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WELCOME FROM
HARPAL KUMAR & IAIN FOULKES

Cancer Research UK is entering a new era. Next year will see the publication of our new five-year strategy and we are confident this will be a bold and exciting new phase for the organisation.

Our strategy will continue to uphold the principle of funding only the highest-quality research and will seek to facilitate collaboration and partnership working, as well as encouraging the UK’s best researchers to help us tackle cancer.

We are very proud of the work and researchers we fund. In the past year you have produced some extraordinary findings and moved many fields of research forward. We have seen high levels of achievement across the range of disciplines we fund – from basic, translational and clinical, to population research. We have also seen excellence across all career stages, from the 89 independent early-career researchers we support, to those who have dedicated their life’s work to beating cancer.

Despite this success, it has undoubtedly been a challenging few years as we, along with all research funders, have weathered the economic storm. This has meant taking some difficult decisions, such as stopping basic-science project grants and reducing spend in our Institutes. We have also received many high-quality applications, considered to be fundable by our committees, which we were unable to support. We’re therefore very pleased to see our fundraising income begin to grow for the first time since 2009/10 – this year we reported a six per cent rise in fundraising income to a total of £460 million. This provides us with renewed confidence and ambition in thinking about our future research plans.

As we embark on an exciting new future we would like to thank everyone who carries out the research we fund, those of you who engage supporters with your work and those who support us in reaching our funding decisions. The time and energy you give to us is incredibly valuable and appreciated.

This publication highlights some examples of your incredible work in the past year, celebrates some of your many successes and provides some perspectives on the challenges in cancer research. We hope you enjoy it.

Harpal S. Kumar
Chief Executive

Iain Foulkes
Executive Director, Strategy and Research Funding
PORTFOLIO OVERVIEW 2012–2013

Last year we supported research worth £351 million across all cancer types, making us the largest funder of cancer research in Europe (Figure 1). We work in partnership with others to achieve the greatest impact, providing support through a range of funding schemes and initiatives across the entire research pipeline, from understanding the biology of cancer through to late-phase clinical trials.

We focus our funding on the high quality research and innovative ideas that we believe will have the greatest impact for the public and cancer patients. To do this we balance reactive funding for new research with directed investments in specific initiatives and infrastructure (Figure 2b). Success rates for our committees vary from year to year on the basis of competition and available budget, but are comparable to those of other biomedical funders. More detailed information about what we have funded recently is available on our website www.cruk.org/science/news/latest-funded-awards

Our cancer biology portfolio

Our basic portfolio continues to be an area of major importance, with over half of our research spend invested in understanding the biology and causes of cancer (Figure 2a). 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 substantially – since FY2005/06 it has almost doubled. We drive specific initiatives to support translational research, including investing more than £20 million a year on our core drug discovery programmes and approximately £10 million on imaging programmes and imaging centres. We also support preclinical development and early-phase trials through our Drug Development Office and the Experimental Cancer Medicine Centre (ECMC) Network.

Our clinical portfolio

We currently support over 250 clinical trials. These 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. Our Clinical Trial Units and the ECMC Network support researchers engaged in trials by providing them with dedicated expertise in trial design and analysis.

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### Science Committee (SC)

Awarded 26 programme grants worth £36.5 million and 11 biomarker and drug discovery projects worth £1.8 million

Formed in April 2012, SC supports our basic and translational cancer research activity through programme grants, and project grants in biomarkers and drug discovery.

### New Agents Committee (NAC)

Awarded three Drug Development Office (DDO) Projects worth £1.6 million and one NAC Trial Grant

NAC reviews proposals for the preclinical development and early Phase I and II clinical trials of new therapeutics and diagnostics.

### Clinical Trials Awards and Advisory Committee (CTAAC)

Funded 28 feasibility studies and clinical trials worth £14.2 million and endorsed 13 new trials

CTAAC reviews applications for Phase III therapeutic clinical trials and some large Phase II trials. CTAAC funds single or multi-centre prospective therapeutic, diagnostic or prevention Phase I and II studies (except first-in-man studies), as well as prospective sample collections.

### Population Research Committee (PRC)

Awarded one programme grant worth £1.2 million, five projects worth £1.7 million and three fellowships worth £600,000

PRC supports clinical and public health epidemiology and educational and behavioural research in the disciplines of prevention, screening and early diagnosis. PRC also considers proposals relating to clinical trial methodologies or statistics and secondary (physical) effects of treatment.
Our annual research activity – 2012/13*

£128m
Research that underpins all types of cancer

£41m
Breast

£32m
Includes cervical,…*

£27m
Bowel

£19m
Prostate

£18m
Leukaemia

£18m
Skin

£13m
Lung

£12m
Ovarian

£6m
Oesophageal

£6m
Brain

£6m
Bladder

£7m
Non-Hodgkin lymphoma

£6m
Pancreatic

£6m

£6m

£6m

£6m

£6m

£5m

£351m

Figure 1: In 2012/13, we spent £351 million on research in institutes, hospitals and universities across the UK into a number of different cancers.

Figure 2a: Funding across the research pipeline

Figure 2b: The balance of our research spend by funding route

* Strategic Investment includes Research Programmes (Cancer Imaging Centres and Programmes, NAEDI awards and funding for International Cancer Genome Consortium projects) and Strategic Infrastructure (CRUK Centres, ECMCs, Clinical Trials Units and the Stratified Medicine Initiative).

Figures do not include Research Support and Cancer Research Technology spend.

Tobacco Advisory Group (TAG)
Awarded two programme grants worth £1.2 million and five projects worth £350,000
TAG considers applications for policy research and policy advocacy activities in tobacco control.

Training and Career Development Board
Awarded seven New Investigator Awards worth £11.3 million and four Clinician Scientist Fellowships worth £2.7 million
Our Training and Career Development Board develops, reviews and manages the portfolio and budget for CRUK’s fellowship and bursary awards.

Thanks to our committees
We thank the 150 researchers who sit on our funding committees. Their hard work ensures that we continue to support high-quality applications that will bring significant progress to the field.

More information about these committees, including membership, is available on our website:
www.cruk.org/funding-committees

Contact details of the CRUK teams responsible for these committees can be found on p. 46.
INVESTING IN OUR NETWORK

Providing an environment in which research can thrive is crucial to delivering world-class results. Our investment in infrastructure helps to shape the research environment in the UK so that researchers can make the most of the funding they receive from us and from other sources.

Institutes
Institutes provide an exceptional research environment. Last year we invested over £100 million in our five core-funded Institutes. Our funding ensures that scientists have access to the long-term support, networks, core services and equipment needed to succeed in research.

We recently appointed two new Institute Directors, both with visionary plans for growth and development at their Institutes - Professor Richard Marais at the Cancer Research UK Manchester Institute and Professor Simon Tavaré at the Cancer Research UK Cambridge Institute.

Experimental Cancer Medicine Centres
Supporting the majority of early-phase cancer clinical trials in the UK, the Experimental Cancer Medicine Centre (ECMC) Network brings together researchers and clinicians across multiple sites to deliver an integrated approach to research and recruitment in early-phase trials and experimental medicine. Last year we invested £3.4 million in ECMCs, a figure which is collectively matched by the four UK health departments.

Over the past year we have made significant steps in a five-year programme to build this network across all 18 ECMCs in the UK, enabling greater collaboration, cross-centre sharing and development of training and skills. As part of this, in 2012, the network introduced a suite of new programmes to help share skills and training opportunities.

Centres
Our Centres are a high strategic priority. They form a national network to deliver world-leading research, improved patient care and greater local engagement. They drive local partnerships and high-calibre collaborations between universities and NHS Trusts and other cancer charities, under a united strategy to accelerate the translation of research into the clinic. Last year we spent almost £19 million on Centre infrastructure.

In Manchester, plans for a new research building were approved in March 2012, marking an important new phase in cancer research in the area. It will be completed and ready for use in summer 2014 and will ensure that the Manchester Cancer Research Centre\(^1\) provides outstanding opportunities and a vibrant environment for researchers, clinicians and external partners to work collaboratively.

