

CANCER RESEARCH UK'S RESEARCH STRATEGY REPORT 2011

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# CANCER RESEARCH UK'S RESEARCH STRATEGY REPORT 2011

## 1. Executive Summary

This is the second annual report on our Research Strategy, in which we report on progress in the two years since our strategy was published in November 2008.

Many factors beyond the control of the Charity impact our ability to deliver the Research Strategy. At this time last year, our primary concern was to understand what impact any new Government would have on how we operate or how we work with others. As we anticipated, the new coalition Government has since introduced a raft of changes that fundamentally alter the environment in which cancer services are delivered, and in which research is conducted. During the past year we have used our influence to protect public investment in research, and the outcome of the Spending Review was a great success for the medical research community. Nevertheless, public sector funding for the research base will reduce in real terms, and CR-UK will carefully monitor the consequences of change for our research environment. Change will continue to play out across a legislative, policy, regulatory and fiscal landscape and we will continue to use our influence to try and engender an operating environment that best helps us deliver our strategy.

Following a sustained period of rapid growth since 2002, the increase in our research expenditure has been more modest in the past two years. The Research Strategy has helped us adapt and prioritise our research ambitions in a considered way in response to our projected income. We have developed a five-year financial plan, approved by our Trustees in March 2009 and reviewed on an annual basis, which supports our ambitious programme of work in the context of a challenging economic environment.

Over the past two years income has held up well, but we must continue to exercise careful control of expenditure and maintain the flexibility to adapt to changing financial circumstances and emerging research opportunities. In 2009/10 controlled expenditure saw the total cost of annualised research expenditure drop, albeit only to the levels seen in 2007/08. Despite this we have been able to invest in some bold initiatives and continue to fund research of the highest scientific quality and clinical impact. We expect that final figures will show that our research spend increased again in 2010/11. Looking forward, our research strategy will assist us in the difficult choices we must make about where to invest for the greatest impact.

Over the past two years we have broadly sustained our support for **areas of research strength** such as basic biology and epidemiology. At the same time we have continued to increase the proportion of our research investment in areas of strategic importance, particularly in clinical and translational research. We have invested significantly in drug discovery, establishing new small molecule programmes at the Beatson and Paterson Institutes in 2009. Our drug discovery strategy is now fully implemented, and there has been significant growth in application volume to the Discovery Committee. During 2011 we will consider our future priorities in this area. Over the past two years our Drug Development Office has made significant progress in streamlining processes, and delivering growth in Clinical Development Partnerships and combination studies. Our drug development strategy was refreshed in 2011. We have also reviewed our mechanisms for providing programme grant support for translational research, and will provide new funding opportunities for applicants in 2011.

Many of the **areas of new opportunity** discussed last year have seen steady progress, with some very significant successes.

We have taken the first steps towards realising new opportunities in imaging and in biomarker development. To become fully established in the portfolio these areas will need further development in coming years, particularly as progress will be largely dependent on developing new approaches in partnership with others. Unfortunately efforts to grow investment in animal model systems and in biomarkers through Innovative Medicines Initiative applications were unsuccessful.

In early detection, the National Awareness and Early Detection Initiative (NAEDI) reached an important milestone in 2010, with the release of a first round of funding for research into symptom awareness and early detection and a second application round now underway. In a major breakthrough during 2010, the outputs of CR-UK's 16 year investment in flexible sigmoidoscopy bowel screening research have translated into a Government commitment to change the screening programme, which should save around 3,000 lives per year in the UK. Despite these successes, barriers to the effective development of diagnostic technologies remain.

Our stratified medicines programme has made rapid progress in the past year, building strong relationships and brokering significant investment from the Technology Strategy Board, and key pharmaceutical industry partners. And our work with two prospective International Cancer Genome Consortium (ICGC) teams, which grew from an initial debate at SSAG, reached fruition, with funding for oesophageal and prostate cancer projects commencing in 2011. Our work on both of these programmes has put us in a strong position to deliver highly cost-effective access to Next Generation Sequencing services. In January we launched a new genomics initiative through our Centres that will capitalise on this unique opportunity to fund whole genome sequencing of well annotated clinical samples to answer important biological questions. Together these activities demonstrate a significant commitment to delivering discoveries through cancer genomics and leadership in ensuring their translation for patient benefit.

In **capacity building priority areas**, we have seen sustained progress in radiotherapy and radiobiology, with important recruitment taking place across the Centres network, and a groundswell of activity stimulated by the NCRI Clinical and Translational Radiotherapy Research Working Group (CTRad) (to which we are the major funding partner). There are encouraging plans for investment in surgery in our Centres, backed up by a range of training and career development activity. In key disease areas our investment in pancreatic cancer has grown significantly largely through our Centres, and oesophageal cancer is one of two disease foci for our ICGC work. Lung cancer has not seen a significant increase in activity over the past year although group leaders have been recruited to our Institutes who will focus on lung cancer and our Institutes are exploring opportunities for coordination and collaboration. There is already a great deal more clinical research in lung cancer than was the case 3-4 years ago.

2011 will see the review of a significant portion of our investment in **the research environment**, including three of our five institutes, and all of the CR-UK / DH funded Experimental Cancer Medicine Centres.

The establishment of Cancer Research UK Centres has been a key component of our strategy for the research environment. We have established Centres in 16 locations over the past two years, and this phase of the programme is nearing

successful completion. Cancer Research UK Centres will play a key role in delivering our Research Strategy, particularly for areas in which we aim to build capacity.

Our Centres and ECMCs are also a growing focus for industry interactions, where activity across the partnerships outlined last year has grown significantly. Our relationships with industry are manifold and complex, changing in response to developing needs. Many steps have been taken over the past two years to enhance our work with this important sector, and we will continue to identify areas where collaboration could be mutually beneficial to both the Charity and industry. In this year's report we provide an overview of interactions with one major industry partner to illustrate the breadth of our activity.

Although our institutes have their own individual strategies, they also have an important role to play in contributing to our broader Research Strategy. To help facilitate this, since September 2010 our Institute Directors have attended Scientific Executive Board meetings and over the next year we will continue to explore our strategic agenda with them. Planning for the UK Centre for Medical Research and Innovation (UKCMRI) continues apace, and critically this year we have secured the commitment of the new Government to invest. Construction work will start on site in the spring.

In the autumn of 2010 we completed the restructuring of our Research Operations and Funding activity and launched our new electronic Grants Management System (eGMS). These changes were important components of our drive to deliver streamlined and consistent support to applicants and grantees. They build on the earlier delivery of simplified terms and conditions for grants and awards that increased financial flexibility and clarity for award holders while reducing the burden of administration.

Our priorities in **providing the right people for research** have moved forward this year, with the delivery of training accounts in our Centres, and changes to response mode funding schemes to meet anticipated need. Work has also begun to identify the next generation of epidemiologists. As we noted last year, our ambition to increase the number of international leaders in cancer research working in the UK has seen least progress. Given the current financial constraints, this is an area that has not been prioritised. The establishment of 16 of our Cancer Research UK Centres has led to a large number of senior positions becoming available in the UK, although there have been issues with recruitment to senior clinical posts. In the medium term the UKCMRI will provide a strong focus for international recruitment.

By the end of the 2011/12 financial year we will be four years on from when we pulled together the thinking for our current research strategy and more than three years since we published it. Moreover, the external operating environment has changed and new opportunities in research are opening up all the time for us to consider. While recognising that the current strategy still provides a sensible but ambitious plan against which we can prioritise investment decisions, it is nonetheless appropriate that we now begin to think about the next planning cycle.

## 1.1. Introduction

In November 2008, Cancer Research UK published its Charity Strategy, setting out how we intend to work towards achieving our 2020 goals over the years 2009-2014. The strategy is directed at reducing mortality from cancer and will guide our decision-making, investment and funding plans and annual operations. A key component of the Charity Strategy is the five-year Research Strategy<sup>1</sup>.

This is the second annual report on our Research Strategy. The purpose of this document is to update Cancer Research UK's Trustees on progress with implementing the Research Strategy, to highlight issues that are impacting or are likely to impact our ability to deliver the strategy, to communicate our future plans and to stimulate ongoing debate about our strategic priorities.

The three themes of the Research Strategy are: focussing our research on scientific quality and clinical impact; providing the right environment for research; and providing the right people for research. This report follows the same structure.

Our strategic aims are to:

### Focus our research – scientific quality and clinical impact

1. Enhance research programmes in early diagnosis, screening and prevention.
2. Ensure that we have the best mechanisms in place to translate research discoveries into clinical advances in diagnosis and treatment.
3. Maintain and, where possible strengthen, a broad and balanced portfolio of world-class research in the UK directed at understanding the biology and causes of cancer.
4. Promote research in areas with the highest levels of unmet medical or research need.

### Provide the right environment for research

5. Establish a UK-wide network of Cancer Research UK Centres to improve outcomes, engage the broader public and increase the knowledge flow from laboratories to patients and vice versa.
6. Continue to maintain a balanced portfolio of research in different venues, including our five core-funded Institutes.
7. Create space for bold initiatives.
8. Continuously review whether we have the right governance and funding streams to meet the needs of our Research Strategy.
9. Identify and provide access to the key new technologies and infrastructure that are needed to make the fastest progress in cancer research.

### Provide the right people for research

10. Increase the number of international leaders in cancer research working in the UK.
11. Continue to develop and maintain schemes for training and career development to ensure that the UK is developing a cancer research workforce for the future, pioneering the development and provision of relevant training in our Institutes and Cancer Research UK Centres.
12. Continue to invest in and foster national and international collaborations to deliver the best research output.

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<sup>1</sup> Available as a downloadable pdf at <http://science.cancerresearchuk.org/research/research-strategy/>

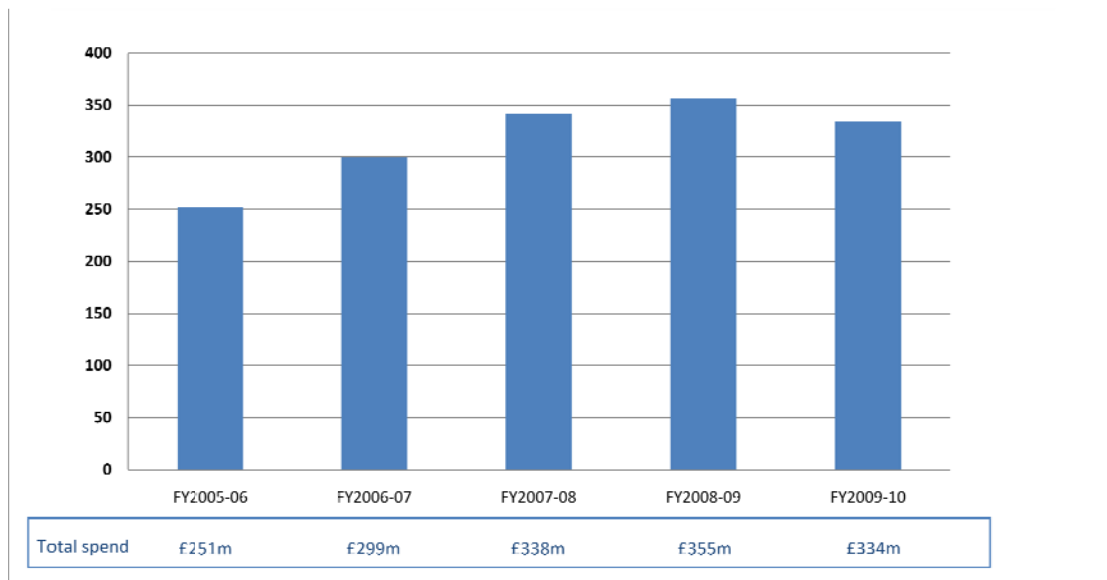
## 1.2 Portfolio overview

The progress report provides an opportunity to examine the make-up of the portfolio and to question if it is sufficiently broad, ambitious and balanced. The figures contained in this section are designed to help stimulate these discussions.

### 1.2.1 Total Research Expenditure

Our Research Strategy was published in December 2008, towards the end of a period of exceptional growth that began in 2002. As we developed and implemented components of our strategy, over the three years from 2005 to 2008, we were able to invest in priority areas during that period.

In our first progress report we saw that research expenditure continued to grow, but at a much reduced rate. In 2009/10, for the first time since 2005/06, the total cost of work done in the year fell (referred to here as annualised research expenditure), albeit only back to the levels seen in 2007/08 (Figure One). This is in part due to the cautious approach to funding that was taken at the beginning of the year in response to the financial climate - income actually rose by 3% in the same time period.



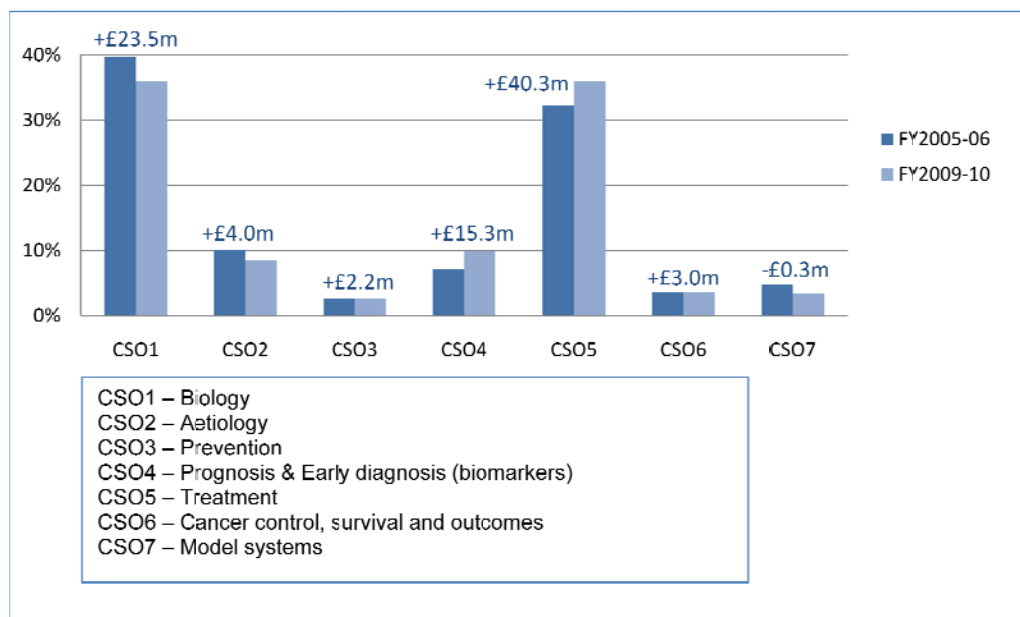
**Figure One: Annualised Research Expenditure for FY2005/06-2009/10<sup>2</sup>** Expenditure is presented for research activities only, and excludes cancer information & advocacy.

### 1.2.2 The Balance of Our Portfolio

In each of the past four years investment in basic science has accounted for around 37% of the portfolio, disease site specific research about 26% of the portfolio and research relevant to all disease sites about 27%. This balance has changed little.

When broken down by type of research (using the Common Scientific Outline coding system), a five year analysis reveals a modest but significant change to the shape of the portfolio (Figure Two).