Clinical Trials Units
Clinical research is one of our most successful and internationally high-profile activities. Central to this success is our network of seven CTUs\(^2\), which provides the UK cancer community with expertise to design and run clinical trials. Last year we invested £7.6 million in our CTUs.

In October 2012, the CTUs were successfully reviewed by an international panel that assessed progress over the past five years and evaluated their respective trials portfolios. The panel highlighted that many CTU-run trials have led to improvements in the care of patients both in the UK and worldwide. Many of these trials (notably in radiotherapy and surgery) would not have been possible outside the UK and would not have been supported by industry, indicating the unique and crucial role our CTUs play in changing clinical practice.

\(^1\) The new Manchester Cancer Research Centre building is a partnership between CRUK, the University of Manchester and The Christie NHS Foundation Trust.

\(^2\) This is in addition to the Cancer Prevention Trials Unit (Barts & The London School of Medicine and Dentistry) and the Clinical Trials Service Unit (Oxford), which both focus on Population Research studies.
4,000
We fund more than 4,000 researchers, doctors and nurses throughout the UK

70
We support research in over 70 institutions across the UK

44%
We fund 44% of cancer research activity in the UK**

Key locations where we supported research infrastructure in 2012-13.

*Calculated from NCRI Cancer Research Database (CaRD) 2012 expenditure figures
We are proud to be a founding partner of this world-class centre for interdisciplinary medical sciences. At 3.6 acres, The Francis Crick Institute will be Europe’s largest building dedicated to research, and will be opening its doors in 2015 in north London.

The Francis Crick Institute will have the vision, scale and expertise to tackle challenging scientific questions underpinning health and disease, including cancer, circulatory disease, infectious diseases and the multiple degenerative conditions associated with ageing.

Researchers at the Cancer Research UK London Research Institute, the MRC National Institute for Medical Research and the Crick’s university partners (Imperial College London, King’s College London and UCL) will be amongst the global pool of talented researchers at the institute. They will form a diverse team of 1,500 biologists, chemists, engineers, physicists, computer scientists and mathematicians who will work together, with the shared aim to accelerate research breakthroughs and develop new ways to prevent, diagnose and treat different diseases. The majority of group leaders at the institute will remain there for no more than 12 years before being supported to find scientific leadership positions elsewhere, with a strong emphasis on UK institutions. This will expand the talent pool for biomedical science across the UK.

In June 2013, a ‘topping out’ ceremony was held to mark the completion of the main structure of the building. More than 600 people attended this event including the Chancellor, George Osborne, and the Minister for Universities and Science, David Willetts. The event marked the launch of the Crick’s research strategy, which details how it plans to advance science and innovation in the UK.

We have committed to raise £100 million to complete our contribution to the £650 million cost of the institute. This amount is being raised in addition to our usual fundraising activities through a separate dedicated appeal called ‘Create the Change’. We are the only partner raising its contribution philanthropically in what is CRUK’s largest ever capital campaign. To date, we have raised £40 million towards our target which is a tremendous achievement and ahead of budget.

We are confident that the institute will be a driving force in promoting better training and networking and building links to support the biomedical research endeavour across the UK.
INVESTING IN CANCER IMAGING

Imaging is a vital area of cancer research, where remarkable technological advances are opening up new opportunities to tackle cancer. In March 2013, following our previous investment in this area, we made a five-year commitment to support cancer imaging centres and to improve the integration of cancer imaging activities in the UK.

In partnership with the Engineering & Physical Sciences Research Council (EPSRC) we have allocated over £35 million to four Cancer Imaging Centres – one of our largest single investments this year. Following two rounds of rigorous review by a panel of international experts, four Cancer Imaging Centres of the highest international calibre were funded at:

- King’s College London and University College London
- The Institute of Cancer Research
- The University of Oxford
- The University of Cambridge and The University of Manchester

Our investment will enable the Cancer Imaging Centres to integrate preclinical and clinical research to facilitate the improved detection and treatment of cancer and will play a fundamental role in translational research.

The new Cancer Imaging Centres will endeavour to bring together imaging with genomics, molecular and clinical information in order to improve pre-treatment patient stratification and assessment of treatment response.

Importantly, the Cancer Imaging Centres will work together to develop a national Cancer Imaging Network that will harness additional imaging expertise, skills and capabilities found across the UK. Multidisciplinary teams will bring together a breadth of insights and approaches from engineering, physical sciences and information and communication technology to accelerate innovation and progress in cancer imaging.

Our strategic investment in imaging began in 2008 and is already beginning to produce excellent results. For example, the King’s College London and University College London Cancer Imaging Centre have been developing pioneering imaging technologies using the photoacoustic effect to characterise tumours. The technique has the high contrast and specificity of optical imaging techniques, but without their limited spatial resolution. As well as being extremely useful for visualising tumour vasculature, functional information (such as blood oxygen saturation and blood flow) can also be obtained using the technique. This work led to the award of the prestigious 2010 Roberts Prize for the best paper in Physics in Medicine and Biology (PMB).

In March 2012 Cancer Research Technology (CRT) and the European Investment Fund (EIF) took a bold step to help address the considerable challenges in UK drug discovery by jointly creating a £50 million Pioneer Fund. This aims to bridge the gap between cancer drug discovery and early development in the UK and to pave the way for potential new cancer drugs to be taken into Phase I clinical trials.

In April 2013 the CRT Pioneer Fund (CPF) made its first investment to develop a promising class of drugs called MPS1 inhibitors, in collaboration with the Cancer Research UK Cancer Therapeutics Unit at The Institute of Cancer Research (ICR) in London. MPS1 belongs to a family of mitotic checkpoint kinases. Increasing levels of MPS1 have been associated with increased genetic instability in many different types of tumour – making MPS1 an attractive target for cancer drug discovery. Investment by the CPF will not only allow the ICR team to accelerate the development of MPS1 inhibitors, but will also fund early clinical trials of potential drugs developed as a result of the collaboration.

Without this vital investment, development of these promising compounds might have been delayed for years. We’re delighted that this collaboration will progress these new treatments from the laboratory right through to completion of the first clinical trial – accelerating research to bring potential new treatments to patients as quickly as possible.

Dr Keith Blundy, Chief Executive of Cancer Research Technology

At least two-thirds of the fund will be used to develop the most exciting scientific discoveries emerging from CRUK-supported research. The remaining projects may come from other academic groups or from the UK industrial sector.

Our share of the investment fund comes from CRT profits derived from licensing our discoveries to industry partners. This innovative model allows us to expand our research portfolio at no additional cost to CRUK. With two further deals close to completion, this new initiative aims to accelerate the rate at which new drugs are made available to those with cancer.
STRATIFIED MEDICINE

Personalised medicine is increasingly recognised as the future of cancer therapy, but its potential is yet to be fully realised. As more targeted therapies become available, clinicians will need to be able to routinely stratify their patients.

We want to tackle the significant challenges facing the delivery of stratified medicine in the UK by providing a model for national screening of patients. This model should enable recruitment onto nationwide trials and ultimately be integrated into routine clinical diagnosis and treatment. Our Stratified Medicine Programme (SMP) is helping us establish a proof of principle to take a vital step towards this goal.

We're pleased to report that the first phase of this programme, a £6 million initiative led by us, in partnership with AstraZeneca, Pfizer and the Government, has been successfully piloted across a network of 26 hospitals and three genetic testing laboratories. In delivering the first phase, we were able to demonstrate the feasibility of embedding large-scale molecular analysis in the NHS, combined with securing patient consent for the routine collection and storage of genetic and clinical data for use in research. Highlights of phase 1 include:

- Successfully setting up a network reaching across UK clinical teams, NHS trusts and academic, clinical and industry sectors. This resulted in more than 200 people working together to tackle the challenges involved in making targeted therapies in the UK a reality.
- Genetically testing tumour samples from 99.6% of the ambitious 9,000 patient target.
- Positioning our labs at the forefront of introducing Next Generation Sequencing (NGS) into the NHS – technology that will make clinical genetic testing faster and more economical.
- Catalysing necessary changes to existing NHS processes, from pathology sample preparation to electronic reporting.