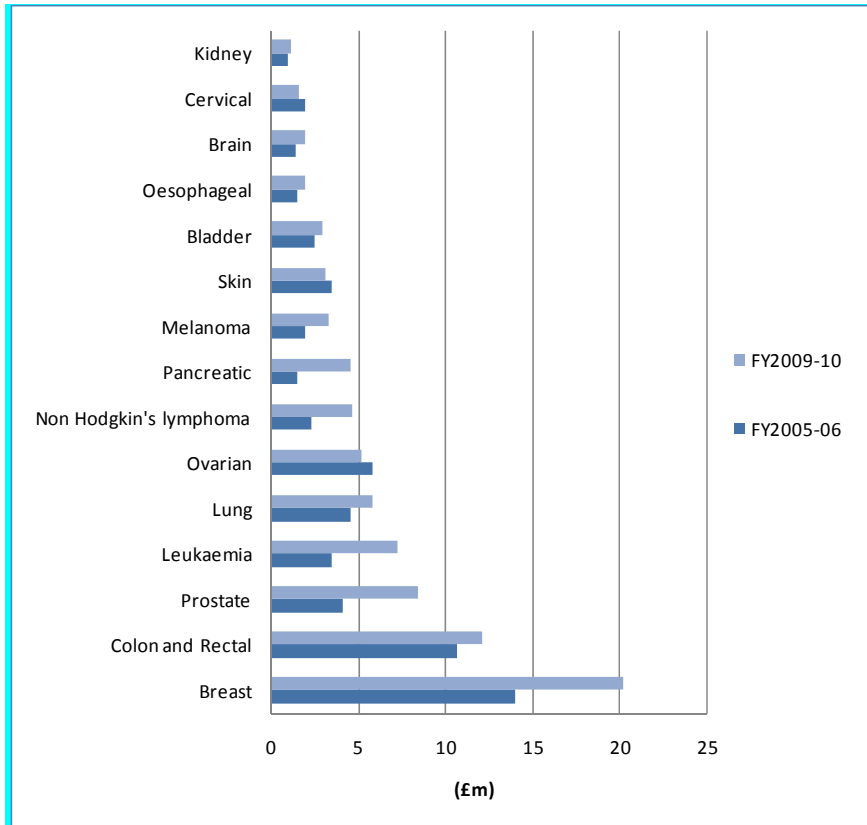
<sup>2</sup> Annualised Research Expenditure is also known as 'Cost of Work Done'



**Figure Two: Change in spend by CSO Code.** The bars represent the proportion of the CR-UK portfolio in each CSO category; the overlaid figures represent the difference in research expenditure in each CSO category between the same time points. Because our overall research spend has increased since 2005/06, all areas except CSO7 have seen increased investment in real terms.

In proportionate terms, there has been roughly a 4% decrease in fundamental research (CSO1 - Biology), and a corresponding 4% increase in funding for drug discovery, development and clinical trials (CSO5 - Treatment). Together these activities make up 67% of the portfolio. Importantly, growth in clinical and translational research has not been achieved at the expense of other areas of the portfolio. All areas except CSO7 have seen increased investment in real terms.

Given the disease specific priorities in the Research Strategy (pancreatic, oesophageal and lung), it is important to review the balance of our portfolio of site specific research (Figure Three).



**Figure Three: Spend by disease site**

The percentage of our site specific portfolio invested in each site has been quite stable in the last four years, but significant areas of growth stand out.

Of the 29% of our portfolio that is invested in site specific research, breast cancer research receives the largest investment (20% of our site specific portfolio, £20.2m in 2009/10 Figure Three). In 2009/10 the annualised research expenditure for breast, colorectal, prostate and leukaemia constituted about 14% of our entire investment in cancer research. This has increased from 12.8% in 2005/06. Investment in breast cancer exceeds any other cancer by over £8m per annum.

Over the same period, investment in prostate has doubled and investment in pancreatic cancer has trebled. Spend on oesophageal and lung cancer have not increased by a significant amount. As this report indicates, decisions made during 2010 mean this is likely to change going forward.

## 2 Focus Our Research

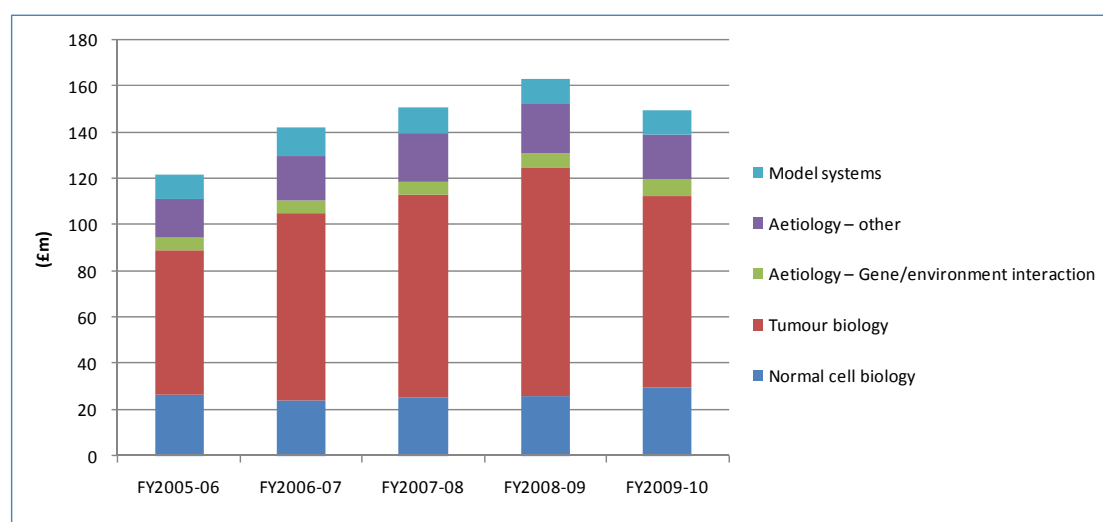
### 2.1 Build on our strengths

#### 2.1.1 Basic Science

Basic science in the CR-UK portfolio is funded largely through the Biological Sciences Committee and the CR-UK Institutes with some funding also through our Fellowships schemes. The fundamental insights generated from this research are critical for driving the charity's translational and clinical aspirations. Our strategy in basic science is to maintain a strong portfolio and to continue to raise the quality of this research in both our Institutes and response-mode portfolios. We have also said we would increase our focus on tumour biology, gene environment interactions and model systems in preference to increasing spend on more fundamental biology.

#### Spend on Basic Science

Overall, investment in basic science increased by 22% in the period from 2005-6 to 2009-10, but decreased in line with spending decreases across other areas between 2008-9 and 2009-10. Spend as a proportion of the total research portfolio has decreased from 49% in 2005/06 to 45% in 2009/10.



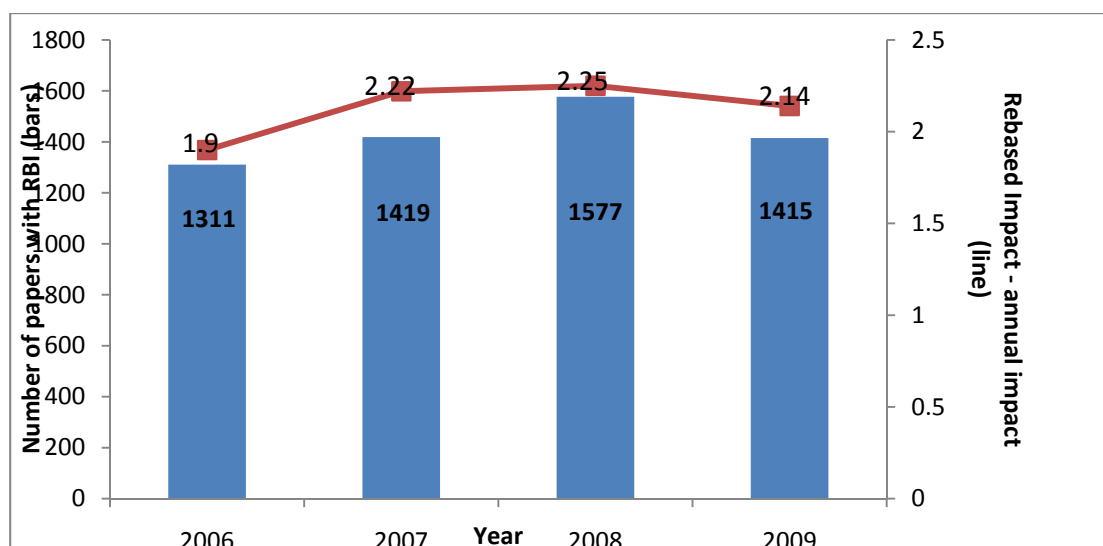
**Figure Four: Spend on basic science.** Basic science is here defined to include all normal and tumour cell biology (CSO1), endogenous and exogenous factors in the causes of cancer (CSO2), and model systems (CSO7)

As Figure Four shows, the spend on tumour biology increased steadily (from £62m to £98m in the years up to 2008-09) but then decreased in line with the overall funding trend in 2009/10 (to £82.7m). Investment in all other categories has remained relatively constant.

#### Basic Science Quality (Publications)

Figure Five shows the total number of primary research and review papers resulting from Cancer Research UK funded research, with the mean rebased impact figure for each year.

Rebased impact compares the citation impact of our papers to the world averages in the relevant subject fields, and indicates that overall our publications consistently have about twice the world average impact.



**Figure Five: Research Quality (Publications).** Number of primary research and review papers resulting from our research during 2006 to 2009, with mean rebased impact. The 'rebased impact' of a paper is the ratio of the actual number of citations to that paper to the mean number of citations for papers in the same subject area published in the same year. Citation counts and subject categories are derived from the Thomson Reuters Science Citation Index.

### Biological Sciences Committee (BSC)

- BSC continues to support a significant proportion of CR-UK's basic science portfolio, covering a broad spectrum of research that addresses all the original "Hallmarks of Cancer" (as proposed by Hanahan and Weinberg): self-sufficiency, insensitivity to growth inhibitors, invasion and metastasis, immortality, evasion of apoptosis and modulation of angiogenesis, as well as the more recent hallmarks characterised by Kroemer and Elledge; evasion of immune surveillance and the stress phenotypes of cancer.
- Over the last year the BSC has funded research utilising a wide range of experimental models, including yeast, *Drosophila*, Dictyostelium, *C.elegans*, zebrafish and mice as well as primary and cultured human cells.
- Since April 2010, the Committee has met 3 times, funding 18 programmes, 50 projects, and 5 Equipment awards.
- The funding rate for programme grants in the same period is 60% (64% of renewing programmes and 50% of new applications). This compares with a 2009/10 funding rate of 42% (45% of renewing programmes and 30% of new applications). Funded programmes in 2010/11 include research into the genomics and molecular pathology of pancreatic cancer, cellular responses to DNA damage and an investigation into the development of bone metastases in breast and prostate cancer.
- Demand for programmes appears to be rising and competition is likely to remain high in 2011. Since March 2010 only two programmes scoring below Forefront were funded and some renewing programmes have had their funding cut by up to 50%.
- In October 2010, a preliminary application stage was introduced for programme applications to manage increased demand. Since then we have considered 18 preliminary applications, with 10 (55%) invited to proceed to full submission.
- We have recently made a change to the way in which programme applications to the BSC are reviewed. All programme applicants now have a face to face meeting with a review panel composed of BSC members and external experts in advance of the BSC meeting at which a decision is made. This has been introduced in response to discussions held with the SSAG last year and will

provide a more robust and equitable process for programme applicants. The first panel meetings took place in February and March 2011, in advance of the April 2011 meeting of the BSC.

- The funding rate for project grant applications at the 3 meetings since April 2010 is 25% compared to 18% for 2009/10.
- Our funding rates this year, particularly for project grants, have compared very favourably with those of other funders including the MRC, AICR and Wellcome Trust. We have been actively maintaining a balance between programmes and projects based on feedback from last year's SSAG about the importance of project funding.
- Funding from the BSC continues to form much of the research foundation of the CR-UK Centres.

### **Institutes and Centres**

- Please see sections on "Providing the right environment for research: Institutes" and "Providing the right environment for research: Centres" (Sections 3.1 and 3.2).

### **Future plans, challenges and opportunities**

- Although we have had a good year in terms of the breadth, quality and quantity of basic research we have been able to fund, the current environment does present some challenges. Applications for programme grants to BSC and for fellowships are increasing and whilst this will push standards ever higher, we anticipate that in the next year we will be unable to fund all of the high quality programme applications that we see.
- Furthermore, the external environment continues to change and the impact of this is as yet uncertain; while the impact of the government spending review on the MRC seems limited, the impact of changes to HEFCE and Research Council funding and changes to funding mechanisms at the Wellcome Trust may still affect CR-UK grant demand.

### **2.1.2 Epidemiology**

Epidemiological research provides new leads for both behavioural and medicinal approaches to preventing, diagnosing or treating cancer. Our strategy is to maintain and grow an active portfolio of epidemiological research, and in particular to support the increasing application of molecular techniques to population studies.

#### **Progress so far**

##### Maintain, and grow, an active portfolio of epidemiological research

- The largest epidemiology programme grant in the Population Research Committee (PRC) portfolio, Dame Valerie Beral (2010 New Years Honour list), had a successful site visit in October 2009.
- In 2010/11 the Population Research Committee (PRC) started to accept new programme grant applications in an effort to strengthen and diversify the portfolio. Two outline programme grants were considered in April and one was invited to submit a full application for consideration at the November 2010 meeting. This programme, which aims to develop and validate models for risk stratification, early detection and diagnosis of ovarian cancer, was funded.
- Funding rates remain strong with a 31% success rate for project grants.
- To date, six of the CR-UK Centres have identified epidemiology as a key focus area (QM-UL, Birmingham, Southampton, UCL, Dundee and Oxford). These will be in addition to the high quality research funded in Cambridge, Leeds and Oxford.

### Correct workforce capacity and training deficit

- CR-UK has a long standing reputation for funding some of the most important epidemiological studies ever undertaken. If we are to achieve our Goals we must take a proactive approach to maintaining excellence. A one day strategy meeting with a small group of epidemiologists was held in February 2011 to discuss mechanisms for identifying and attracting rising stars to the portfolio. In addition, the issue of the lack of uptake of existing funding opportunities was discussed.
- Succession planning for retiring programme grant holders remains a priority and discussions with key Host Institutions have commenced.
- The PRC has identified a shortage of HEFCE supported posts for junior group leaders as a limiting factor in the development of research leaders of the future. Partly to address this, SEB decided to create some ring-fenced postdoctoral fellowship positions early in 2010. The first call was however disappointing.
- The second call for post doctoral Fellowships in Population Research closed in December 2010. Encouragingly, double the number of applications were received, compared to the previous year. Applications will be triaged at the April 2011 meeting and candidates will be invited for interview by a subset of the PRC.

### Genetic Epidemiology

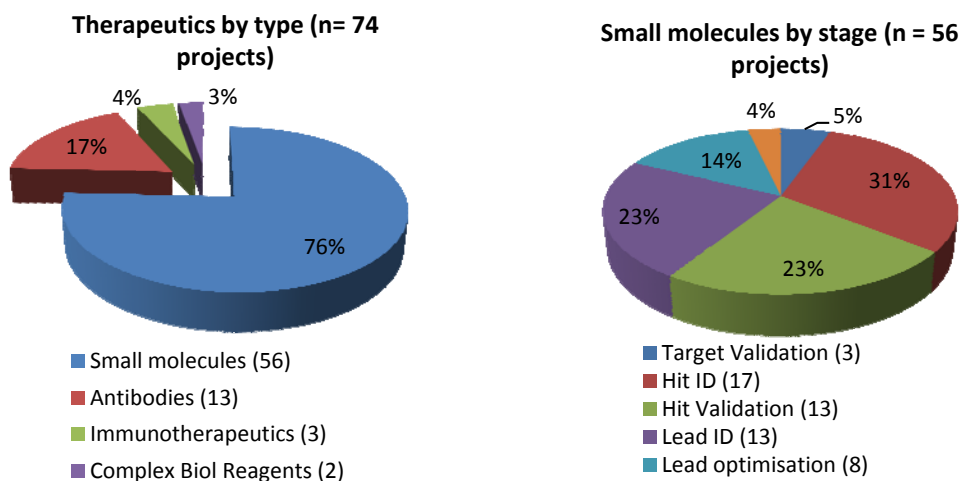
- Response mode funding for genetic epidemiology moved to the remit of the Biological Sciences Committee after the publication of the Research Strategy. One programme dissecting genetic predisposition to colorectal cancer was renewed in 2010/11.
- In recent years, Cancer Research UK has invested heavily in genome wide association studies aimed at understanding genetic predisposition to colorectal, prostate, breast, ovarian and lung cancer. The initial funding for most of these projects came to an end during 2009/10, although CR-UK funded follow-up studies on breast and prostate continue. Insights generated by the lung, ovarian and colorectal cancer projects will be pursued by the investigators through response mode funding from CR-UK and other agencies. These studies generated considerable interest and a number of high profile publications.
- An update on International Cancer Genome Consortium funding is presented in section 2.2.7).

### **Future plans, challenges and opportunities**

- Discussions have commenced with the International Agency for Research on Cancer (IARC) regarding potential opportunities for joint working (e.g. IARC representation on the PRC, potential joint Fellowships).
- Discussions with other funding agencies (e.g. Wellcome and the National Cancer Institute) have also commenced in order to identify key themes emerging in the area.