More work is needed for stratified medicine to become the standard of care in the future – pathology practices need to be standardised and investment is needed into data systems across the NHS. Over the next six months we will be working to share our knowledge and findings with clinicians, policy-makers and relevant organisations to ensure these changes are on the national agenda.

We know this is only the beginning. Real success will be measured when we begin to see patients receiving appropriate treatments through this process. We're now developing phase 2 of the programme, which aims to maintain the existing network and infrastructure and expand nationally to bring in new sites. Crucially, phase 2 will pilot a transformation in how we recruit people to clinical trials of targeted therapies in the UK. It will focus on testing patients with advanced lung cancer (Stage 3 and 4) to determine which clinical trials will be most beneficial for them to join. This capitalises on the UK's unique clinical infrastructure, ensuring we remain at the forefront of stratified medicine research and, importantly, will allow patients to access emerging new lung cancer treatments.
We have tested tumour samples from 99.6% of the ambitious 9,000 patient target
NEW FUNDING APPROACHES

The boundaries between basic and translational research are increasingly blurring and our funding structures need to be flexible enough to meet these new challenges. In response to this, in April 2012, we successfully established a new funding committee – the Science Committee. This sets the stage for researchers across the spectrum of cancer research to be able to contribute to the translational agenda. This transition is also reflected in the work at our core-funded Institutes, as described in Professor Julian Downward’s perspective piece on taking insights from basic research findings to drive changes in clinical practice.

The Science Committee merged our former basic and translational research funding committees, enabling us to effectively evaluate the increasing numbers of applications that bridge these areas.

Researchers are now able to submit proposals that have both basic and translational elements, without the need to modify applications to fit the criteria of our funding committees. The breadth of the Science Committee’s remit means that we not only support research arising from the bench-to-bedside paradigm, but also biological investigations that answer questions arising from the clinical setting.

We are looking for proposals that help us to understand cancer better and ultimately have tangible patient benefit. These could be firmly in the basic research space, for example, using appropriate model organisms to address underlying cancer biology questions. They do not necessarily have to address basic mechanisms, but should be based on a strong biological rationale and clear clinical need. We are also keen to see proposals that span both basic and translational research.

It is important to us that we ensure there is a route at CRUK to assess the work researchers want to undertake. Our committees are supported by teams of Research Funding Managers who are available to advise applicants on all aspects of the application and funding process. To find the relevant contact or for more information on any of our funding committees please visit: www.cruk.org/funding-committees

Highlights

Now into its second year, it is great to see that our vision for the Science Committee is becoming a reality. We have funded 11 clinicians to date through this committee. Two recently funded teams that are aiming to take a personalised approach to the treatment of cancer are led by Dr James Brenton and Professor Jude Fitzgibbon. Their work exemplifies the type of research – bridging basic and translational boundaries – that we aim to support.

A collaborative effort led by Dr James Brenton at the Cancer Research UK Cambridge Institute and Professor Iain McNeish at the University of Glasgow aims to measure tumour progression and develop prognostic biomarkers for ovarian cancer patients. They are taking advantage of new technologies to develop techniques to identify circulating tumour DNA. This cutting-edge study is at the forefront of developing genomic technologies to support personalised medicine.

The second team, led by Professor Jude Fitzgibbon at Queen Mary, University of London, aims to take a personalised approach to the treatment of follicular lymphoma. Professor Fitzgibbon’s group is developing genetic tools that will be used to inform future biomarker-led clinical trials. The ultimate goal of this work will be targeting treatment based on a patient’s epigenetic mutation profile. This innovative programme of work is the first of its kind for follicular lymphoma research, as discussed on p.19.
In my lab at the Cancer Research UK London Research Institute, I have worked for many years trying to understand the growth and survival signals generated by activated oncogenes, to which cancer cells become addicted during the process of tumour evolution. We particularly focus on identifying unique dependencies of oncogene addicted cancer cells that might be targetable in the therapy of human cancer. My special interest throughout this time has been on the KRAS oncogene, which encodes a small GTP binding signalling protein and is the most commonly activated oncogene in human cancer.

KRAS has proved extremely difficult to target directly using small molecule drugs and is often referred to as ‘undruggable’. As KRAS mutation underlies some 20% of human cancers, including many diseases with the worst prognosis, such as lung and pancreatic tumours, there is a pressing need to develop new therapeutic approaches to block its action. We have employed functional genomic screens using RNA interference technology to look for genes whose function is essential for cancer cells expressing mutant KRAS, but not for other cells. We found that KRAS mutant lung cancer cells rely upon a novel gene, GATA2, for their continued survival.

These findings were followed up using genetically modified mouse models of KRAS mutant lung cancer. The development and continued maintenance of KRAS induced lung cancer is uniquely dependent on the expression of GATA2; when this is blocked, the lung adenocarcinomas regress completely. Although, as a transcription factor, GATA2 itself is not likely to be a good drug target, we have identified a number of pathways downstream from GATA2 that can be inhibited by existing drugs. Using a combination of two such drugs, we have been able to show an impressive therapeutic response in KRAS induced mouse lung cancer models1.

My aim is to take the understanding of mutant KRAS signalling that we have gained in the laboratory into clinical practice. To help in this, I have started a small translational laboratory at the Institute of Cancer Research. We are investigating the possibility of studying drug combinations based on KRAS/GATA2 synthetic lethality in the clinic with colleagues at the Royal Marsden Hospital. We have also been using methods that we developed in mouse models to investigate the possibility of early detection of KRAS mutant cancers in asymptomatic individuals in a screening setting. This involves the analysis of circulating free tumour DNA in the bloodstream. Ultimately, we are aiming to develop interventions that make a real difference for those with cancers caused by mutant KRAS.

My research has always been themed around genomics, having gained my BA degree in Genetics at Trinity College Dublin and my PhD at the Galton Laboratory at University College London using irradiation cell hybrids to map chromosome 9q. The Human Genome Mapping Project (HGMP) was, at that time, in its infancy, and my first experiments were a world away from the high-throughput technologies at our disposal today.

Having worked on follicular lymphoma (FL) for more than 10 years, I feel that we are finally getting inside the mindset of the disease. It’s an incurable cancer, more remarkable considering that 20% of patients are managed on a watchful waiting approach. For those who are treated, the majority initially respond well to immuno-chemotherapy. Sadly, most patients will relapse, and for some 20% – 30% of cases it returns in an aggressive form. This makes it a fascinating disease to study, gaining insight into the molecular pathogenesis of FL and the twists and turns taken over the course of the disease.

I am very much indebted to past members of the CRUK Barts Centre, who, with funding from CRUK, created a haem-onc tissue bank in the early 1970s. Their policy of repeat biopsying at FL recurrence is now allowing us to chronicle not only the clinical, but also the genetic evolution of the disease, using next generation sequencing approaches. We know that each new episode of FL originates from an ancestral B-cell population, which seems to have acquired an ability to evade treatment and somehow propagate lymphoma. This is the cell we need to remove if we are to see an improvement in patient outcome.

Epigenetic reprogramming lies at the heart of these progenitor B-cells, with most FL tumours harbouring a mutation in one or more histone-modifying enzymes. These mutations are generally stable over the course of a patient’s disease and target methyl (MLL2, EZH2) and acetyl (CREBBP) transferases or histone linkers (HIST1H1/2). The new sequencing data has therefore led to a fundamental shift in our understanding of how normal B-cells become malignant and is set to direct efforts to develop novel agents for the treatment of FL and related lymphomas, based on the underlying gene mutation.
In March 2012, a landmark study led by Professor Charles Swanton at the Cancer Research UK London Research Institute, used next-generation sequencing technology to carry out the first genome-wide analysis of the genetic variation between different regions of the same tumour. This revealed that about two-thirds of genetic faults were not repeated in other biopsies from the same tumour, furthering our understanding of intra-tumour heterogeneity.

**METABRIC study**

Further insight into the complexity of cancers came in April 2012, when Professor Carlos Caldas of the Cancer Research UK Cambridge Institute concluded a five-year international study cataloguing genetic changes in 2,000 breast cancers. The METABRIC study identified several new genes that drive the disease. This data demonstrated that breast cancers fall into 10 subtypes, each with its own suite of mutations relating to particular clinical features. Revealing this level of inter-tumour heterogeneity could enable classification of tumours according to genetics rather than by tissue structure. This could revolutionise the way breast cancer is approached, both in the laboratory and in the clinic.

It is increasingly apparent that since no two tumours share the same characteristics and each tumour is not a homogeneous mass, it is unlikely that a single-agent treatment will be relevant to the whole tumour. It is also becoming clear that tumour heterogeneity is not a static condition, and that temporal evolution of tumours adds another layer of complexity to contend with. This underscores the significant challenges in developing effective new drugs, to understanding and preventing drug-resistance and to personalising approaches to cancer therapy. We therefore need to invest in new ways of thinking to help us understand how to translate this knowledge into tangible benefits for patients.

**TRACERx study**

TRACERx – Tracking Cancer Evolution through Treatment (Rx) – demonstrates the type of innovative thinking required to tackle one of the key cancer challenges of the 21st century, and is a practical step towards an era of precision medicine. At £14 million, it’s the biggest single investment in lung cancer research we’ve ever made, reinforcing our strategic focus on the disease. We hope investments such as this will transform our understanding of lung cancer and help us make real progress for people with the disease.

Professor Swanton has devised a novel way to uncover mechanisms of temporal evolution and how lung cancer responds to treatment. The TRACERx study will analyse the intra-tumour genetic changes of more than 850 lung cancer patients, from the point of diagnosis and throughout their treatment. This will give unprecedented insight into the impact of treatment on the genetics of the disease and the effect on patient outcomes. TRACERx also profits from the knowledge that exists across our network of cancer researchers. Experts from different disciplines will help to integrate clinical and genomic data to give a comprehensive understanding of how the disease progresses over time.

The data generated will help us to better understand tumour evolution and diversity and to identify patients who could benefit from drug trials of newer, targeted treatments. The study has already gained the attention of several drug companies, interested in setting up more trials in the UK. There is also an exciting opportunity to link this work with the Stratified Medicine Programme (p. 14) where lung cancer patients could be assigned to trials testing the drugs that are likely to be most effective for them.

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ENABLING DRUG DEVELOPMENT

CLINICAL DEVELOPMENT PARTNERSHIPS

Cancer Research UK is in a unique position to drive academic drug development in the UK. We have a wealth of experience in early clinical development and we aim to increase the number of promising therapeutic agents under development. Our Clinical Development Partnerships (CDP) initiative is central to this objective, providing a simple route for companies to progress oncology agents that would not otherwise be developed. We’re excited to report that the first project supported through this initiative, the IMA950 trial, is soon to reach completion.

Although we considered IMA950 very promising, our small company was lacking the resources to start clinical development of the vaccine. CRUK’s DDO made it possible to perform an extensive multi-centre trial in which many interesting scientific aspects could be addressed.

immatics biotechnologies GmbH

The CDP model

This model combines the drug development expertise of our Drug Development Office (DDO) with the business development experience of Cancer Research Technology. The companies we work with may license the trial data we gather about their drug in exchange for future royalties to CRUK or, failing that, the DDO may license to another company to ensure the drug’s continued development. If the drug is approved for the clinic, the royalties we receive are used to fund more research.

For more information about the CDP initiative, visit our website: www.cruk.org/clinical-partnerships
Professor Roy Rampling is Emeritus Professor of Neuro-Oncology at the University of Glasgow. Here he gives his account of the IMA950 trial, which was funded through our New Agents Committee and is one of the first examples of a CDP project to reach completion.

In 2008, immatics biotechnologies GmbH sought a partner to develop IMA950, their glioblastoma multiforme (GBM) vaccine. Through the Clinical Development Partnerships initiative, CRUK’s DDO negotiated with immatics to run a Phase I trial of IMA950.

GBM is universally fatal, with a median survival of between one and two years. Optimal conventional management of GBM comprises surgery and radical chemo-radiotherapy. No substantial improvement has arisen from research into biological agents and recent attention has turned to stimulating the immune system or reversing the powerful immunosuppressive properties of brain tumours. The former strategy is the most advanced.

From October 2010 to February 2013 the IMA950 trial recruited 45 patients across seven CRUK-affiliated centres. The design added IMA950 vaccination to standard surgery and chemoradiotherapy in newly diagnosed patients. Two vaccination schedules were investigated, one prior to and the other post-chemoradiotherapy, with the primary endpoints being the safety and immunogenicity of IMA950. The DDO managed the entire conduct and clinical analysis of the trial. Immatics provided the vaccine and analysis of immunoresponse.

Early results suggest strongly positive results to both primary endpoints, supporting the case to further develop IMA950. The close and mutually supportive collaboration between the company and CRUK’s DDO was instrumental to the success of the trial. The recruitment of experienced trialists from CRUK Centres into a collaborative unit is therefore a good model for the implementation of a complex study in a rare tumour type.

As our understanding of the complexity of cancer develops, so does the recognition that combinations of therapies will be needed to combat the disease. The multitude of potential combinations, doses and treatment regimens is daunting, but this presents a promising route towards a more effective approach to treatment. It is important that we continue to develop an understanding of how, and in which patient populations, new therapy combinations might be used most effectively in the clinic.

Testing novel drug combinations
The Combinations Alliance allows early-phase researchers to access experimental drugs from companies to test in new combination trials, consequently providing UK patients with more therapy options. The initiative is a collaboration between our Drug Development Office (DDO), the Experimental Cancer Medicine Centres (ECMCs) and industry.

The initiative, now in its third year, has a growing portfolio of novel combination studies across a range of cancer types and early and late phase development agents available to UK patients. During this time, we have held several combined workshops with the NCRN AZ alliance, to support paving the way for a seamless transition from early to late stage development.

We currently have nine Combinations Alliance trials running and are planning more for the future. The first trial we launched is a Phase Ib/Ia clinical trial led by the Glasgow ECMC and the Clinical Trials Unit at the CRUK Glasgow Centre. It is testing an experimental drug called AZD4547 (an FGFR inhibitor), in combination with standard chemotherapy, to treat patients with advanced stomach or oesophageal cancer. AZD4547 is provided by AstraZeneca, the first pharmaceutical company to join the Alliance.

In order to expand the work of the initiative we want to get more industrial partners on board. We will also begin to address some of the challenges involved in these studies. For example, preclinical models can be insufficiently predictive of the clinical activity of novel compounds. We therefore intend to invest more in the preclinical studies needed to provide a convincing rationale for our combinatorial trials.

For further information please visit: www.ecmcnetwork.org.uk/collaborations/combinations-alliance

Combining different treatment modalities
The benefits of a combinatorial approach to treatment are by no means solely restricted to drug-drug combinations. The fact remains that around 95% of people cured from cancer undergo surgery and radiotherapy, which is why research into these important areas will continue to be a strategic focus for us in the coming years.

Combining, for example, radiotherapy with molecularly targeted agents has the potential to improve treatment efficacy and results in a need for fewer, less radical surgical interventions.

Currently few drug discovery units and pharmaceutical companies are able to exploit the opportunities that such combination approaches can offer. This highlights the importance of new initiatives such as The Radiotherapy-Drug Combinations Consortium, a collaborative partnership between the DDO and the National Cancer Research Institute Clinical and Translational Radiotherapy Research Working Group (CTRad). The group aims to produce packages of preclinical radiation and drug data that will decrease the time needed to perform proof-of-principle studies into potential combinations and thus provide the preclinical evidence needed to initiate much needed Phase I trials. This new initiative, along with directed funding for preclinical combinations work, represents a new strategic direction for the DDO.