### **2.1.3 Drug Discovery**

CR-UK has a long history of success in drug discovery. In order to build on this platform and exploit the outcomes of our basic research portfolio, the 2005 strategic review recommended increasing activity in small molecule drug discovery and therapeutic antibody research. We are now at a stage of full implementation of the strategy and are closely monitoring the progress and impact of our investment.



**Figure Six: The configuration of our 2009/10 drug discovery portfolio.**

The portfolio consists of 74 active projects. Small molecule approaches make up the largest proportion (76%) with over 50% of these at the stage of Hit Identification or Hit Validation. N.B. "Projects" include DC funded projects or sub themes of work from within a drug discovery programme (usually focussing on a defined molecular target)

### Progress to date

- The number of applications submitted to the Discovery Committee over the last two years has increased nearly 3-fold (10 applications were submitted in 2008 over 3 meetings, 26 applications submitted in 2010 over 3 meetings).
- In 2009, Cancer Research UK invested £16 million over 5 years in two new drug discovery programmes at the Paterson and Beatson Institutes. The first year of both programmes was marked by a period of extensive laboratory refurbishment and staff recruitment. Following successful annual reviews, both programmes are now in their second year and each has an active portfolio of research projects focussed on novel drug targets.
- A one-day Small Molecule Drug Discovery Colloquium was hosted in March 2010 which was attended by the Drug Discovery Leadership Group (DDL<sup>3</sup>) and approximately 50 members of the disparate drug discovery programme teams. The aim of the colloquium was to foster interactions between the groups, to share best practice and to discuss the challenges of drug discovery research in the academic arena. The meeting was very well received and has initiated a number of continuing discussions between the groups.
- In 2010, a new group, the Drug Discovery Advisory Group (DDAG) was constituted to replace the Discovery Coordinating Committee (DCC), with the remit to conduct an annual scientific review of all our activity in this area. The recommendations from the inaugural meeting held on June 30<sup>th</sup>/July 1<sup>st</sup> 2010 were ratified by CTCR and the SEB.
- The Therapeutic Antibody programmes initiated in July 2009 (at Oxford and Southampton universities) underwent a successful annual review at the recent DDAG. The therapeutic antibody portfolio has grown from three projects in 2008 to 13 projects in 2009/10 and now represents approximately 17% of the active drug discovery portfolio.

<sup>3</sup> The DDL group consists of leaders of the 5 major small molecule drug discovery programmes (Institute of Cancer Research, Cancer Research Technology, Northern Institute of Cancer Research, Paterson and Beatson Institutes) and meets to share best practice, identify common issues and seek opportunities for collaborative solutions.

- During the course of the last year, the drug discovery programmes have leveraged an additional 56 full time equivalents (FTEs) of resource from commercial collaborators based on the potential of the portfolio; this represents approximately 18% additional resource beyond that funded by CR-UK.
- During 2009/10 CRT developed exciting new collaborations around early drug discovery projects with Cephalon and Astra Zeneca. Both of these collaborations are going very well with the commercial partners commenting on the professionalism and quality of CRT's work. Further industrial collaborations are under discussion.
- CRT has also established collaborative consortia of scientists working in a specific biological area, with a view to then providing a mechanism for these consortia to interact with industry. To date consortia have been established in cellular senescence and stem cells and a third consortium in lipid metabolism is under review.
- A small scale expert workshop was held in Q2 2010 to explore the drug discovery opportunities arising from advances in synthetic lethal approaches. Discussion mainly focussed on high through put genetic screening (HTS) approaches. The group agreed that the impact of HTS exploiting synthetic lethal interactions had been limited to date and that the technology required is expensive, relatively immature at this time and dependent on thinly spread expertise. The group recommended that a larger workshop be convened to explore the level of ongoing activity and access to appropriate expertise within the community, and to further develop strategy in this area.
- CRT and Medical Research Council Technology (MRCT) have agreed to 'swap' medical discoveries to accelerate the translation of early scientific research into patient benefit. MRCT will offer CRT the opportunity to manage, develop and license certain intellectual property with an application in cancer.
- The CR-UK Cancer Therapeutics Unit, directed by Professor Paul Workman, underwent a successful quinquennial review in December 2010. The CTU has contributed to the identification of 13 pre-clinical development candidates, five of which have progressed in to clinical study.

### **Future plans, challenges and opportunities**

- A review of our drug discovery strategy will be undertaken during 2011 to assess the progress made since the 2005 Science Plan Review and the desired future direction. The review will also conduct a capabilities analysis (access to enabling technologies with which to support drug discovery) as a current lack of High Throughput Screening capacity may be an issue which is negatively impacting our small molecule drug discovery activities.
- We will continue to monitor progress of the drug discovery portfolio on an annual basis at the DDAG and will seek commercial partners at an early stage.
- A second small molecule Drug Discovery Colloquium will be held in Q1/Q2 2011.
- In Q1 2010, CRT entered into a 3-year multi-project research alliance with Astra Zeneca (AZ) to develop therapeutic agents targeting cancer metabolism. CRT is currently exploring the possibility of further collaborative opportunities with Pharma/Biotech companies in specific areas of tumour biology; including tumour microenvironment, DNA repair and epigenetics.
- The Discovery Committee has seen a significant increase in fundable applications over the past year beyond the capacity of the current budget (6 of 17 fundable projects were unfunded). The collaborative consortia established by CRT (above) have to date sought (part or full) funding from the Discovery Committee and, given the funding requirements of the multiple partners, this has put added pressure on the Discovery Committee budget. We are proposing to

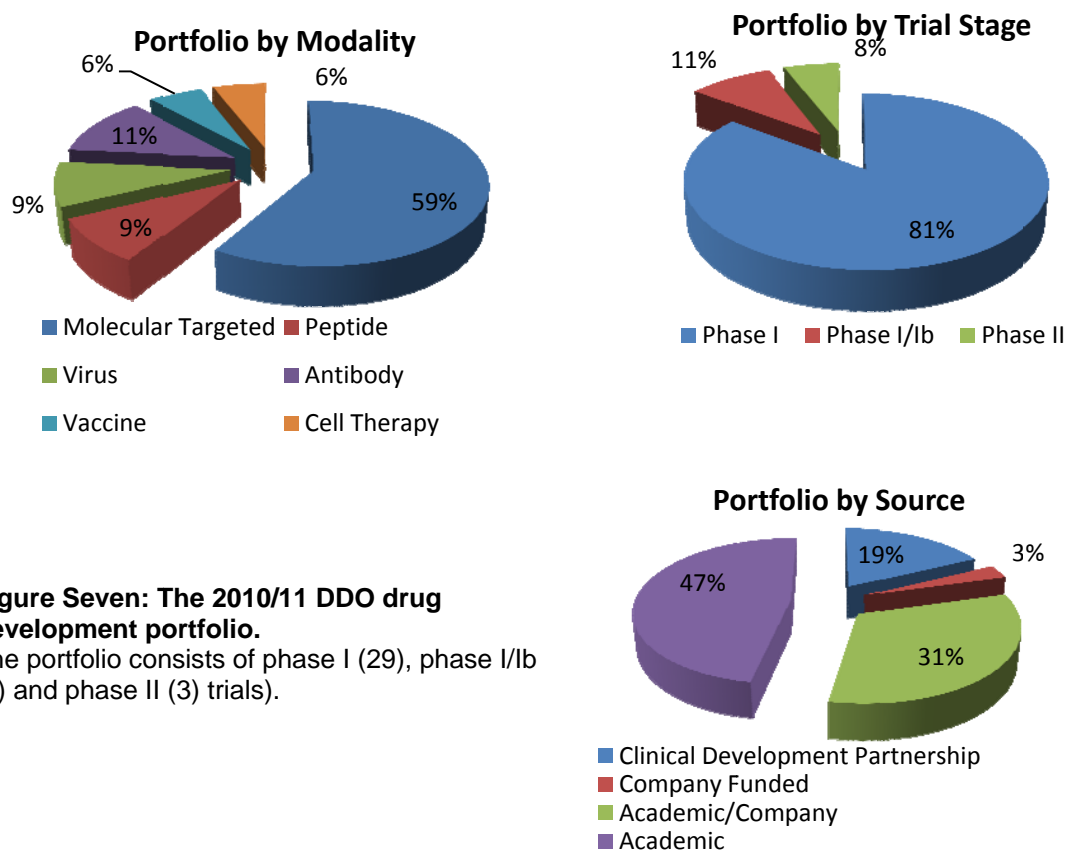
increase the DC budget by 33% during 2011/12 to reflect the increase in demand.

### 2.1.4 Drug development

Drug development was the first area within the CR-UK portfolio to develop its strategy in 2005. As such we have renewed the drug development strategy earlier than other areas within the portfolio. The DDO implemented a new 5 year strategy in May 2010, the key aims of which are to:

1. Focus on delivering phase I/II clinical trials incorporating novel study designs, biomarker strategies and/or imaging.
2. Bring promising new medicines to cancer patients that might otherwise not be available, particularly through:
  - a) Academically developed experimental therapeutics considered too complex or risky by Industry
  - b) Promising agents from CR-UK funded labs/institutes
  - c) Therapeutics from biotech requiring resource and the capability of the DDO to progress into clinic
  - d) Partnering with Industry through the Clinical Development Partnership (CDP) initiative to take shelved agents and novel combination treatments into trials.
3. Balance the portfolio to focus the majority of DDO resource on drugs with a clear development pathway.

In line with the CR-UK Research Strategy, the DDO is particularly looking to increase the number of projects in our portfolio supporting first in class, hypothesis testing phase II studies, rationally targeted combination studies or novel therapies for lung, pancreatic or oesophageal cancers.



**Figure Seven: The 2010/11 DDO drug development portfolio.**

The portfolio consists of phase I (29), phase I/Ib (4) and phase II (3) trials).

## Progress so far

- The DDO has been focussing on developing tools, processes and working practices that will help deliver projects on time and within the approved budget.
- The DDO has successfully implemented a portfolio management system which focuses on balancing our portfolio to maximise the potential for patient benefit through focussing the majority of DDO resource on drugs with a clear development pathway. A full review of our portfolio has been completed.
- The first study using electronic data capture (EDC) went live in Feb 2010 with the first patient data collected in May. There are currently 4 studies live in this system.
- There are currently seven projects in the portfolio (two studies now open to recruitment) which have been identified and run through the Clinical Development Partnership (CDP) initiative.
- Combination studies are an important avenue for future cancer drug development and will be considered on a case-by-case basis should they demonstrate a specific fit with the CR-UK strategy or be an area where DDO can add some specific value. For example:
  - providing peer review for studies that can be sponsored by an NHS Trust
  - brokering agreements where an applicant approaches us with a study where the agents are from two separate companies
  - providing business expertise and acting as a co-ordinator where a company is interested in entering into an alliance with Phase I oncologists
- In 2009/10, the DDO entered negotiations with Astra Zeneca regarding setting up a collaborative model to support the progression of novel combination Phase I studies with new agents from their pipeline through UK clinical centres. The first proposals for combination studies of novel molecularly targeted agents resulting from the AstraZeneca/ECMC combination alliance were submitted to the Nov 2010 NAC meeting and two out of three were funded.
- To reflect our strategy to support the development of novel imaging agents we have recently opened our second study in this field.
- In May 2010 we opened our first phase I study to incorporate a novel statistical design. The design will accelerate the dose escalation of a combination of molecules targeted at pancreatic cancer patients (**see Box 1**).
- European legislation now requires companies to also test their new drugs within the paediatric population so the availability of new medicines for children is expected to become less of an issue in the future. Currently, however, we have not seen any significant signs of improvement in this area and there still remains a significant unmet need in the paediatric population.
- The first paediatric study with an aurora kinase inhibitor opened to enrolment in 2009 and has exceeded recruitment targets.
- The newly built Biotherapeutic Development Unit (BDU) at Clare Hall passed its MHRA inspection in March 2010 and received its licence in May.

### Box 1: Novel statistical design

A clinical study with a Notch inhibitor and gemcitabine is currently being sponsored by Cancer Research UK at three centres in the UK. The Notch inhibitor has previously been trialled in healthy volunteers, patients with Alzheimer's disease (for which the drug was originally developed) and breast cancer. Gemcitabine is standard of care for patients suffering from pancreatic cancer. Laboratory work has suggested that a combination of the Notch inhibitor with gemcitabine may be beneficial to patients with pancreatic cancer.

This is the first time that this combination of drugs has been given to man. The initial part of the study (Phase I) has been designed to investigate the safety and tolerability of the two drugs in combination and to establish a recommended dose which can be used to establish efficacy (Phase II). Dose escalation is guided by adaptive Bayesian dose-escalation methodology rather than a more traditional design. It allows the statisticians working on the study to predict the probability of dose-limiting toxicities occurring at a given dose based on previous occurrences in patients treated at lower doses. It is intended that this approach will reduce the number of patients exposed to the lower (potentially less efficacious) dose-levels of the combination of drugs. This will be the first time that this methodology has been employed by the charity.

- The NAC role and remit has expanded to include grant funding of Phase I studies sponsored by ECMCs<sup>4</sup>, and more funds have been released to DDO to support this change. To date five studies have been approved through this mechanism.

#### **Future plans, challenges and opportunities**

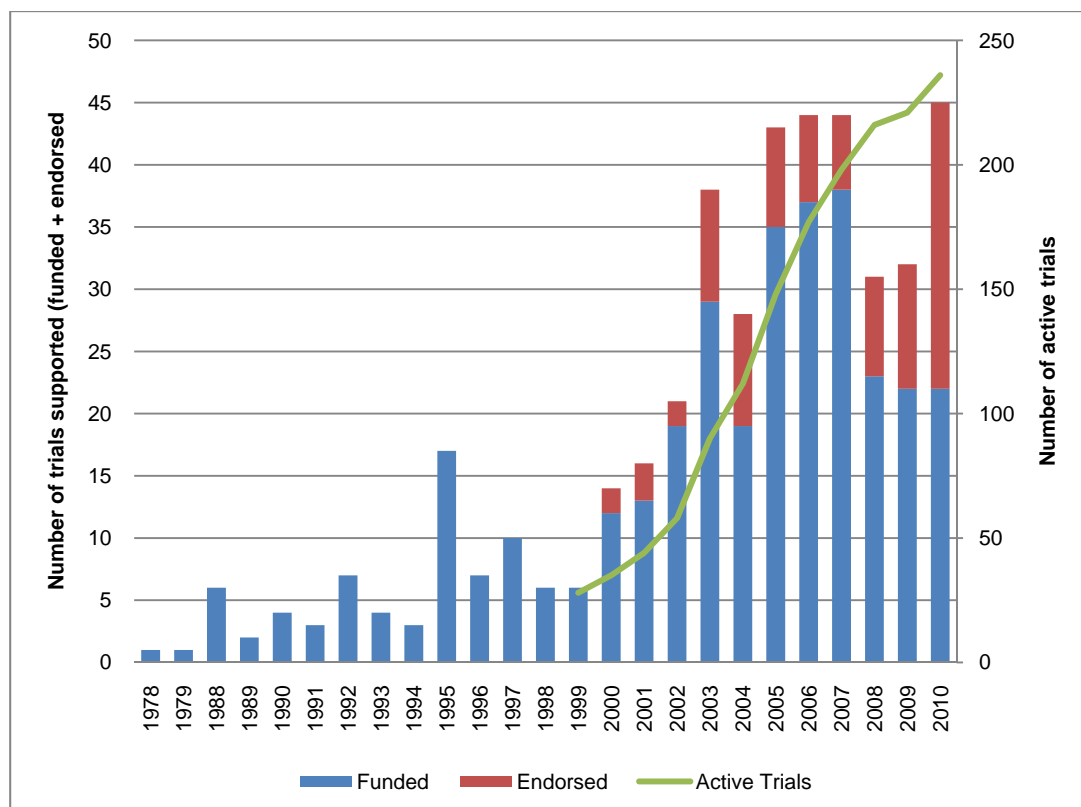
- DDO will continue to support the CDP (Clinical Development Partnerships) initiative. There are now seven ongoing CDP projects within our portfolio, with further deals in negotiation.
- The DDO will continue to work closely with and ensure we exploit more effectively the knowledge and expertise of the clinicians and scientists within ECMCs and CR-UK Centres.
- While the DDO Portfolio generally ensures our preclinical development and manufacturing capabilities (which are unique in the European non-commercial drug development arena) are constantly busy, we will continue to explore opportunities to ensure they are fully utilised at all times.
- Johnson & Johnson recently indicated that they wish to exercise their option to license the clinical data from the ongoing DDO Phase I/II trial of Abiraterone in breast cancer. The DDO has also received an expression of interest from another pharmaceutical company in licensing the data from a second ongoing DDO Trial.
- We are in discussions with Pfizer regarding the potential to set up a development programme with one of their drugs via the CDP route. With this initiative we hope to build a strong working relationship with Pfizer that will be as successful as our current relationship with AZ.

#### **2.1.5 Late phase clinical trials**

CR-UK supports new interventional, therapeutic trials via project grants or endorsement by the Clinical Trials Advisory and Awards Committee (CTAAC). In addition, we support 8 late phase Clinical Trials Units (CTUs) (seven adult and one paediatric) across the UK. Core funding to the Trials Units is essential in that it provides long term support for key staff with expertise in areas such as statistics and governance to develop and manage trials.

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<sup>4</sup> Previously all DDO studies were sponsored by CR-UK



**Figure Eight: New and cumulative late phase clinical trials funded and endorsed by CR-UK**

With one CTAAC meeting remaining in 2010/11, we have funded and endorsed a total of 35 new trials. There are over 236 active trials in the CTAAC portfolio (156 late phase trials and 80 feasibility studies), including those trials in set-up by the Trials Units, trials open to recruitment and those in follow-up. The introduction of the Feasibility Studies Committee (FSC) in 2006 saw the number of studies supported rise rapidly up to 2006 and 2007. In 2008 FSC and CTAAC merged and the NIHR HTA programme introduced response mode funding for trials. Furthermore the Clinical Trials Units underwent their QQRs in December 2007 and hence submitted fewer applications for review and funding.

### Highlights of 2010

- Figures from the National Cancer Research Network (NCRN) show that last year almost 31,000 cancer patients entered a trial supported by CR-UK; in the previous year 25,000 patients were recruited, hence this is a major increase of 24% in one year. 73% of all patients taking part in NCRN trials are entered into CR-UK funded trials, and 68% of patients taking part in randomised trials were on CR-UK supported trials (13,049 out of 19,274 patients).
- 21 CR-UK trials were presented at the American Society for Clinical Oncology Conference this year (8 more than last year), including the first major findings of 5 trials.
- A key aim of the feasibility study scheme was to encourage and support new investigators and the scheme is succeeding in fulfilling this objective. Of 182 applications to the scheme since 2006, 82 (45.1%) have been from new investigators. Of these 82 applications from new investigators, 38 (46.3%) have been supported; this compares favourably with a success rate of 54% (54/100) for applicants already in receipt of CR-UK support.
- One study, initially funded via the feasibility study scheme, has been funded as a phase III trial this year.
- A partnership with the Samantha Dickson Brain Tumour Trust resulted in 3 proposals being considered by CTAAC in March 2010, 2 of which were supported and are now co-funded with CR-UK. There was a disappointing response to this initiative, in part due to the lack of therapeutics in development.

- Over the past 2 years, from November 2008 to July 2010, CTAAC has terminated funding early for 8 studies due to poor accrual. The amount of money and time already committed to a study and the efforts made by the investigators to 'rescue' the trial is considered by the Committee.
- The newly-established CR-UK Children's Cancer Trials Team at the University of Birmingham became fully operational as of 1st April 2010, and has already won support for five new trials (three funded by CR-UK).
- The future funding of the two recently-established adult CR-UK Clinical Trials Units in Liverpool and Southampton has been agreed.
- A review of CR-UK support for the European Organisation for Research and Treatment of Cancer (EORTC) resulted in continued support. Efforts continue with the EORTC to overcome legislative hurdles through-out Europe and to increase joint working.
- An analysis of the level of support from pharmaceutical companies illustrated that for 63% of trials, the various Chief Investigators had leveraged financial support from 23 different companies.

#### **Future plans, challenges and opportunities**

- **Facilitating long-term follow-up:** We have begun receiving applications to fund the long term follow-up of a number of breast cancer trials; to date the most expensive application we received was for £1million over 9 years. We have established a CR-UK Data Standards & Information Systems Working Group that includes representatives of our Clinical Trials Units, and are liaising with the broader group of NCRI CTU Heads on the use of a standard long term follow-up form. This could reduce the burden on both staff in Networks and on the CTAAC budget. Discussions with NCIN are underway to explore the collection of this data within the National Cancer Data Repository (NCDR).
- **Innovative trial designs/large scale trials:** The multi-arm, multi-stage (MAMS) design allows researchers to assess multiple therapeutic approaches simultaneously by using an intermediate assessment of outcome. This design increases the chance of a single trial providing a positive result and saves time and potentially money compared to separate sequential trials. CTAAC funds several trials of this design, including STAMPEDE in prostate cancer. We anticipate an increasing number of studies using innovative designs, such as MAMS or Bayesian adaptive designs; Professor Max Parmar (Director of the MRC Clinical Trials Unit) and Dr Emma Hall will be speaking to CTAAC on 'Complex trial designs' in Spring 2011. Once the process for continual assessment of the drugs being introduced/discarded during the lifetime of a trial have been developed, we will work with our CTU statisticians to promote CR-UK's inclusive approach to innovative trial designs at national and international meetings. Specifically, we are exploring hosting a workshop at the NCRI Cancer Conference in November 2011. A paper will be discussed at SEB in April 2011.
- **Stratified medicine:** The clinical community currently face the dilemma of whether to design 'smarter' trials using molecularly targeted drugs *in selected groups of patients*, or to evaluate targeted agents *in a broad population* and rely on retrospective analysis to determine those groups who benefit, who may not always be the same population as expected. We are undertaking a project to determine the likely cost, volume and design of biomarker-driven trials (BDTs) that will be submitted to CR-UK for funding. This project will feed into the planned review of Funding Committees during 2011.
- **Extensions:** Between 2007 and 2009 less than 20% of the new money available to CTAAC was spent on funding extensions to existing grants. In 2010, over 50% of the new money available to CTAAC has been spent on funding extensions to existing grants. The number of trials supported by CTAAC increased dramatically

from 2002 onwards, and we now know that it takes almost 2 years to get the first patient onto a trial. It is therefore feasible that the number of extension applications will peak over the next 2-3 years and then decrease as the CTAAC portfolio changes to include more feasibility studies, for which extensions are not given.

- **Astra Zeneca /NCRN Initiative:** This is a partnership that gives NCRN access to promising novel drugs for early and phase II trials in areas of opportunity/unmet need. Eighteen studies have been supported in 14 tumour types involving drugs from the AstraZeneca (AZ) pipeline that would not have been pursued in these tumour types otherwise. The majority of these studies are in tumours classed as rare tumours.
- **International Trials:** As many common cancers are increasingly being re-classified into sub-types of rarer cancers, there is an increasing need for international collaboration. In October 2009, Harpal Kumar and Kate Law joined a UK delegation led by Dame Sally Davies (DH) to the US National Cancer Institute (NCI) to explore the potential for collaborations around trials in rare and lethal tumours and patient sub-populations. An international initiative is being set up between the UK, supported by the British Embassy in Washington, the EORTC and the NCI, which aims to increase collaboration between the UK and other countries. A CR-UK International Liaison Officer has been appointed to facilitate this initiative and is driving forward progress on behalf of the international leaders involved. In January 2011 we presented to MEPs attending the Forum Against Cancer Europe (FACE) Workshop on Rare Cancers, that aimed to highlight the need for policy on rare cancers.
- **Trial Start-Up Times:** As part of a project evaluating the impact of the new Co-ordinated System for Permissions, baseline data on the time taken to set up trials demonstrated that it took a median of 621 days from funding committee decision to the first patient entering a trial. We are analysing the processes the Clinical Trials Units have to undertake before submitting studies for regulatory approval, including Host Institution approvals, finalising contracts, liaison with remote Chief Investigators, staff recruitment, obtaining patient approval, to determine how CR-UK might influence these processes and reduce the delay in study start-up. Reducing start-up times is a major objective for 2011.
- **Excess treatment costs:** We support the recommendation of the AMS Review on the regulation of health research that 'the forthcoming re-organisation of NHS commissioning arrangements provides an important opportunity to improve the provision of Excess Treatment Costs and remove the current difficulties' around the definition and allocation of research costs for non-commercial research. We will continue to work with the Department of Health to embed health research as a core function of the NHS. If accepted, this would reduce the concerns relating to treatment costs. However, there is little sign of these recommendations being implemented at present.

## 2.2 Realise new opportunities

### 2.2.1 Early detection and diagnosis

The 2007 Cancer Reform Strategy identified earlier diagnosis of cancer as crucial to further increasing survival and decreasing mortality due to cancer. Early diagnosis has previously not been a major area of investment for CR-UK in comparison with basic biology and clinical research (see Figure Two). Our strategy is to increase our investment in symptom awareness and early diagnosis and we co-lead the National Awareness and Early Diagnosis Initiative (NAEDI).

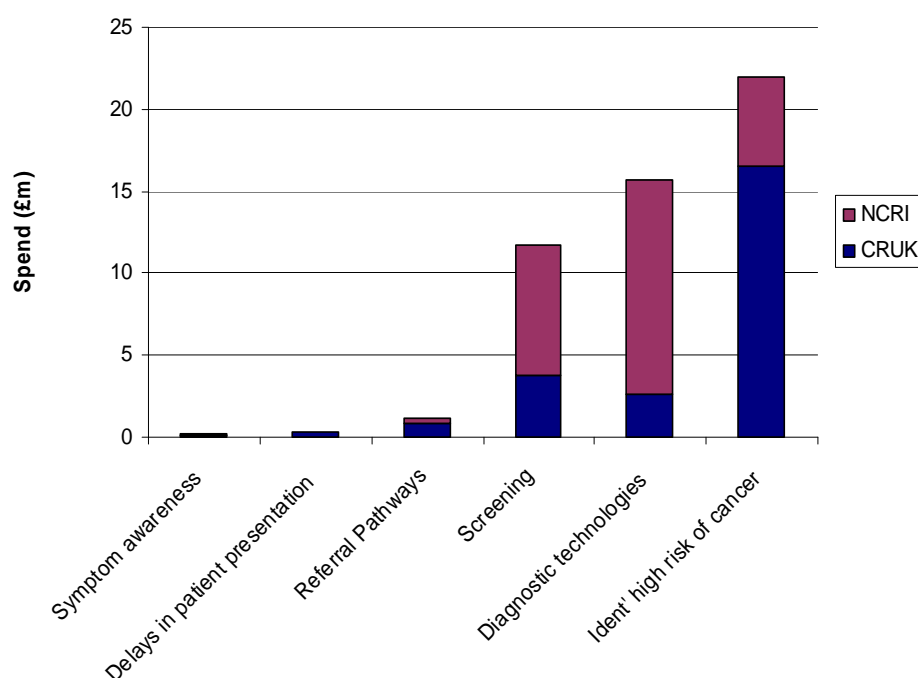


Figure Nine: NCRI and CR-UK annualised spend on early detection and diagnosis research (2007)<sup>5</sup>

### Progress to date

#### NAEDI Workstream 4: Research, evaluation and monitoring

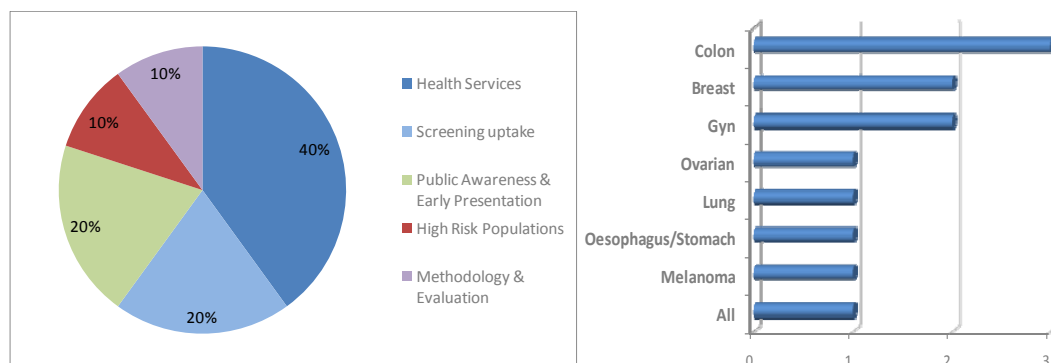
- A British Journal of Cancer supplement on early detection and diagnosis was published in December 2009, brought together by CR-UK working with the National Cancer Director. For the first time it comprehensively described the evidence base suggesting that late diagnosis contributes to poorer outcomes and showed some of the approaches being used to promote earlier presentation.
- In 2009/10 Cancer Research UK agreed to invest up to £5m in project grants through the NCRI/NAEDI Research Call, as part of a joint fund of up to £7.5m over five years<sup>6</sup>.
- CR-UK has managed the first call for project grants and pilot studies in the following areas: Targeting higher risk populations; Public awareness and reasons for late presentation; Health services; Methodology for, and evaluation of, early detection and awareness research.
- Of 61 Expressions of Interest, 49 were invited to submit full applications and in September 2010 the NAEDI Scientific Committee recommended 10 projects for funding (20% success rate, Full duration cost of approx £1.7 million). 70% of

<sup>5</sup> Editing note: data from last year's report – update not yet available from NCRI.

<sup>6</sup> NAEDI Funders to date: Cancer Research UK, Department of Health (England), ESRC, Scottish Government, Northern Ireland Health and Social Care R&D Office, National Institute of Social Care and Health Research (Wales)

projects have a 2 to 3 year duration. Projects were funded across the UK (with the exception of Northern Ireland).

- Of the funded projects, four focus on Health Services research with all of them proposing to design interventions to respond appropriately to symptoms as they present in primary care; two projects focus on screening uptake and determining the triggers for and barriers to screening behaviour; two focus on raising public awareness and early presentation; one focuses on High Risk populations; and finally, one focuses on methodology and evaluation of early detection and awareness interventions.



**Figure Ten: Distribution of funded projects by research area and disease site**

### The International Cancer Benchmarking Partnership (ICBP)

- The ICBP is working to identify the root causes of survival differences between countries/areas with comparable health care systems and high quality cancer data. Modules 2-5 of the programme are being managed by CR-UK, and several CR-UK Programme grant holders are involved; most notably Professor Michel Coleman leading on Module 1 comparing contemporary survival data, and Professor Jane Wardle, co-leading Module 2, which will analyse differences in population awareness, attitudes and beliefs about cancer, early diagnosis and screening. The ICBP should generate insights on policy and practice to help all partners improve cancer survival and mortality outcomes.

### Clinical trials

- In a breakthrough publication in May 2010 a trial of once-only flexible sigmoidoscopy screening in colorectal cancer led by Professor Wendy Atkins<sup>7</sup> reported a major impact of screening on colorectal cancer incidence and mortality. Subsequently we persuaded the Government to introduce flexi-scope into the national bowel screening programme; £60million will be invested in the latest bowel cancer screening technology over the next four years. Results indicate this could cut the number of cases of bowel cancer by a third and deaths from the disease by almost half (43 per cent) among those attending screening.
- In September 2009, just 6.5% of all National Cancer Research Network (NCRN) trials open or in set up were in screening, early detection or diagnosis.<sup>8</sup>

### **Future plans, challenges and opportunities**

- The first call for the NAEDI research workstream included a significant number of applications that contained good ideas, but failed because the committee were

<sup>7</sup> WS Atkin et al, Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. The Lancet, Volume 375, Issue 9726, 8 May 2010-14 May 2010, Pages 1624-1633

<sup>8</sup> Latest available data

not convinced that the proposed methodologies were robust. A research conference for NAEDI grantees held in February 2011 included engagement with some of the unsuccessful candidates.

- A second call for the NAEDI research workstream was launched in December 2010. It is similar in remit to the first broad based call with applications in the area of cervical screening and decision support systems being particularly encouraged. The committee meeting will be held in September 2011.
- There is no recognised process for the development of early diagnostic technologies, and this is an area that requires further investigation. Diagnostic companies do not have the same level of funding or IP protection as Pharma that would enable them to fund large studies in the same way that Pharma do.