Drug Development Office
We are committed to helping research scientists bring their work into the clinic and giving promising new therapies a chance of becoming the treatments of tomorrow. Our Drug Development Office (DDO) is at the forefront of early-phase cancer drug development, providing the expertise and facilities needed to advance new cancer treatments in the non-commercial sector. With access to a UK-wide network of Clinical Trials Units and Experimental Cancer Medicine Centres, our DDO is able to lead the way in developing new experimental cancer treatments and diagnostics and running early, and often first-in-man, clinical trials in close collaboration with academics throughout the UK. The agents come from academic research groups as well as biotech and pharmaceutical companies throughout the world.
Professor Dion Morton is Director of the Birmingham ECMC and Director of Clinical Research at the Royal College of Surgeons of England. Here he highlights the importance of engaging surgeons in clinical trials.

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It is tempting to imagine that as multiple novel targeted therapies are introduced for the treatment of cancer, the role of the surgeon will inevitably diminish. However, there is a unique opportunity for multidisciplinary teams to make substantial improvements in cancer outcomes in the next few years. We are faced with significant challenges in selecting the correct patients for targeted therapies, in remodelling complex care pathways, and in reducing the morbidity from our treatments. Surgeons can make a major contribution in all these areas, and the treatment of colorectal cancer provides a good example of this.

As our cancer treatments continue to improve, the importance of providing effective, safe surgery with minimal morbidity has never been higher. Screening and early detection of tumours permits more limited surgical procedures to be performed, so reducing the ‘surgical insult’. The greatest benefits from minimal access approaches, such as laparoscopic surgery, are likely to be realised in treating these early stage tumours. Providing safe and effective laparoscopic surgery, with optimised post-operative care, has recently been evaluated in the EnROL trial1, and local surgery for selected early-stage rectal cancer is currently being explored in the TREC trial2. Minimally invasive techniques, to replace major surgery, are also being evaluated in trials such as CReST3, which compares endoluminal stenting with emergency surgery for obstructing colon cancer. This trial is especially challenging because it requires patients to be approached in the emergency setting – demonstrating another key role for engaging surgeons in clinical trials.

The treatment of colorectal cancer, like most solid tumours, involves a complex pathway of multidisciplinary care. Changing this pathway could also realise benefits to our patients. By offering chemotherapy before surgery, there is a chance that tumours can be down-staged, disease-free survival could be improved and perhaps, in future, the size of operation could be reduced. This possibility is now being explored in the FOxTROT trial4, where chemotherapy is being given prior to operation, with encouraging early results.

CRUK provide a multidisciplinary forum for developing and delivering new diagnostic and therapeutic trials. Surgeons have been increasingly engaged in this process, which has been greatly assisted by the Royal College of Surgeons initiative (with the Rosetrees Trust) to develop five new surgical trials centres across the United Kingdom. This has helped to move the UK into the vanguard of surgical trial development, substantially increasing our research activity. This will provide essential support for advances in cancer treatment over forthcoming years.

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1. EnROL: Conventional versus laparoscopic surgery for colorectal cancer within an Enhanced Recovery Programme, CRUK/07/019
2. TREC: Transanal endoscopic microsurgery (TEM) and radiotherapy in early rectal cancer, CRUK/09/032
3. CReST: The role of endoluminal stenting in the acute management of obstructing colorectal cancer, CRUK/08/005
4. FOxTROT: Fluoropyrimidine, Oxaliplatin and Targeted Receptor pre-Operative Therapy: a controlled trial in high-risk operable colon cancer, CRUK/07/014
NOVEL CLINICAL TRIAL DESIGN

As cancer research moves steadily towards an era of precision medicine, the clinical trial landscape in the UK needs to evolve accordingly. Increasingly, alternative trial designs are needed to deliver the complex information required to prove efficacy.

While the majority of trials for novel targeted agents are still initially in unstratified populations, a large proportion feature translational research or sample collections to retrospectively identify responding populations.

The FOCUS 4 trial, led by Professor Tim Maughan, from the University of Oxford, is a recently approved trial which exemplifies how unique design can help us take a major step forward in understanding how best to tailor treatments. This study will take an adaptive multi-arm, multi-stage (MAMS) biomarker-driven approach to testing a number of new ‘targeted’ cancer drugs in patients with different subtypes of colorectal cancer.

The trial aims to provide a greater understanding of the molecular diversity of the disease and its response to novel therapeutic approaches.

FOCUS 4 is an integrated clinical trial programme which enables us to identify and allocate patients at an early point in their disease for entry into a randomised evaluation of novel targeted therapies, which are tailored for their subtype of cancer. This is a radical departure from the ‘one size fits all’ approach – which fails to take note of the variability of cancer. It is highly adaptable, allowing us to evaluate the clinical effect early and stop specific comparisons if they are not working. It also allows us to bring in new biomarkers and new treatments during the course of the trial. Crucially, this builds on the success of cancer research networks in improving participation in trials, the expertise of the Experimental Cancer Medicine Centres (ECMCs) in the delivery of early phase trials, the collaboration of expert molecular pathology central laboratories and the statistical expertise at the MRC trials unit. This study therefore enables the UK colorectal cancer research community to be at the forefront of clinical research in this very common and challenging cancer with great hope of improving outcomes for our patients.

Professor Tim Maughan

FOCUS 4 will provide proof-of-principle for the design of future complex trials. We are keen to explore the potential for using MAMS trials to inform tailored treatment for other cancer types. This will present us with new challenges of how best to deliver more complex and, consequently, considerably more expensive clinical trials in the UK.

1. FOCUS 4: Molecular selection of therapy in metastatic colorectal cancer – a molecularly stratified randomised controlled trial programme, CRUK/11/054
Other emerging designs of note are that of the WCTU PIN trial in lung cancer, which uses induction chemotherapy to identify patients less likely to recover from DNA tumour cell damage and therefore eligible to be randomised to a DNA repair targeted agent, and the ICR-CTSU TO-PARP trial in prostate cancer, where Stage 1 is to detect predictive biomarkers, Stage 2 to validate the biomarkers and Stage 3 is a randomised Phase II trial using the validated biomarkers.

As a CRUK core-funded Clinical Trials Unit we, and our sister CRUK Clinical Trials Units, work closely with the National Cancer Research Institute Clinical Studies Groups to develop clinical trials using the most appropriate designs. We still face some challenges in clinical trials design, but methodological advancements have allowed us to add new techniques to our armoury of possible designs.

Multi-arm, Multi-stage (MAMS) designs

With more and more experimental therapies becoming available, we needed to think about the most efficient way to simultaneously assess multiple experimental arms. This gave rise to the MAMS design, which has one control arm and multiple experimental arms. Each experimental arm is assessed at certain stages for safety, activity and efficacy to determine whether that arm should be dropped early or continue to be included in a final Phase III comparison. The design also allows new arms to be included while the trial is still running. An example of a CRUK-funded MAMS trial is the Medical Research Council CTU FOCUS 4 trial in colorectal cancer, which also makes use of developments in CRUK’s Stratified Medicine Programme genetic testing by including biomarker-defined subpopulations.

Bayesian designs

As part of the International Rare Cancer Initiative (IRCI) we have been faced with the challenge of designing trials where there are only small numbers of patients available. In some cases, this has given rise to a move away from classical ‘frequentist’ designs (which make a conclusion based solely on the patient data collected), to studies that use ‘Bayesian’ methods. A Bayesian approach combines a prior distribution of clinicians’ beliefs of the effect size with the actual patient data collected, to create a posterior distribution which can be used to determine the confidence with which we can say there is evidence of a treatment effect. Examples of CRUK-funded trials using this methodology are the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) led InPACT trial in penile cancer and Glasgow CTU’s BALLAD small bowel adenocarcinoma trial (which uses both a frequentist and Bayesian approach).

A global partnership for rare cancers

Rare cancers make up around a fifth of all cancer diagnoses in Europe, making them more widespread than any single common cancer. Because the numbers of people with each of these cancer types is low we need international collaboration to recruit enough people to run clinical trials.

In an attempt to address this, the International Rare Cancers Initiative (IRCI), a joint initiative between ourselves and the National Institute for Health Research Cancer Research Network (NCRN), the National Cancer Institute (NCI) and the European Organisation for Research and Treatment of Cancer (EORTC), was established early in 2011. It aims to encourage the use of innovative methodologies to advance knowledge of these cancers and facilitate the development of international clinical trials.