### **2.2.2 Prevention**

Prevention is the most effective form of cancer control and, using the knowledge we gain from intervention studies and trials in prevention, we can devise practical strategies to help reduce the risk of developing cancer. In order to work towards our Goals, our prevention research must be strengthened in terms of quantity, quality and infrastructure. We stated in the Research Strategy that over the next five years, a significant proportion of our prevention research would be focused on medical intervention studies, such as research in primary or secondary chemoprevention, vaccines, and in identifying and monitoring people at high risk. We also stated that we would only fund research into prevention interventions with a significant benefit for other major diseases (eg obesity, alcohol) in partnership with other funders.

#### **Progress to date**

##### National Prevention Research Initiative (NPRI)

- The NPRI is a national initiative made up of government departments, research councils and major medical charities that are working together to encourage and support research into chronic disease prevention. Its core aim is to develop and implement successful, cost-effective interventions that reduce people's risk of developing major diseases by influencing their health behaviours.
- To date, the first three phases of NPRI have supported 55 research projects with a combined commitment of £23 million on behalf of 16 funding partners (including approximately £10 million awarded for Phase III in July 2008).
- For the first three phases, most of the NPRI's work focused on alcohol, obesity and exercise. In Phase III, three out of 16 awards were smoking related.
- Phase IV was announced in September 2010 and the partnership has been expanded to include the Wellcome Trust. The call invites cross-disciplinary research which develops or tests interventions that can potentially have a major impact on population health, using the full range of evaluation methods, including experimental and quasi-experimental (or observational) designs and natural experiments. Research funded through the Call will be translational in the sense that it must be relevant to, or directly impact on, policy and/or practice.

##### UKCRC Public Health Centres of Excellence (UKCRC PHCOE)

- Following recommendations from a UK Clinical Research Collaboration report, "Strengthening Public Health Research in the UK" the UK Clinical Research Collaboration created five centres of excellence in public health research to strengthen the field in the UK by bringing leading research experts together with practitioners, policy makers and wider stakeholders.
- The annual reports of all five UKCRC PHCOE's were approved by the Funders Group in July 2010.

- A mid-term review was carried out at the Newcastle Centre in July 2010 further to an original condition at the time of the award. CR-UK was represented on the site visit party and the Centre successfully passed the mid-term review.
- A joint meeting of the Centre Directors and Funders Group was held in July 2010. Further plans were made for closer interactions between the Centres and the Funders Group.

### **Infrastructure**

- Network support (NCRN etc.) has been identified as an issue for trials in screening and prevention as, except in the case of secondary prevention, high risk groups are not seen in cancer clinics. Network support for accrual to screening and prevention trials should be facilitated through the recently established Comprehensive Local Research Networks. The initial bid for an NCRN Deputy Director for Screening and Prevention was turned down by the Department of Health. A subsequent re-submission was also unsuccessful.

### **Trials**

- There are few candidates for primary chemoprevention. Key candidates at the moment are vitamin D, aspirin and metformin for which a number of pilots are either planned or underway. CR-UK is likely to be involved in all of these.
- In secondary chemoprevention, CTAAC has supported the long term follow-up of patients in the aTTom trial. The findings of this and other trials demonstrated that the use of tamoxifen beyond 5 years reduces recurrence; new funding will fully evaluate whether there is a cancer-specific survival advantage following 10 years of follow-up.
- Aspirin is still under consideration for the chemoprevention of colorectal cancer. A meeting will be held in May to consider the current data and identify whether there is a need for further research.

### **Tobacco control**

While there have been some key successes in tobacco control in recent years, most notably legislation to make all work and enclosed public places smokefree, one fifth of the population still smokes and over a quarter of all cancer deaths are caused by tobacco. So the ability to support research, through the Tobacco Advisory Group (TAG), that provides evidence for the effectiveness of policies and rebuts the falsehoods propagated by the tobacco industry remains of paramount importance.

- TAG continues to support key groups. ASH, which is co-funded by CR-UK, BHF and the Department of Health, produces a range of timely research, the most recent being a series of analyses showing that tobacco control policies are highly cost effective.
- CR-UK's Centre for Tobacco Control Research (CTCR) runs the Youth Tobacco Policy Survey which tracks young people's exposure and attitudes to tobacco and industry tactics to target them. In 2009 Professor Hastings, Director of the CTCR, received an OBE in recognition of his contribution to the field of social marketing.
- TAG also supports the research coordinator for the UK Centre for Tobacco Control Studies (UKCTCS), one of the five UKCRC Public Health Centres of Excellence. It has succeeded in attracting considerable additional funding for research that is addressing key issues in the field as well as supporting numerous fellowships and studentships.
- The original research in the major Royal College of Physicians report "Passive smoking and children" was funded by TAG. The report updated the epidemiology on the harms caused to children by secondhand smoke and estimated that up to 25,000 children start smoking every year in the UK as a result of exposure to

smoking in the home, showing that the best way to prevent youth uptake is for adults to quit or not to smoke in front of children.

- ASH Scotland was funded to prepare 2 reports, one on the content of a comprehensive tobacco control strategy for Scotland, and the second to detail industry interference in recent legislation
- TAG-funded research, as part of our EU Smokefree Partnership, revealed the extent of tobacco industry involvement in the Better Regulation agenda, as a result of which economic impact is prioritised over health and environmental considerations. The report, by industry document researcher Professor Anna Gilmore of Bath University, was presented at a high profile event in the European Parliament.
- TAG reports have on several occasions played a vital role in campaigning for key tobacco control measures: for example an evaluation of the removal of point of sale displays in Ireland by Professor Ann McNeil, Nottingham University, which countered misinformation from the tobacco industry, was presented to Ministers and in Parliament.

### **2.2.3 Imaging**

Following a comprehensive review of imaging in 2008, CR-UK launched a new strategic initiative in partnership with the Engineering and Physical Sciences Research Council (EPSRC). The aim of the initiative is to significantly enhance the level of cancer imaging research in the UK and to improve the integration of cancer imaging activities. This initiative has received additional contributions from the MRC and the National Institute for Health Research (NIHR), resulting in an investment of over £50 million over 5 years. Four Cancer Imaging Centres (Imperial, KCL/UCL, ICR and Oxford) and five Cancer Imaging Programmes (CCLG in Birmingham, Royal Surrey Hospital, Newcastle, St Andrews and Sheffield) have been established.

#### **Progress to date:**

- The Cancer Imaging Review Group (CIRG) was established in 2010 to review progress of the Cancer Imaging Centres and Programmes on an annual basis. In the first review, that took place in March 2010, the work of the four Imaging Centres was positively received. The second review will take place in April 2011.
- Following feedback from the CIRG, CR-UK has facilitated two meetings between members of the Cancer Imaging Programmes/Centres to investigate methods to integrate biomarkers from different imaging platforms (PET, MRI, ultrasound etc) in a common imaging space. In the second meeting (October 2010), a number of representatives from software development companies were invited in order to evaluate what industry can offer for the biomedical informatics needs of the academic imaging community. A follow up meeting in February 2011 will explore how to take this forward (finalise needs and explore funding sources).
- The inaugural annual cancer imaging conference was held in Oxford in March 2010. The conference was open to groups outside the CR-UK/EPSRC/MRC/NIHR imaging initiative and aimed to support integration and facilitate networking between UK imaging groups. The conference was oversubscribed and the feedback from attendees was extremely positive; attendees felt that this was the only conference of its kind in the UK that brings together the imaging community and covers diverse modalities in preclinical and clinical research. The next conference is organised by the ICR Cancer Imaging Centre and will take place on 12<sup>th</sup> April, 2011.
- CR-UK has held discussions with the NCI to explore ways to create common resources and drive a consensus on validation methods and related quantitative imaging standards. A number of collaborations have been set up as part of this

initiative including a recent publication in Neoplasia (<http://www.neoplasia.com/pdf/manuscript/v13i02/neo101102.pdf>).

- A joint proposal was submitted to the Innovative Medicines Initiative (IMI) call by EORTC, CR-UK and the European Association of Nuclear Medicine (EAMN). The assembled applicant consortium consists of 12 academic partners, including 5 from the UK (Imperial College London, Kings College London, Cambridge Research Institute, Manchester, Institute of Cancer Research) and eight industry partners, including Astra Zeneca, GSK, Pfizer and Roche. The consortium was ranked first by the EU and was successful in obtaining funding with a budget of 14m euro. The project will validate three imaging biomarkers of tumour cell proliferation, apoptosis and necrosis and is expected to commence in April 2011.

#### **Future plans, challenges and opportunities**

- We will continue work to ensure that the Imaging Centres & Programmes are fully integrated with the broader imaging community in the UK (e.g. NCRI-PET initiative, Experimental Cancer Medicine Centre (ECMC) Imaging group, other imaging groups). A number of investigators from the Cancer Imaging Centres and Programmes are involved with the EORTC imaging Group, the NCRI PET initiative and the ECMC Imaging group.
- We will work with the ICR to organise the second annual Cancer Imaging Review Group and the associated Cancer Imaging Conference that will take place in April 2011.
- We will work closely with the Cancer Imaging Centres and Programmes to facilitate development of common bioinformatics tools for integration of imaging biomarkers in a common space.
- We will continue to work closely with the NCI and EORTC and strengthen plans for international collaboration.
- CR UK is in discussion with the Canadian Institute of Health Research and the NCI about a potential tripartite initiative to support cancer imaging. A workshop with scientists from the three countries, hosted by the Canadian High Commission in London, is planned for June 2011 to explore areas of potential mutual interest.

#### **2.2.4 Biomarkers**

Biomarkers have the potential to improve outcomes for patients in several ways including better diagnosis, screening, prognosis and stratification of treatment. Our strategy for biomarker research is to focus on establishing and facilitating a clear pathway for the discovery and development of all types of biomarkers.

A new funding stream dedicated to the support of biomarker research was established (Biomarkers and Imaging Discovery & Development – BIDD). In addition, a set of clear pathways (roadmaps) for the discovery and development of all types of biomarkers (risk/predisposition, diagnostic, prognostic/predictive, pharmacological/surrogate response) were created and launched to the scientific community in April 2009. In the past year, our efforts have continued to implement the recommendation of the strategic review and coordinate our portfolio of biomarker research.

#### **Progress to date:**

- The BIDD portfolio has been categorised and analysed by disease type, analytical technology and marker type and “mapped” to the biomarker roadmaps.
- Although to date there has been little demonstrable progress of projects along the roadmap (the vast majority of awards are in BM Discovery Stage 2 where the relationship between the biomarker and the clinical outcome is studied

retrospectively), this reflects the fact that BIDD is a young committee, and progress in this area of research is typically slow.

- Historically, the biomarker portfolio has been dominated by predictive biomarkers (51% of all awards made since the establishment of the former TRICC committee) as the vast majority of awards were tied to CTAAC-type clinical trials. Since the establishment of BIDD, the portfolio is no longer so closely tied to late-phase clinical trials and as a result there has been an increase in other types of biomarker.
- A poster of the roadmaps was presented at the 4th AACR “Molecular Diagnostics in Cancer Therapeutic development” meeting in September 2010.
- CR-UK led a pan-European academic consortium as part of the Framework 7 IMI on Molecular Biomarkers. The focus for this expression of interest was on pharmacological and predictive biomarkers. An “Expression of Interest” (EoI) was submitted in February 2010, but was unsuccessful.

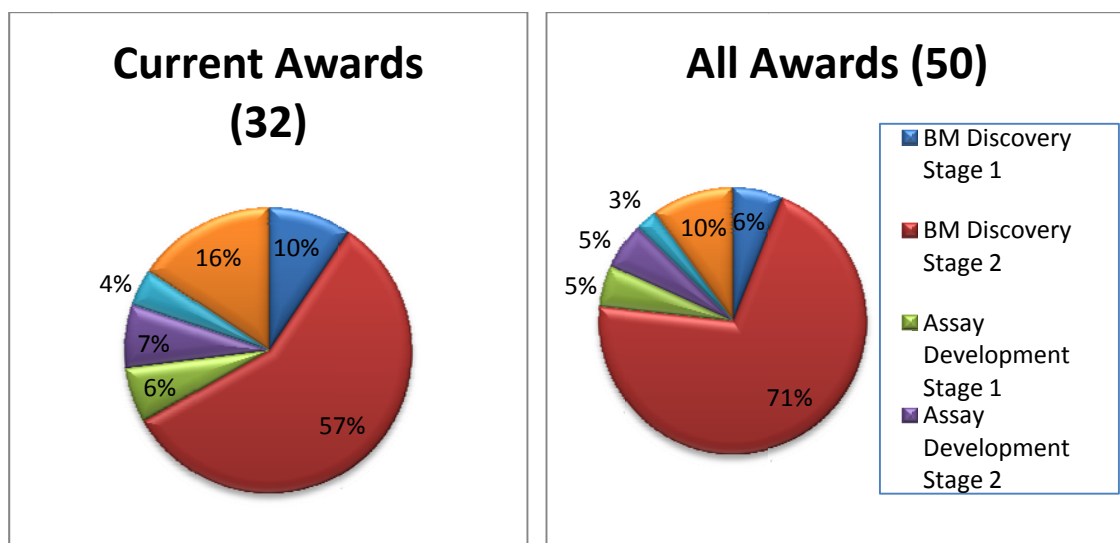


Figure Eleven: BIDD portfolio by biomarker stage.

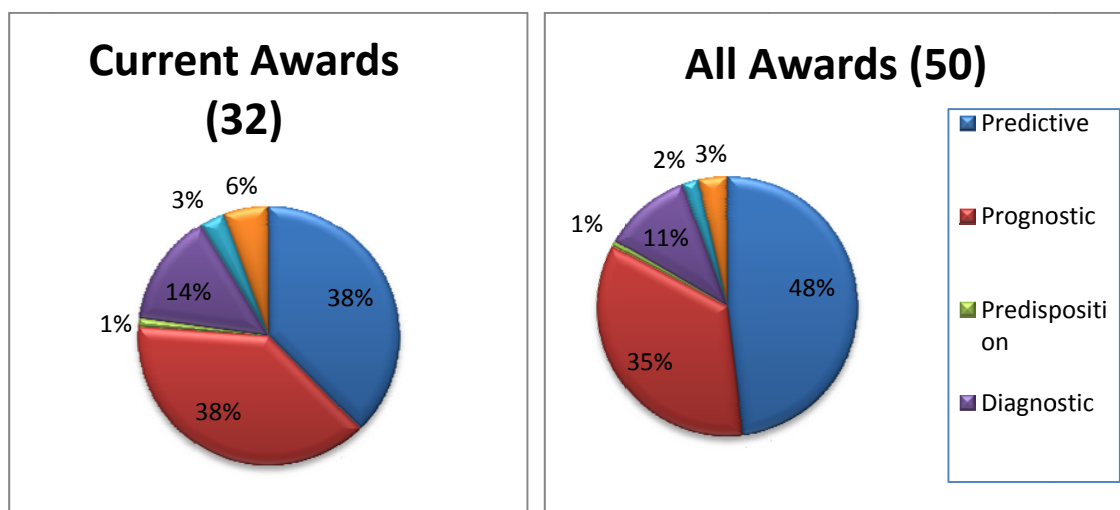


Figure Twelve: BIDD portfolio by Biomarker type

**Future plans, challenges and opportunities:**

- We have seen a 100% increase in the number of outline applications submitted to BIDD during 2009/10 (37 outlines submitted in 2009, 74 outlines submitted in 2010 over 2 funding meetings) and a 43% increase in the number of full applications submitted in the same time frame (21 full applications submitted in

2009, 30 full applications submitted in 2010 over 2 funding meetings). This has led to an increase in fundable projects beyond the capacity of the allocated budget. We are therefore proposing to increase the BIDD budget by 30% in 2011/12 to reflect the increase in demand.

- Categorisation of biomarker studies according to the biomarker roadmaps will need to be extended beyond BIDD to the rest of the CR-UK portfolio.
- Qualification of biomarkers in prospective clinical trials is an area that requires attention. Funding routes and budgets for such studies will need to be identified and agreed.
- A very high number of Expressions of Interest for Biomarker programmatic funding were submitted to CTRC resulting in a high number of outline applications. Given the linear process of biomarker development dictated by the roadmaps, an agreement on what constitutes a biomarker programme as opposed to a number of BIDD projects grants needs to be reached. It is anticipated that the review of the Funding Committees structures will look into the overlap of CTRC and BIDD.
- We will continue to work with academia, pharma and regulatory authorities through the establishment of joint consortia for the development of biomarkers.
- Sixteen of the 32 applications to CTRC are entirely biomarker programme applications (see section 2.2.9).

### **2.2.5 Model systems**

To improve the efficacy and efficiency of the drug discovery process we aim to develop models which more accurately recapitulate human disease and hence can help us evaluate the potential efficacy of novel cancer treatments more effectively. The combination of these new models with modern developments in imaging and biomarker methods offers a real chance to improve the predictability of the human response to new treatments. Furthermore, such models may also offer an appropriate platform to study combinations of drugs which will be a critical component of developing broadly effective cancer treatments.

### **Progress to date**

- In 2009 we facilitated the recruitment of Gerard Evan to the Chair of Biochemistry at the University of Cambridge, which he took up at the beginning of October 2009. This year he successfully applied for programme grant funding from CR-UK.
- Four Cancer Research UK Centres (Cambridge, Cardiff, Manchester and Glasgow) have identified laboratory models as a particular focus. In addition UKCMRI and LRI will have a major focus on laboratory models, and the BICR is building a new biological resources unit.

### **Future plans, challenges and opportunities**

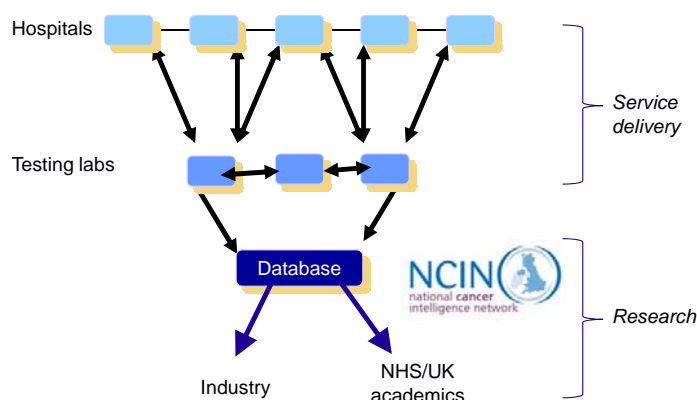
- In 2010, a consortium, consisting of Gerard Evan (Cambridge), Anton Berns (NKI), Mariano Barbacid (CNIO), Doug Hanahan (ISREC, Switzerland) and Daniel Louvard (Institut Curie, Paris) was established to apply for Innovative Medicines Initiative (IMI) funding under the Target Validation call. Unfortunately despite great enthusiasm from the consortium the IMI bid was not successful.
- The remit for a workshop on laboratory models convened to build on the successful collaboration of investigators brought together for the Target Validation IMI call is being discussed with the new Chief Scientist. At this time there are no plans for additional CR-UK funding.

## 2.2.6 Stratified Medicines

Government, charity and commercial organisations have formed a partnership to help the UK health service adopt new targeted therapies, as well as making the UK a better place for stratified medicines research.

The vision of the Stratified Medicine Programme is a national molecular diagnostics service delivering high quality, cost effective tests for patients, with routine consent for the collection, storage and research use of population-scale data including genetic, treatment and outcomes data.

### A workable model for stratified medicine in the NHS combines service delivery with research



7

### Figure Thirteen: A Model for stratified medicine in the NHS

During the pilot phase, the programme will designate three laboratories, two NHS and one private, as the technology hubs to run the genetic tests. This will allow the greatest level of centralisation as well as allowing quality assurance and peer review across the sites. The main focus of the hubs will be to deliver high quality, cost effective testing within clinical turnaround times.

Six hospitals from the ECMC network will collect samples from breast, ovary, lung, prostate, melanoma and colorectal cancer patients. Other hospitals who pass the programme's inclusion criteria will be held in reserve in case the initial six hospitals cannot supply sufficient samples, or if the programme has spare capacity.

### Progress to date

- Five work-streams each with an Advisory Group, (Research & Clinical, Technology, Informatics, Service Delivery and Funding), addressed the relevant issues and developed appropriate implementation plans culminating in the production of a detailed report which was approved by SEB in September and also provided to the Technology Strategy Board (TSB) and other partners.
- Pfizer and Astra Zeneca signed agreements with Cancer Research UK in December 2010 to support the programme, which has a budget of £5.5 million.
- The TSB committed £5.6 million to support commercially led research that will support the aims of the CR-UK Cancer Stratified Medicine Programme and on 12 October 2010 David Willetts (Minister for Universities and Science) announced that this will be part of a five year, £50 million investment in a new Stratified Medicines Innovation Platform to develop stratified medicine in the UK. CR-UK is on the programme board of this Innovation Platform and we believe that cancer is likely to be the focus of the next £10m funding round.
- Calls for proposals were issued on 25<sup>th</sup> January inviting ECMCs to bid to become "Clinical Hubs" to collect samples and inviting genetic testing laboratories to bid

to become “Technology Hubs”. The first 6 Clinical Hubs and 3 Technology Hubs will be selected in the summer 2011.

- Phase 1 will collect up to 9,000 samples and test them for a broad panel of mutations within clinical timeframes to demonstrate a possible service model, as well as storing and linking genetic and NHS routine datasets on these patients.
- Phase 1 will also enable pre-stratified cohorts of patients to be entered for clinical studies.

#### **Future plans, challenges and opportunities**

- It will be important to ensure that the companies funded by the TSB to develop panel testing of genetic mutations work closely with the technology hubs to validate their tests for use in the NHS.
- During Phase 1 we need to put in place all the processes for a smooth transition into a national UK service. We have support from Paul Burstow (Minister for Cancer), David Willets (Minister for Science), Mike Richards (NCD Cancer), Ian Barnes (NCD Pathology), and Sally Davies (acting CMO) and hope to leverage this during handover to the NHS in 2013.
- A key challenge will be the interaction with routine service provision: does the CR-UK testing require additional biopsies, and how will the gene panel test interact with existing services such as EGFR and KRAS?
- We have not yet established the best role for the charity and the partnership beyond Phase 1, and are considering this.
- The programme is based on our confidence in the increasing number of stratified medicines approved in the UK. If no further stratified medicines are approved, national rollout is likely to be delayed.

#### **2.2.7 International Cancer Genome Consortium**

In 2009 CR-UK indicated its intention to invest in the International Cancer Genome Consortium (ICGC), with a specific focus on oesophageal adenocarcinoma and prostate cancer. ICGC aims to obtain a comprehensive description of genomic, transcriptomic and epigenomic changes in 50 different tumour types and/or subtypes which are of clinical and societal importance across the globe. Each project aims to analyse a minimum of 500 cancers and 500 control samples. Over 20 projects are now listed on the ICGC website, although not all of these have yet commenced.

#### **Progress to date**

- Following a call for proposals during 2010, CR-UK has agreed to fund two ICGC projects. The project in oesophageal adenocarcinoma will be UK based and led by Dr Rebecca Fitzgerald in Cambridge and funded in its entirety by CR-UK, whilst the prostate cancer project will be funded jointly by CR-UK, Prostate Cancer Canada, the Ontario Institute for Cancer Research and also potentially by INCA (France).
- An invitation to tender was published for organisations interested in supplying sequencing services to CR-UK, in particular to carry out the whole genome sequencing required for the ICGC projects. Eleven organisations responded and five were invited to present to the panel. The top two organisations agreed to take part in a test of their service at their cost; data was provided in mid-January on a triplet of samples from each tumour type. We are waiting for the comparison of the data quality from the lead bioinformaticians and expect to have identified a supplier by mid-February.

#### **Future plans, challenges and opportunities**

- The initial funding for the oesophageal project is for an extended pilot project in which the effect of pre-treatment by chemo-/radio-therapy will be assessed. The timetable for a review of the pilot and consideration of funding for the full project is being finalised.
- The review panel recommended that we ensure as much synergy as possible between the two consortia so that they share solutions to common issues, such as data storage, collection logistics etc. We will need to ensure that we maintain a close working relationship between the consortia and CR-UK.

### **2.2.8 Genomics**

The past decade has seen genomics contribute fundamental knowledge about biology and its perturbation in disease. Genome studies of the genes and pathways associated with disease-related traits require comprehensive catalogues of genetic variation, which provide both genetic markers for association studies and variants for identifying candidate genes. Through our previous funding of Genome Wide Association Studies (GWAS), we made a major contribution to identifying genomic loci associated with several different cancers. Technology development drives genomic research and has led to huge interest in throughput and reduction in costs of DNA sequencing. The cost of whole genome sequencing (WGS) is fast approaching a threshold at which this approach will be the most cost effective to answer a variety of clinical and biological questions. CR-UK is seeking to enhance its investment in genomics by increasing access to whole genome/exome sequencing using next generation sequencing (NGS) technology. We propose to provide our scientists with rapid, cost effective access to NGS services from a third party supplier.

#### **Progress to date**

- SEB has agreed that the scientific rationale for increasing CR-UK's investment in genomics is compelling and that a strategic investment would be likely to put CR-UK in a world-leading position in the application of this technology.
- A call for proposals was issued on 17<sup>th</sup> January 2011 to CR-UK core-funded Institutes and Centres. Proposals will undergo scientific review by BIDD in June 2011 and the prioritised list will then be considered by SEB which will make the final funding decisions.

#### **Future plans, challenges and opportunities**

- To date no new money has been set aside for this initiative. The Call has been operated by a new mechanism, no information has been issued about how much funding may be available; this will allow SEB to make a decision based on the quality of the scientific proposals.
- We aim to run a second call in 2012.

### **2.2.9 CTRC Programme Grants**

In October 2010, SEB approved the launch of a major new funding scheme for clinical and translational programmatic research through CTRC from 2011. This scheme is intended to bridge the gap in programmatic funding for clinical and translational research that does not fit into the remit of the BSC, including research areas of strategic priority such as surgery and radiotherapy. Given the current CR-UK strategic initiatives in drug discovery and imaging, new applications in these areas will not be considered until 2013.

This funding scheme is designed to fund innovative translational research to drive scientific discoveries with clearly identifiable clinical outputs, such as clinical trials,

novel screening procedures, novel diagnostic tools, novel radiotherapy techniques, or any other relevant clinical applications. Thirty two outline applications will be reviewed by the CTRC in March 2011, with up to 4 programmes being awarded funding in the Autumn.

### **2.2.10 Other New Opportunities**

With an increasing move towards large scale science, it is more important than ever to invest in and foster collaborations in the UK and across the world. We continue to be involved in many ongoing partnerships and collaborations and a number of new opportunities highlighted last year have seen significant progress.

#### **Progress to date**

- Updates on progress with new opportunities reported in 2009 are provided in other sections of this report (stratified medicine (section 2.2.6), ICGC (section 2.2.7), links with the EORTC Imaging Group and an application for Innovative Medicines Initiative (IMI) funding for imaging biomarkers (section 1.7), NCI collaborations in trials of 'rare and lethal' tumours (section 2.1.5 (late phase)).
- Two other collaborative Expressions of Interest to IMI (in animal models and biomarkers) were not successful.

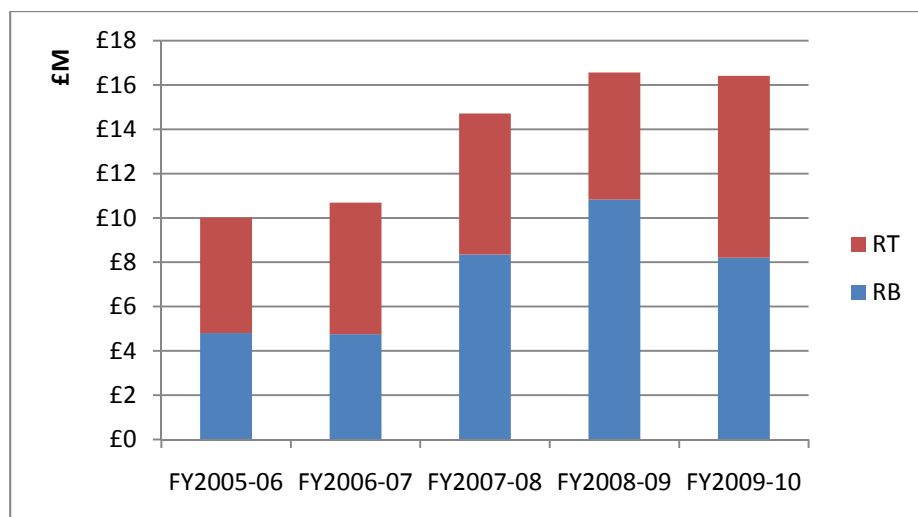
#### **Future plans, challenges and opportunities**

- In February 2010 the International Human Epigenome Consortium (IHEC) was launched. As its first phase, the consortium plans to map 1,000 reference epigenomes within a decade. CR-UK is working with other NCRI or UK partners to maintain a dialogue with the consortium. It is anticipated that commitment to ICGC funding will naturally lead to an expansion of investment in epigenomics.
- We are considering how to develop the next phase of engagement with cancer research in China, building on relationships developed through current interactions including our programme of fellowships for Chinese post-doctoral scientists.

## **2.3 Building capacity**

### **2.3.1 Radiobiology and radiotherapy**

It is estimated that half of all cancer patients require radiotherapy at some point in their care pathway, to either treat the disease or alleviate symptoms of advanced cancer. Over the past five years CR-UK has invested heavily in radiotherapy and radiobiology research. Our strategy is to revitalise radiotherapy and radiobiology research by supporting the Gray Institute for Radiation Oncology and Biology (GI-ROB) in Oxford and strengthening activity in other places. As shown in Figure Thirteen our spend on radiobiology has more than doubled since financial year 2005-06, with our spend on radiotherapy largely being maintained.



**Figure Fourteen: Radiotherapy and radiobiology measures**

The figures include all funding at the Gray Institute in Oxford. The COMARE (Committee on Medical Aspects of Radiation research in the Environment) definition of radiation biology is used. Radiotherapy research includes related imaging awards and a proportion of the spend at Cancer Imaging Centres. Please note that despite the fact that the absolute spend has declined slightly in 2009-10, the percentage of funding relative to the whole portfolio has actually increased slightly.

### Progress to date

#### Gray Institute for Radiation Oncology and Biology (GI-ROB)

- The Gray Institute for Radiation Oncology & Biology (GI-ROB) is now the largest centre for radiobiology research in the world, housing more than 200 basic and clinical scientists.
- Preclinical imaging facilities at GI-ROB are now fully commissioned. These include the housing of CT-PET, CT-SPECT, ultrasound, MRI (4.3T, 7T and 9.4T), visible and near infrared light imaging and both confocal and multiphoton imaging. These imaging facilities are coupled with a wide range of experimental radiation sources that can be used for irradiation, including ultrasoft and orthovoltage X-ray sets, 6MeV pulse electron linear accelerator, <sup>137</sup>Cs gamma-irradiators, <sup>238</sup>Pu alpha-particle irradiator and access to the <sup>60</sup>Co gamma-ray facility on the MRC Harwell site. A small image-guided x-ray irradiator is also being purchased.
- The GI-ROB underwent a successful Interim Review in June 2009. The facilities were considered to be state-of-the-art and were well managed.
- The major challenge for the Institute was considered to be building presence in the clinic in Oxford and to establish early phase clinical trials activity within clinical oncology.
- Training the next generation of radiation oncology and radiobiology researchers is an essential part of re-invigorating this academic discipline. A Masters course covering all aspects of radiobiology is now in its second year. Clinical and non-clinical DPhil courses are now well established with 8 and 43 students respectively.
- Over the past 18 months there has been significant restructuring within the Oxford Radcliffe Hospitals NHS Trust which has enhanced the service-academic interface and will facilitate the translational ambitions of GI-ROB over the next few years.
- Tim Maughan has moved from Cardiff to the GI-ROB as the Clinical Director and one of his main roles is to organise and improve service provision in radiotherapy.

- GI-ROB has now opened its first radiotherapy trials to recruitment and, as a result of this interaction with the NHS Trust, for the first time in Oxford, patients have been treated with highly conformal radiotherapy, image-guided radiotherapy (IGRT), intensity modulated radiotherapy (IMRT) and intra-arterial brachytherapy (selective internal radiotherapy).