For more information about this initiative, visit: www.irci.info

1. InPACT: International Penile Advanced Cancer Trial (International Rare Cancers Initiative study - IIRC 004), CRUK/13/005

2. BALLAD: A global study to evaluate the potential benefit of adjuvant chemotherapy for small bowel adenocarcinoma (International Rare Cancers Initiative study - IIRC 002), CRUK/12/041


4. TO-PARP: Trial of Olaparib in patients with advanced castration resistant prostate cancer, CRUK/11/029
Having had two cancers and participated in five trials myself, I think the consumer perspective will always offer something fundamental to successful cancer research.

Shirley Harrison and I are the two consumers on CTAAC. We have each previously sat on clinical studies groups and on other research bodies, and without this kind of background our CTAAC role would be very difficult. We are full members of the committee and we expect to make a contribution that is as professional as everyone else’s.

The committee meetings are both long and densely packed with business, so we tend to listen a lot and contribute if and when we think something has been missed. We also make suggestions about using specific consumer input where the committee feels a study is addressing an important question but needs a different approach. More researchers are involving consumers in the early stages of trial design and we feel that those proposals are often of a higher quality.

At the meetings I am often lost in detailed methodologies or complex treatment regimes, particularly as trial designs are ever more complicated. But I always keep patients in mind – once all the decisions are made, somebody has to put this trial in front of a patient and ask them to participate. So I consider, if it were put in front of me, would I say yes or no – and why?

Richard Stephens is a member of our Clinical Trials Awards and Advisory Committee (CTAAC). Richard has participated in a number of cancer trials as a patient and is one of two ‘consumer’ representatives on the committee. Here he tells us about his CTAAC experience.
Early diagnosis of cancer is critical to effective treatment. One route to detecting cancer earlier is through developing effective screening techniques. While the advantages of screening for some cancers, such as cervical cancer, are evident – where pre-malignant changes can be detected and cancer prevented – there is less certainty around the benefits of screening techniques for other cancer types.

TRIALS OF SCREENING

This year, along with the National Cancer Director, we commissioned an independent review of the evidence around breast screening, chaired by Professor Sir Michael Marmot. This was published in The Lancet in October 2012. It showed that, as well as saving lives, the current breast screening programme also brings a risk of over-diagnosis, with economic implications. The review highlights the need for further research to help increase benefits and minimise risks of breast screening in the future. Professor Per Hall discusses this in his Perspective piece on p. 34.

Other issues that need to be addressed include understanding the differences in screening uptake and help-seeking behaviour between different segments of the population, as highlighted by Professor Jane Wardle in her Perspective p. 35. Effective processes to discover and validate novel screening biomarkers also need to be put in place and we have identified this as a priority in our forthcoming research strategy.

The pros and cons of breast cancer screening have been discussed for a number of years and the debate continues. Surprisingly, few discuss possible improvements to current routines. A short version of the Marmot report on mammography screening was recently published in The Lancet, which concluded that mammography screening reduces breast cancer mortality by 20% but increases over-diagnosis by 11%. If we agree that early detection of a disease is better than postponing diagnosis and therapy, the focus of the discussion should be: how do we make screening more efficient?

Mammography screening has been used in more or less the same way over the last 40 years. Most screening programmes assume the risk of breast cancer to be solely age dependent, that is, women will benefit equally from screening as long as they are within a certain age range. However, there are emerging possibilities to better target the women who are most likely to benefit from screening and thus avoid spending time and money on those where screening merely induces anxiety.

The first step is to identify women at high risk of breast cancer. There are several established breast cancer risk models, e.g. Gail, Boadicea, Tyrer-Cuzick, that use lifestyle factors and family history to predict risk. Adding mammographic density, a strong risk factor, would add substantially to the prediction since women with high mammographic density are hit twice: they have an increased risk of breast cancer and cancers are ‘masked’ and difficult to detect. Mammographic density is a comparatively simple measure of individual breast cancer risk, but there are currently no established standards for measuring density in an automated and objective fashion, independent of what type of machine is being used for imaging.

Through an international collaborative project, partly funded by CRUK, a large number of genetic alterations that influence breast cancer risk have been identified. Armalagamating lifestyle information, mammographic density and a polygenic risk score would enable identification of individual breast cancer risk.

If individualised screening is adopted, a number of challenges face health care providers, politicians and the general public. Acceptability to the public is crucial, but also probably the least problematic. The organisational aspects are challenging, e.g. if selection is based on genetic tests, who should provide counselling and give advice? It is difficult to predict how acceptable a change to an individualised screening programme would be to professionals. In addition, there are ethical, legal and social challenges.

Lastly, we have not even touched on what to offer women in the highest risk strata. Let’s assume that some women will end up in a group where one in three will develop breast cancer. Will intensified screening be accepted or looked upon as too passive an intervention?

2. www.nature.com/icogs
In 2010, research into a new bowel screening technique called flexible sigmoidoscopy (FS) showed it could reduce the risk of individuals dying from bowel cancer by 43%. The NHS piloted the technique in six regions of England in March 2013, aiming to offer this screening programme to all 55-year-olds in England by 2016.

Historically, behavioural research in cancer has focused either early in the cancer pathway – on modification of behavioural risk factors, or later – on the emotional consequences of diagnosis. Interest is now growing in the behavioural influences on the timing of diagnosis. Diagnosis at an earlier disease stage can reduce mortality and, in some cases, incidence, but this depends not only on advances in diagnostic technologies but also understanding the behaviour of the target population.

The Health Behaviour Research Centre has a particular interest in early diagnosis, with research into the psychosocial predictors, decision-making processes, and emotional consequences of screening and symptomatic presentation. All these domains have featured in a long-standing collaboration with Professor Wendy Atkin, Imperial College London, to investigate the potential of FS screening. The research began with a trial demonstrating that colorectal cancer screening information did not, as was feared, increase cancer worry and went on to develop materials to promote public understanding.

We used interviews with patients, endoscopists and nurses in the pilot centres to optimise workflow, staff-patient interactions and results letters. We administered a baseline questionnaire to investigate people’s motives for accepting or declining screening, and supplemented this with qualitative interviews – demonstrating the influence of perceived risk, costs and benefits. Follow-up questionnaires showed high acceptability and no adverse effects on health behaviours. Once the FS trial was in progress, we analysed uptake patterns on a large-scale, gaining insights into socioeconomic inequalities to inform future interventions. The success of this collaboration between epidemiology, gastroenterology and behavioural science is demonstrated in the recent introduction of FS into the NHS cancer screening programme.
**FUTURE LEADERS**

Recruiting, developing and retaining world-class cancer researchers is essential to securing the future success of cancer research. Each year we spend over £35 million on training and career development, helping to develop the next generation of leaders in the field. This includes vital funding for new investigators who are starting out in their research careers (through our prestigious fellowships and other funding schemes). We also provide support in the form of career advice, workshops and training events.

**Supporting the first steps**

Last year we funded 14 new fellows. These include early-career researchers setting up their research groups for the first time, as well as clinicians committed to combining an academic research career with their existing clinical role.

**Dr Rita Sousa-Nunes** and her team at King’s College London are investigating mechanisms of neural tumourigenesis in Drosophila. Central nervous system tumours are the most common type of cancer in children after leukaemia. Treating them can be very challenging, and even successful treatment can have long-lasting side effects, so new approaches are urgently needed.

> "The Cancer Research UK Career Development Fellowship is invaluable in allowing me to start a new team investigating fundamental properties of cancer cells relevant to combat human disease. Furthermore, the Cancer Research UK network promotes networking between cancer researchers around the UK, fostering the exchange of ideas and collaboration."  

The quality of applications this year was exceptional and, although it was extremely difficult to choose, we’re confident that the individuals selected are truly outstanding. The next few years will undoubtedly be difficult for these researchers as they seek to establish themselves in this highly competitive field. But with the extra funding and support they will receive from Cancer Research UK I have no doubt these individuals will go on to achieve great things in the future.