#### Centres

- Radiotherapy and radiobiology have been identified as a strategic focus for 5 Cancer Research UK Centres - Belfast, Liverpool, UCL, Manchester and Oxford.
- The UCL Cancer Research UK Centre core award will support an academic radiotherapy research programme to be led by a new Professor of Radiotherapy funded by the University.
- The Leeds Cancer Research UK Centre will establish an academic unit in Clinical Radiology (imaging) and appoint a Chair in Radiation Oncology.
- The Cancer Research UK Centre in Belfast will employ medical physicists alongside clinicians and scientists to develop an extensive programme in radiation oncology.
- The Liverpool Centre is particularly strong in experimental cancer radiotherapy, and will form a research hub linked to other University research departments, the cancer treatment centre and also to strong cancer units around Merseyside and Cheshire where some radiotherapy is delivered.
- Our University and industrial partners in Manchester will provide funding towards positions and infrastructure in radiation-related research.

#### Clinical and Translational Radiotherapy Research Working Group

- Supporting radiotherapy research is a priority for NCRI partners and has resulted in the establishment of the NCRI Clinical and Translational Radiotherapy Research Working Group (CTRad), initially led by Professor Tim Maughan and now led by Professor Tim Illidge, which is funded by CR-UK in partnership with others. The thrust of the new initiative is to maximise the opportunities for high quality radiotherapy research in the UK.
- Professor Tim Maughan, the CTRad Chair, has put out 2 calls for radiotherapy research proposals to be discussed and developed at open meetings. 29 proposals were received and given feedback in the first call and the second call is currently still open. Nine out of the ten studies finalised using this process have been submitted to CR-UK for support; 5 have been supported, 1 declined, 1 invited as a full application and 2 are in progress. Nine ECMCs (Leeds, ICR, Cambridge, Imperial, Manchester, Cardiff, Belfast, Sheffield and Liverpool) submitted proposals for the second call.
- The Chairs of the CTAAC, NAC and BIDD Funding Committees, along with representatives of the NIHR Health Technology Assessment Programme, received personal invitations to the CTRad Methodology Workshop held in May 2010. One of the aims of the Workshop was to build an understanding with research funders on the use and validity of approaches to technology evaluation other than randomised controlled trials. One output will be a position paper on research designs for evaluating radiotherapy technologies.

#### Radiotherapy trials

- Since April 2007, 34 early phase studies involving radiotherapy have been reported as using ECMC support, 11 of which involved radiotherapy as the primary purpose of the trial. Twelve ECMCs have reported participating in trials using radiotherapy, with eight Centres reporting trials where radiotherapy is the primary purpose.

- CTAAC has supported 5 new trials evaluating radiotherapy in four different cancers over the past year.
- Two phase I trials have been supported by the New Agents Committee (the DREAM trial and more recently the PARP CRT study); these studies are the first to have been issued with NAC grants, rather than being conducted by the Drug Development Office.

### Future plans, challenges and opportunities

- In the medium term, retirement of key experts in radiation physics may have a negative effect on research capacity.
- The GI-ROB will undergo a full review in 2011.
- We will develop a set of metrics to help monitor the impact of the CTRad on the CR-UK and national trials portfolio.
- A survey we carried out recently showed that public awareness of the importance of radiotherapy in cancer treatment is low. We are currently discussing with the Royal College of Radiologists and others how best to use this information to drive up capacity and standards of radiotherapy delivered to cancer patients.
- Programmatic funding for clinical and translational research will be made available in 2011, providing a new opportunity for applicants for radiotherapy-based research.

### 2.3.2 Surgery

Surgery continues to be the primary modality for the treatment and management of cancer. Research investment into novel surgical techniques is significantly outweighed by investment in biological and chemical therapeutics. We have recognised the need for increased and targeted research investment in surgical oncology and hope to build capacity through the mechanisms outlined below.

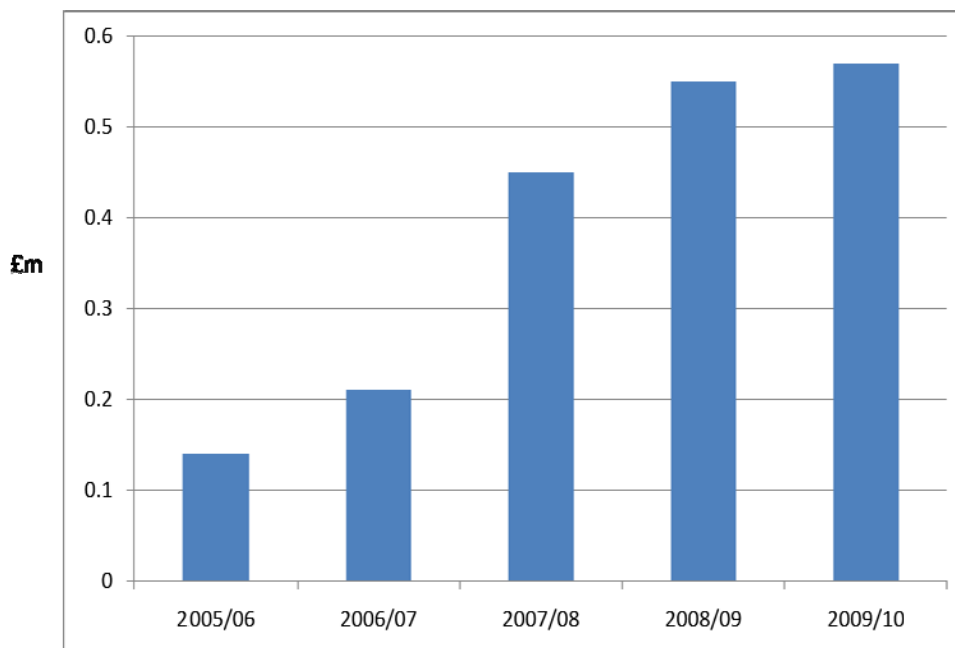


Figure Fifteen: Annual investment in surgery research.

This only includes research where development of new surgical techniques is the primary aim. There are other examples of surgeon-led research that are not included.

## Progress to date

### Ensuring surgery is a key focus in our Centres

- As we established our Centres, together with our partners we committed to providing additional support for surgery research, mainly in the form of senior salaries.

Centre	CR-UK	NHS Trust	University
Birmingham		✓	
Cambridge	✓		
Imperial	✓	✓	
Liverpool			✓
Southampton	✓	✓	
UCL		✓	

**Table One: Commitments to Invest in Surgery Research in a Centre.** The table indicates where CR-UK or a partner has committed to providing additional resource for surgical oncology research.

- As part of our commitment to invest in surgical oncology, funding has been made available for a series of three year post-doctoral research training positions. The scheme is to focus on producing cancer-specific surgical researchers capable of applying for personal awards following completion of the scheme. Applications were open to CR-UK Centres that had made surgery a significant component of their research strategy and were prepared to meet 50% of the support costs. Awards will be made to Cambridge (3 posts), Oxford (2 posts), UCL (1 post), Southampton (1 post) and Imperial (1 post).
- Surgery trials are classified as those studies having a surgery question as a primary endpoint. CTAAC has funded three new trials in the past year (one in head and neck cancer in November 2009 and two in renal cancer in 2010).

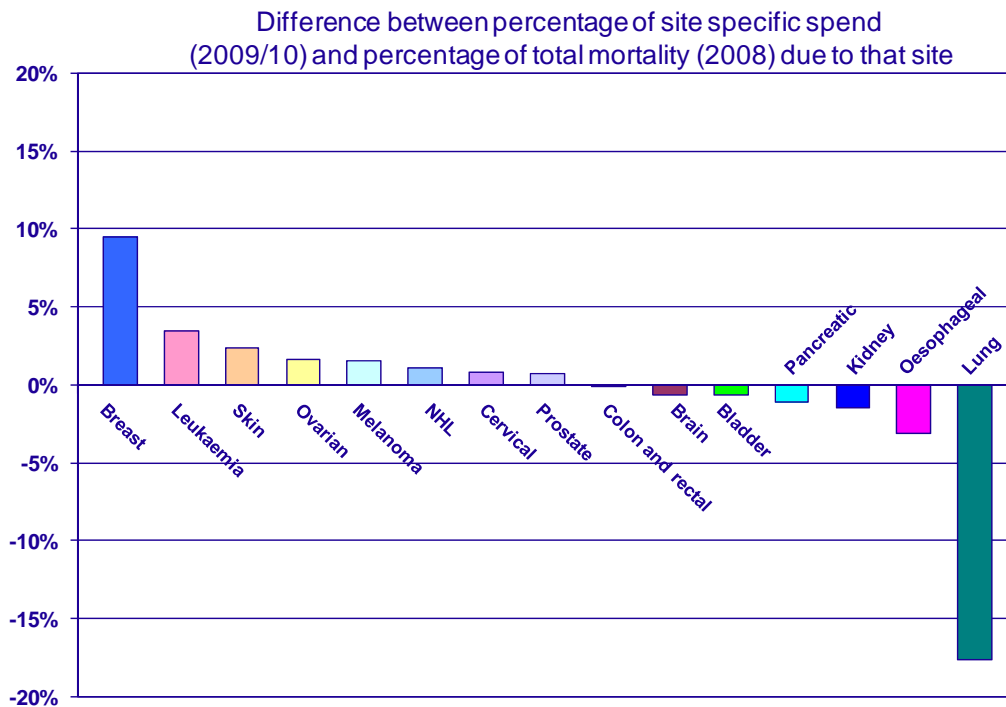
### **Future plans, challenges and opportunities**

- Professor Dame Sally Davies has established a NIHR Surgical Specialty Sub-Group (UKCRN Surgical Taskforce) to address the challenges related to surgery trials support within the NHS. This group is led by Professor John Scholefield with support in the cancer field from Professor Dion Morton.
- The Clinical Trials Team will continue to monitor the activities of this group and identify emerging opportunities for cancer trials, and the Vice-Chair of the Taskforce will lead a discussion on the issue with CTAAC.
- A surgical research collaborative has been established in the West Midlands region. CR-UK will explore with other partners whether this model can be expanded in order to grow surgical research activities in the UK.

### **2.3.3 Cancers with the highest levels of unmet clinical need**

Figure seven illustrates that for some cancers with particularly high mortality (pancreatic, lung and oesophageal) we invest relatively little in research. In 2009/10 we invested three times more in breast cancer than we did in lung cancer. However, some changes can be seen in the portfolio. For example, investment in pancreatic cancer has more than trebled since 2005/06 (see Figures Three and Eighteen).

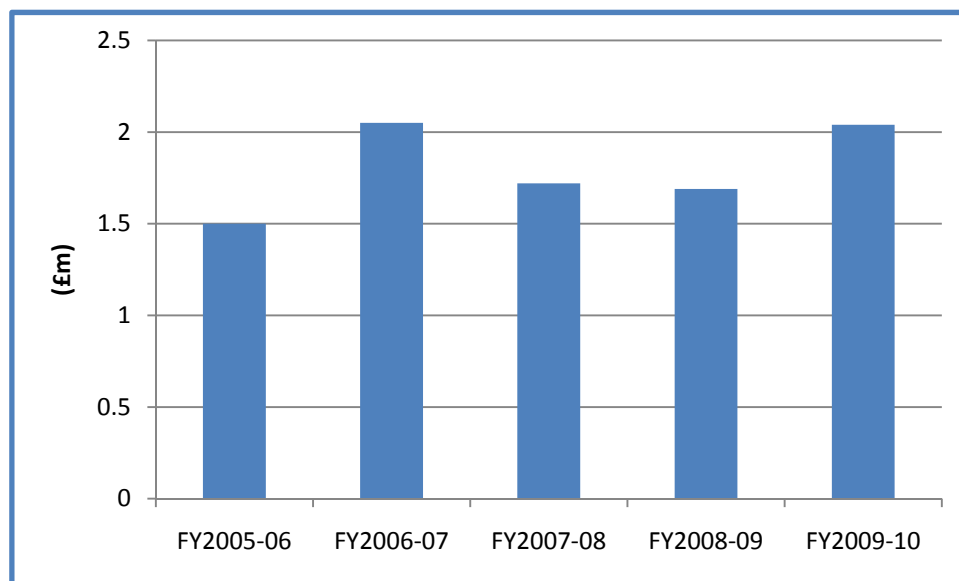
Three of the cancers on the right hand side of the graph in Figure Sixteen have been or will be the subject of a disease specific review.



**Figure Sixteen: Analysis of spend on disease site in comparison with mortality.**

### 2.3.3.1 Oesophageal cancer

Rates of oesophageal cancer have increased alarmingly since the 1970s and today only 8% of patients are alive five years after diagnosis. Although oesophageal cancer caused almost 5% of all cancer mortality, in 2009/10 it received just over two percent of our site specific investment (as shown in Figures Three and Seventeen). In the Research Strategy we committed to developing the recommendations from the Disease Specific Review of oesophageal cancer and to funding at least one major initiative in this disease.



**Figure Seventeen: Spend in oesophageal cancer over the last 5 years**

## Oesophageal cancer indicators

	Oesophageal cancer 2008/09	Oesophageal cancer 2009/10
Number of CR-UK trials on NCRN database*	8	8
Total number of people registered on above trials**	6,813	4,307
Annual recruitment to the above trials	1,817	1,398
Number of oesophageal trials using ECMC support since 2007		15
Oesophageal grant application success rate (CY_08,09)	32.5%	28.4%
Average site specific success rate of applications	31.3%	37.3%

**Table Two: Oesophageal cancer indicators**

\* These are trials supported, funded or endorsed by CR-UK that are included in the NCRI trials register. These are trials that we have funded and that are in recruitment rather than those that are just funded. Only trials that have recruited at least one person in the time period shown have been counted.

\*\* This includes non-patients e.g. people on studies such as AsPECT and is a cumulative total of all patients on trials since they opened

- The large drop in annual trial recruitment was due to the closure of AsPECT which last year recruited over 900 people in 08/09. Only one new trial in oesophageal cancer started recruitment in 09/10 (321GO).
- The number of grant applications in oesophageal cancer has fluctuated since 2005, but in recent years there could be a trend towards fewer applications (data not shown), however the success rates of applications are largely in line with the average for site specific applications.

### Progress to date

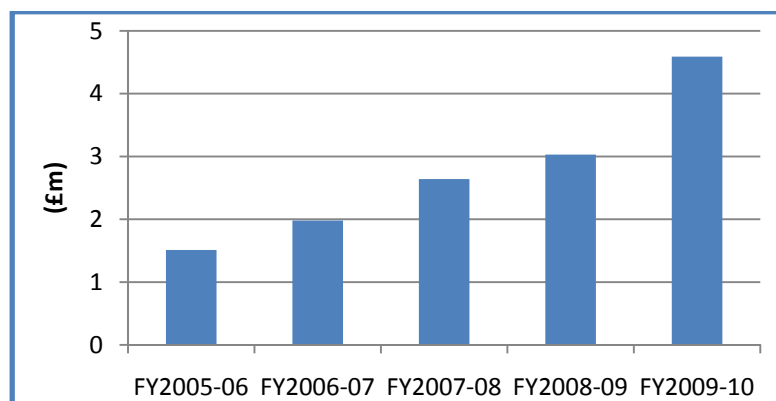
- In 2010, we funded a project grant through PRC for a phase III trial to evaluate a non-endoscopic screening device for Barrett's oesophagus.
- CR-UK has agreed to fund an ICGC project in oesophageal adenocarcinoma. This will be UK based and led by Dr Rebecca Fitzgerald in Cambridge and funded in its entirety by CR-UK (please refer to Section 2.2.7 for further details).
- As the precursor to the projects funded above, three working groups (epidemiology, early detection and biomarkers of disease) were established to help CR-UK further develop priorities emerging from the Disease Specific Review which took place in 2008.
- Whilst improving the understanding of the epidemiology of oesophageal cancer is very important, it became apparent that there was a lack of clarity about the most important question to ask. With such uncertainty, SEB declined to provide dedicated funding for an epidemiological study although applications will be welcome through normal channels. SEB appreciated the importance of biomarkers in helping to identify which patients will and will not respond well to treatment, and again welcomed applications through normal channels.