**Establishing careers**

We have supported a number of researchers from the early-stages of their careers, through to securing programme grant funding.

**Dr Prabhakar Rajan** is a surgeon at the University of Glasgow, investigating alternative splicing in prostate cancer metastasis. He will use next-generation sequencing to understand the functional complexity of the cell transcriptome during cancer progression to identify new therapeutic targets.

> "I am extremely grateful to Cancer Research UK, the Royal College of Surgeons of England, and their generous supporters for this Clinician Scientist Fellowship. With this essential funding, I will be able to develop my own independent and novel research programme to pursue my passion to identify effective treatments for advanced prostate cancer."  

**Dr Claudia Wellbrock** from the University of Manchester was one of the first recipients of our Career Establishment Awards. The scheme, established in 2007, aims to support researchers at the start of their independent careers in cancer research.

After carrying out her PhD and postdoctoral positions at the University of Wuerzburg in Germany, Dr Wellbrock moved to the UK to work with Professor Richard Marais at the Institute of Cancer Research. In 2007 she was appointed a Reader in Molecular Cancer at the University of Manchester and a year later was awarded the Career Establishment Award. Dr Wellbrock’s research has gone from strength to strength and this year she was awarded a programme grant to continue her work.

Dr Wellbrock’s programme of work aims to understand the cellular signalling that is linked to melanoma initiation and progression, in order to improve current treatment strategies and identify new therapeutic targets and new prognostic markers for the disease.

**Professor Margaret Frame**, Director of the Edinburgh Cancer Research UK Centre and Chair of the New Investigator Awards interview panel.
Future Leaders Prize

The Future Leader in Cancer Research Prize recognises exceptional individuals at the start of their careers. This year’s prize was awarded to two remarkable Junior Group Leaders at our Institutes – Dr Ivan Ahel at the Cancer Research UK Manchester Institute for his work to understand the mechanisms of DNA damage responses and Dr Nitzan Rosenfeld at the Cancer Research UK Cambridge Institute for his excellent record in developing cancer biomarkers and diagnostic strategies. More information about this prize and how to send in your nominations can be found on our website: www.cruk.org/prizes-in-research

Dr Mark Rutherford is based at the University of Leicester and holds one of our PRC Postdoctoral Fellowships. Here he discusses how he applied his skills as a statistician to the field of cancer research.

“I finished my PhD at the University of Leicester towards the end of 2011, having previously studied BSc Mathematics at the University of York and completed an MSc in Medical Statistics at Leicester. Mid-way through my PhD, I decided that I wanted to continue my career in cancer research and so began the process of drafting a CRUK postdoctoral fellowship proposal. Over the course of my PhD I had been fortunate enough to be allowed the opportunity to travel widely to conferences and workshops, allowing me to build a strong network of collaborators. I have since visited other research institutions (IARC, Lyon, and Karolinska Institute, Stockholm), enabling me to experience different research environments and work closely with experts in the field, which I found invaluable.

I chose to apply for the Population Research Committee Fellowship as it aligned perfectly with my PhD research, and future plans. I was keen to utilise my skills as a statistician to improve the understanding of applied research, and this funding has allowed me to do exactly that.

Population-based cancer survival studies are widely performed in the UK and across the world, and a number of studies make international comparisons using this data. But who are the results of these studies actually aimed at? There are a number of parties interested in such results, be it patients, clinicians or health policy decision-makers. The methodological developments being made as part of my Fellowship build on different methods for optimising the presentation of results to different groups.”
Drug discovery is an important part of our research activity and we make significant investments across a number of centres. Over the years, many important developments that are leading to patient benefit have come from the work we have supported, including those described here.

Professor Laurence Pearl and Professor Paul Workman were recognised this year for their influential contributions to cancer research by being awarded the CRUK Translational Cancer Research Prize. Their collaborative and pioneering work, culminating in the discovery of a potent and well tolerated drug, is showing considerable promise in the treatment of a range of tumour types, including non-small cell lung cancer. Their teams also made major contributions to understanding the molecular mechanism of action of HSP90 inhibitors and the genes involved in drug sensitivity and resistance.

Professor Laurence Pearl, Professor of Structural Biology at the University of Sussex, led the group that elucidated the basic biochemistry and structural biology of the HSP90 system. Their findings provided the rationale for the entire international effort in HSP90 inhibitor development, underpinning the collaborative translational research programme carried out in collaboration with Professor Workman and colleagues.

Professor Paul Workman, the Deputy Chief of the Institute of Cancer Research and Director of the Cancer Research UK Cancer Therapeutics Unit, made huge advances in the discovery, chemical biology and molecular pharmacology of HSP90 and PI3-kinase inhibitors.

Their work is truly interdisciplinary, playing a leading role in moving HSP90 from a poorly understood molecular target, to one that is now most actively pursued by the pharmaceutical industry, with over 20 inhibitors entering clinical trials.

The outstanding contributions of this team, whose research is described as the model for academic drug development, has led to the development of HSP90 inhibitors as effective drug targets. The HSP90 team is an exceptional group that exemplifies the broad skill set needed to build and test small molecule inhibitors.

CRUK Prizes Panel

For more information on CRUK prizes, or to nominate your colleagues for these awards, visit: www.cruk.org/prizes-in-research

The deadline for the next round of nominations is 31 March 2014.
This year Professor Sir Bruce Ponder stepped down as the first Director of the Cancer Research UK Cambridge Institute. His foresight in fostering a focus on translational research and cross-disciplinary working, his major research contributions in understanding inherited predisposition to cancer and his lifetime commitment to furthering our understanding of cancer have all contributed to him being awarded the 2013 CRUK Lifetime Achievement Prize.

Professor Ponder’s accomplishments have been remarkable. In the 1980s, during his early career, he established one of the first familial cancer clinics in the UK, leading to the discovery of the causative gene for inherited thyroid cancer. Later, in collaboration with others in the field, Professor Ponder initiated the International Consortium for breast cancer linkage, which laid the groundwork for gene mapping that led to the identification of the BRCA1 and BRCA2 genes in the mid-1990s. From 1996 he turned his attention to the problem of polygenic susceptibility and, along with Professors Doug Easton and Paul Pharoah, assembled the large case/control sets and expertise that enabled the first successful genome-wide association study (GWAS) in cancer.

In 2007, Professor Ponder not only developed a significant new Cancer Centre in Cambridge, but he also established the first major new cancer institute in the UK for many years – the Cancer Research UK Cambridge Institute. Both these research institutes are recognised to be amongst the leaders in Europe.

The Cancer Research UK Cambridge Institute made an impact from the start. I think that core funding was critical in this. We recruited in selected areas of cancer biology – gene regulation, epithelial cell biology; in areas with a strong technological base – genomics, in vivo imaging, bioinformatics, mouse models; and clinician-led laboratory groups in specific cancers – breast, pancreatic, prostate and ovarian. We also recruited group leaders with joint appointments in mathematics, chemistry, biochemistry.

One of my best memories of the Institute is the feeling of a community of scientific colleagues. Competitive, certainly, but also very engaged and ready to help one another develop their projects.

Professor Sir Bruce Ponder continues to be the Director of the Cambridge Cancer Centre, as well as conducting his own research into the mechanisms underlying polygenic susceptibility to cancer. His hard work and commitment has left an incredible legacy in Cambridge which will continue to bring benefits to people with cancer for many years to come.
As a researcher you know how expensive research is – none of the studies we fund would be possible without the support of the public. We rely entirely on their generosity to fund our research portfolio. We estimate it takes the sponsorship of around 230 Race for Life participants to fund a laboratory for just one week.

We have worked with many of you over the past year to help bring cancer research to life and to show the impact your work could have for people with cancer. Public engagement activities are a very effective way for us to motivate supporters, increasing donations and ultimately allowing us to fund more research. You also play a central role in helping us influence policy-makers, representing cancer research in the media and developing relationships with corporate partners.

**Behind the scenes**

Our Birmingham Centre recently opened its doors to the public, where over 115 researchers came together to allow 300 visitors to go ‘behind the scenes’ and experience what it’s like to be a researcher through hands-on science activities. Following the success of this event, we are rolling out more open days across our network of research Centres this year.

The Showcase was a great opportunity to share our enthusiasm for science with the public and to explain our efforts in the fight against cancer. Working together to plan and deliver the showcase enhanced the team spirit within our labs and created new links with other researchers throughout our centre.

*Dr Ruth Densham, University of Birmingham*

**Fundraising fun**

Many of you get involved in our high-profile campaigns – for example uniting to support our Stand Up To Cancer event, which was televised on Channel 4 towards the end of 2012. Photos of researchers donning eccentric ‘stand-up’ hairstyles were used widely in national and regional press to raise awareness of the campaign. The staggering £8 million raised through the campaign is now funding 12 new clinical trials across the UK.

**Bringing research to life**

Our Research Engagement team at the Cancer Research UK Manchester Institute developed a bespoke lab tour for potential supporters of our ‘More Tomorrows’ campaign. As a result, £100,000 was donated to CRUK, which will help fund the construction of a new groundbreaking research Centre in Manchester.

We were delighted to hear that such a generous donation was inspired by our lab tour. Our group is focused on moving lab-based cancer research into the clinic. Donations, like this one to the Manchester Cancer Research Centre, are essential for the future development of our work, both in understanding cancer biology and translating it to benefit cancer patients.

*Dr Ged Brady, Cancer Research UK Manchester Institute*

**Influencing science policy**

Our recent work has helped raise the profile of medical research, moving it up the political agenda. Ensuring the Government maintains the amount they spend on science is one of our top priorities, as it lays the foundations for investment from funders like ourselves and industry. Last year we worked with members of the research community to provide powerful case studies to politicians that would demonstrate the tangible, life-saving impact of the research you do. We were encouraged to see these efforts rewarded with the news that the science budget for 2015/16 will be frozen at £4.6 billion. We are already gathering evidence to make the case for Government investment in science ahead of the next election.

Keen to input ideas into our policy work? Contact: publicaffairs@cancer.org.uk

**To blog or not to blog**

Kate Williams is a PhD student in Professor Jane Wardle’s lab at the UCL Health Behaviour Research Centre. After attending our graduate communications training course, she offered to write a post for our award-winning Science Update blog, to coincide with the publication of her paper. The post prompted interest and a stream of comments from supporters and patients. Kate is now recruiting people to the trial their lab is running through our Cancer Chat web forum.
How we can help

There are lots of ways we can help you to raise the profile of your exciting work, as well as helping us to demonstrate to the public exactly why their support is needed – from formal communications skills training to simply flagging opportunities that arise. Our Research Engagement team work locally with researchers to assist in developing skills and techniques to deliver inspiring talks and events for the public. If you are interested in any of these activities please contact: researchengagement@cancer.org.uk

For other ways to get involved please visit: www.cruk.org/share-research
THE RESEARCHERS RETREAT

Having the opportunity to hear from you is incredibly important to us. Your opinions and knowledge are vital in shaping our thinking and driving our direction. Sharing ideas, data and expertise is a crucial component of research, which we actively support through a range of different meetings bringing together researchers across the community, both from the UK and internationally.

One example, our inaugural Researchers Retreat, took place in July 2013. An organising committee, made up of senior researchers, helped us design the agenda which brought CRUK staff and over 300 grantees together to stimulate discussion and debate and to help initiate and develop collaborations.

The meeting featured a number of stimulating talks from researchers at varying stages in their careers. Talks focused on topics including the future impact of emerging technologies and how multidisciplinary approaches can be incorporated into cancer research.

“A very positive outcome to arise from the Retreat, was that a piece of research, which I was considering applying for funding for, now has the potential to be carried out through a collaboration I initiated at the conference.

Professor Neil Perkins, University of Newcastle

We will refine the format and content based on the invaluable feedback you provided. As a result of the overwhelmingly positive response we received, we will host the meeting biennially. We look forward to seeing you at the next event.
LOOKING FORWARD:
OUR RESEARCH STRATEGY

Next year will see the publication of our new five-year organisational strategy, including our new research strategy. It has been a long process of development, as we have covered a wide range of topics and have consulted broadly to get a diverse range of views, insights and advice. Over 100 members of the research community in the UK and overseas have provided input, and we are indebted to them for their valuable contributions.

The strategy will set out our priorities for the next five years and the actions we will take to support them. The outlook for fundraising is positive, and so we anticipate being able to increase funding in a number of areas, as well as introducing new funding schemes and launching important new initiatives. The strategy will be ambitious, driving innovation in new areas, but will look to build on the outstanding strengths that exist in UK research. Ultimately, the key strands of the strategy are aligned with our mission: To save more lives from cancer, sooner.

We will continue to support a broad portfolio of basic research to build our fundamental understanding of cancer, while also strengthening our capabilities for effective translational research across the UK. One area where we want to cultivate research activity is in improving cancer prevention and early diagnosis. Another key objective will be to increase the research effort aimed at tackling the cancers with the lowest survival rates, in particular lung, pancreatic, oesophageal and brain cancers. We have already started to make new investments in lung cancer to support our ambitions, including the TRACERx study aimed at understanding the genetic complexity of the disease and its impact on how we treat it, as well as a commitment to establish lung cancer Centres of Excellence.

We will publish the new strategy in April 2014 and you will be the first to know the details. We will engage broadly across the UK to explain the new approach and the thinking behind it. But the publication will only be the start of the journey. Over the coming months and years, we will need your help in making the strategy a reality. We will need your feedback, ideas, creativity and inspiration to help continue the progress, and to develop the new approaches to make headway against cancer.

If you have any comments or questions, please contact:
researcher.comments@cancer.org.uk

Professor Peter Johnson
Cancer Research UK’s Chief Clinician

Professor Nic Jones
Cancer Research UK’s Chief Scientist
WE WANT TO HEAR FROM YOU...

Below are some useful contact details, so you can get in touch to find out about our funding opportunities, how to get involved in our activities and to give us your feedback.

**Funding and research**

[www.cruk.org/science](http://www.cruk.org/science) gives details on how to apply for funding, including our application deadlines.

If you have questions regarding specific funding schemes, please contact the relevant funding team:

- **Clinical Trials Awards and Advisory Committee**
  ctaac@cancer.org.uk

- **New Agents Committee**
  kate.searle@cancer.org.uk

- **Population Research Committee**
  prc@cancer.org.uk

- **Science Committee**
  science.committee@cancer.org.uk

- **Tobacco Advisory Group**
  TAG@cancer.org.uk

- **Training and Career Development Board**
  fellowships@cancer.org.uk or students@cancer.org.uk

**Experimental Cancer Medicine Centres**

Would you like to find out more about the ECMC network? Visit the ECMC website: [ecmcnetwork.org.uk](http://ecmcnetwork.org.uk) or contact: ecmcadmin@cancer.org.uk

**Our policy work**

Help our policy team to identify the issues affecting the research community. Contact: publicaffairs@cancer.org.uk

**Public engagement and fundraising opportunities**

Contact your local Research Engagement Manager: researchengagement@cancer.org.uk

**Publicise your work**

We can help you get your work across to the media, our supporters and the general public. Your story could be featured on our award-winning science blog and podcast: [scienceblog.cancerresearchuk.org](http://scienceblog.cancerresearchuk.org) and [info.cancerresearchuk.org/news/podcast](http://info.cancerresearchuk.org/news/podcast). Contact: pressoffice@cancer.org.uk.

**Get involved online**

If you’re on Twitter or Facebook, we’ve got a huge online community who would love to hear about your work. Go to [@CR-UK](http://twitter.com/CR-UK) and [facebook.com/cancerresearchuk](http://facebook.com/cancerresearchuk)

**Cancer Research Technology**

Do you have an idea or a discovery with commercial potential? Are you interested in working with industry? If the answer is yes, we want to hear from you. Visit: [www.cancertechnology.com](http://www.cancertechnology.com) or contact: enquiries@cancertechnology.com
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