### Oesophageal cancer in Centres and ECMCs

- Since April 2007, 15 early phase clinical trials in oesophageal cancer have been reported as using ECMC support. These have been reported by seven ECMCs.
- Oesophageal Cancer is a focus area for the Cambridge Cancer Research UK Centre. Both Birmingham and Leeds Cancer Research UK Centres are planning specific research in this area.

### 2.3.3.2 Pancreatic cancer

The five year survival for pancreatic cancer is less than 5%, with little improvement in the last ten years. Following a Disease Specific Review in pancreatic cancer, we committed in the Research Strategy to establishing up to three centres of excellence in pancreatic cancer research through our Cancer Research UK Centres. Since 2005/06 our investment in pancreatic cancer has trebled, with a significant rise between 2008/09 and 2009/10, mostly related to new activity at the CRI.



**Figure Eighteen: Annualised research expenditure for pancreatic cancer over last 5 years.**

### Pancreatic cancer indicators

	Pancreatic cancer 2008/09	Pancreatic cancer 2009/10
Number of CR-UK trials on NCRN database*	5	4
Number of patients on CR-UK trials above**	4201	665
Annual recruitment to the above trials	261	360
Number of pancreatic trials using ECMC support since 2007		19
Number of DDO trials	1	1
Pancreatic grant application success rate (2008, 09)	27.3%	47.5%
Average site specific success applications	31.3%	37.3%

**Table Three: Pancreatic cancer indicators**

\* These are trials supported, funded or endorsed by CR-UK that are included in the NCRN trials register. Only trials that have recruited at least one person in the time period shown have been counted. We have not counted trials that are translational elements of other larger trials (e.g. ESPAC T-Plus) as this would double count patients)

\*\* This includes non-patients e.g. people on non-treatment trials and is a cumulative total of all people on trials since they opened

- It should be noted that the largest recruiting trial in pancreatic cancer in recent years, GEMCAP, finished recruiting before 2008/09 and so is not included in these figures.
- The increase in annual recruitment was largely due to ESPAC-4 ramping up recruitment.
- Success rates for pancreatic cancer applications are largely in line with expectations and since 2005 the numbers of applications have stayed largely constant (data not shown), but they do fluctuate year on year. It should be noted

that our increase in investment in pancreatic cancer is largely through non-response mode funding i.e. Professor David Tuveson at the CRI.

### **Progress to date**

- So far, three Centres have identified pancreatic cancer as a particular focus:
  - The Liverpool Cancer Research UK Centre aims to bring together basic, clinical and translational researchers in pancreatic cancer to identify a causative gene for familial pancreatic cancer. Liverpool has also won a £5m grant from the NIHR to establish a Biomedical Research Unit specialising in diseases of the pancreas;
  - Cambridge University and Addenbrooke's will establish a new pancreatic cancer clinic, which through the Cancer Research UK Centre will be linked to the research strengths in the CRI;
  - An objective for the Barts Cancer Research UK Centre is to conduct high-quality basic, translational and clinical activity in pancreatic cancer and to introduce novel therapeutic approaches.
- Additionally, Glasgow and Oxford both have a reasonably strong pancreatic focus, as does the ICR, although it is not yet a CR-UK Centre.
- Since April 2007, 19 early phase pancreatic cancer trials have been reported as using ECMC support. These have been reported across the Network by 11 ECMCs.
- During 2009/10 five ECMCs (Barts, Cardiff, Cambridge, Liverpool and Leicester) noted specific work/ achievements relating to pancreatic cancer trials. Cardiff ECMC's work to identify novel agents for solid tumours has led to the preclinical development of an agent for pancreatic cancer. Leicester ECMC is examining the relevance of cell signalling in pancreatic cancer with the aim of defining new biomarkers for diagnosis/ prognosis and to develop novel therapeutic strategies.

### **Drug development for pancreatic cancer**

- DDO currently has one pancreatic cancer study within its portfolio, a collaboration with Merck to combine a Notch targeting agent with gemcitabine.

### **Clinical trials for pancreatic cancer**

- CTAAC currently funds three phase III trials and three phase II trials in pancreas cancer. The ESPAC 3 study of adjuvant chemotherapy (CI, Professor Neoptolemos) was chosen for 2009's 'Best of ASCO'.

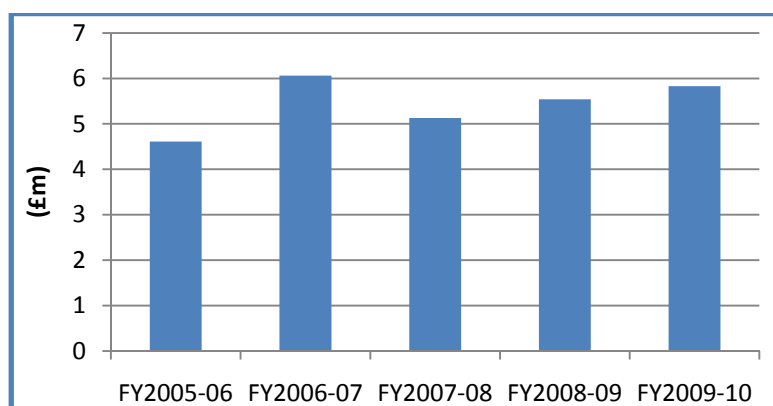
### **Future plans, challenges and opportunities**

- Centres that have identified pancreatic cancer as a focus area will this year be invited to attend a themed workshop, in order to encourage collaborative working to develop pancreatic cancer research.
- It may be useful to learn from the experience of the NCI initiative in pancreas cancer. Since 2000, the investment in pancreatic cancer has risen from \$20m to over \$70m *pa*. In that time there has been an increase in the number of phase II trials but, disappointingly, no increase in phase III trials. In fact, at the current time, there are no NCI phase III/IV trials in pancreatic cancer registered on the [clinicaltrials.gov](http://clinicaltrials.gov) database (36 phase I/II).

### **2.3.3.3 Lung cancer**

Lung cancer remains the largest single cause of cancer mortality in the UK, with very little improvement in survival rates since the introduction of platinum agents in the 1970s. In 2006, the NCRI published a Strategic Review of lung cancer which recommended that efforts in early detection and diagnosis should be increased, and

that the use of spiral CT for screening should be considered. However, the review has had limited impact. In the Research Strategy we committed to conducting a Disease Specific Strategic workshop on lung cancer. In advance of this workshop we continue to fund high quality lung cancer research through our Centres, response mode funding streams and CRT.



**Figure Nineteen: Annualised research expenditure for lung cancer over last 5 years**

#### Lung cancer indicators

	Lung cancer 2008/09	Lung cancer 2009/10
Number of CR-UK trials registered on NCRN database	10	9
Number of patients on CR-UK trials above*	4940	4577
Annual recruitment to above trials	1878	1790
Number of lung trials using ECMC support since 2007		65
Number of CRT projects	7	4 drugs in 5 trials
Lung grant application success rate (2008)	33.7%	41.0%
Average site specific success applications	31.3%	37.3%

**Table Four: Lung cancer indicators**

\* These are trials supported, funded or endorsed by CR-UK that are included in the NCRI trials register. Only trials that have recruited at least one person in the time period shown have been counted.

\*\* This includes non-patients e.g. people on non-treatment trials and is a cumulative total of all people on trials since they opened

- Annual recruitment to trials registered on the NCRN database has decreased slightly. Two trials ceased recruiting (The Chest Study and MARS), and only one new trial started recruiting (The ET Trial).
- The numbers of applications in lung cancer has been broadly steady since 2005, however in 2009 there was a sharp dip in applications. Since 2005 success rates for LC applications have tended to be above average, but in recent years applications look to have a lower success rate, more in line with the average (data now shown). However, in all years given the burden of this disease the numbers of applications has been low, making up only 5% of all disease site specific applications.

## **Progress to date**

### **Update on progress with the Spiral CT Lung Cancer Screening Study**

- The Health Technology Assessment Commissioning Board considered an application for a pilot study of the UK Lung Cancer Screening Trial (UKLS) submitted by Professor John Field in July 2009. Both Cancer Research UK and the Department of Health attended as observers.
- The pilot was funded at the January 2010 meeting of the HTA Commissioning Board and HTA have indicated that they will approach Cancer Research UK and other organisations as potential co-funders of a full trial in due course. The pilot has recently commenced.

### **Clinical trials in lung cancer**

- All of the CR-UK Trials Units have indicated that trials in lung cancer are an area of interest. CTAAC is currently funding 9 phase III trials and 3 feasibility studies in lung cancer/mesothelioma with one new trial being funded in 2010.

### **Lung cancer in Institutes, Centres and ECMCs**

- A significant proportion of our lung cancer research is carried out through our Institutes. Recently our five Institute Directors held a discussion about their individual strategies with respect to lung cancer to identify potential areas of synergy. There is potential for positive overlap and collaboration in the research being carried out. The apparent regional variation in the lung cancer burden in the UK also presents an opportunity for collaboration between Institutes, particularly since each Institute is developing a distinctive focus. It was proposed that a workshop be organised to take place in Manchester in 2011 that would allow for all the groups working in this area to meet together with an aim of increasing collaboration.
- Two Group Leaders have been recruited to our Institutes who will focus on lung cancer, and some others have recently indicated that they plan to switch their focus to lung cancer from other disease sites.
- Since April 2007, 16 ECMCs have reported participating in 65 early phase lung cancer trials including small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC) and mesothelioma.
- The Imperial College ECMC's work using tumour specimens has identified for the first time a biomarker of poor outcomes in NSCLC patients.
- Lung cancer is a focus area for Cambridge, Leeds, Manchester, Oxford and UCL Cancer Research UK Centres.

### **Future plans, challenges and opportunities**

- We plan to carry out a Disease Specific Workshop on lung cancer in the future.

## **2.4 The Research Areas in Which We Operate**

The Research Strategy sets out clearly the areas in which CR-UK will normally operate. As a result, a number of areas for disinvestment were identified, the remits of the relevant funding committees were adapted and discussions with other funders were commenced to ensure that high quality research in the affected areas continues to be supported.

### **Progress so far**

There have been no new CR-UK awards in the areas of:

- End of Life research

- Complementary Therapies (except when comparing complementary therapy with conventional therapy)
- Psychosocial oncology (except as part of larger clinical trials)
- Emotional/practical support for patients (except as part of larger clinical trials)
- Physician training in communication
- Service delivery

#### Supportive and Palliative Care

- Further to the NCRI Rapid Review of Research in Survivorship after Cancer and End of Life Care (SEOLC), a formal proposal to appoint a Chair of the UK Steering Group for research in SEOLC has been put forward by the NCRI. CR-UK supports this proposal as part of our managed transition away from supporting research in this area. The Chair will work with NCRI partners, the NCRI Secretariat and others to give professional and scientific leadership to champion research in SEOLC by facilitating access to resources, fostering collaboration, breaking down barriers, and increasing understanding of the importance of these research areas.
- The NCRI SUPAC collaboratives (CECo and COMPASS) have been informed that funding for the collaboratives will not be provided past June 2011.

#### End of Life Care Research

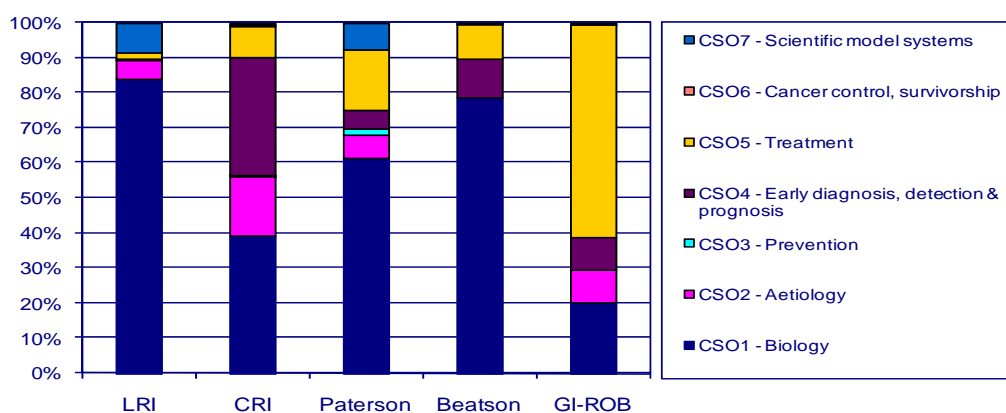
- CR-UK's collaboration with Marie Curie Cancer Care (MCCC) has been established. MCCC has agreed to provide £1 million per year for three years from 2010 to fund a research programme in end of life care. CR-UK will collaborate with MCCC to administer the application process and grant management for the scheme. First funding decisions were taken in November 2010 and grants have been awarded. CR-UK will also assist MCCC to review the research conducted by scientists within the Marie Curie Palliative Care Institute Liverpool and the Marie Curie Palliative Care Research Unit.
- The NCRI Rapid Review of Research in Survivorship After Cancer and End of Life Care report was published in November 2010. This follows on from the NCRI Rapid Review, undertaken during 2009/2010, which considered how best to develop and sustain research in survivorship after cancer and end of life care. Following extensive discussions with researchers, consumers and research funders, an action plan has now been agreed. In addition, the NCRI Survivorship After Cancer and End of Life Care Research Grantsmanship Gateway ([www.ncri.org.uk/grantsmanship](http://www.ncri.org.uk/grantsmanship)) was launched which is a micro-site that directs early career researchers to sources of expert advice on writing successful funding applications.

### 3. Provide the right environment for research

#### 3.1. Institutes

Cancer Research UK has five core-funded Institutes: the Beatson Institute for Cancer Research (BICR) in Glasgow, the Cambridge Research Institute (CRI), the Gray Institute for Radiation Oncology and Biology (GI-ROB) in Oxford, the London Research Institute (LRI) and the Paterson Institute for Cancer Research (PICR) in Manchester. Two of these Institutes are new since 2007.

Together the Institutes represent a major investment for the Charity – an expenditure of over £100m per annum. Our strategy is to continue to maintain a balanced portfolio of research in different venues, including these five Institutes. We are also committed to developing well defined strategies for each of our core-funded Institutes that are distinct, but coordinated with each other. As shown in Figure Twenty, the research profiles of our institutes are quite distinct.



**Figure Twenty: Institute research portfolios by Common Scientific Outline.** Data are presented for 2008/09. 2009/10 data not yet available.

#### Progress so far

During 2010 a number of promotions to Junior or Senior Group Leader positions were successfully reviewed or recruited to, confirming the excellence of the research at respective Institutes and providing valuable new expertise.

#### Beatson Institute (17 Groups)

- In 2009/10:
  - One Senior Group Leader (SGL) was reviewed, scoring Forefront for future work.
  - Two Junior Group Leaders (JGLs) were promoted to SGL.
  - Two new JGLs started, bringing strengths in structural biology and use of *Drosophila* as a model for cancer cell migration.
  - Dr Martin Drysdale was recruited to establish a drug discovery programme.
- In 2010/11:
  - One JGL, Dr Owen Sansom, was promoted to SGL.
  - One JGL, Dr Sara Zanivan, was recruited and will utilise proteomics to investigate the molecular mechanisms of angiogenesis.
  - A new head of the proteomics core service has also been recruited increasing expertise in an important technological research area.
- The Institute of Cancer Studies, formed in 2010, brings together all of the cancer research in Glasgow for the first time. Professor Karen Vousden has been appointed as the Institute's first Director. The Beatson Institute and the CR-UK West of Scotland Cancer Centre are key components of the new Institute.

#### Cambridge Research Institute (21 Groups)

- The process to recruit a successor to Professor Ponder as Director of the CRI will begin in the summer of 2011 after the CRI review.
- In 2009/10:
  - Two SGLs were reviewed, scoring Competitive/Forefront with Forefront potential and Forefront/Outstanding for future work confirming the excellence of the research within the Institute.
  - Two new JGLs started, bringing strengths in biomarker development and proteomics.
- In 2010/11:
  - Two JGLs, Dr Duncan Odom and Dr Jason Carroll, were promoted to SGL after only 4 years in the Institute.
  - Two SGLs were recruited to the Institute, including Professor Shankar Balasubramanian (end March 2010) bringing expertise in chemistry and increasing the focus on drug discovery and development. This will be achieved through close collaboration with Professor David Tuveson (experimental therapeutics) and Professor Duncan Jodrell (pharmacology and early phase clinical trials).
- CRT has finalised a major collaboration with Merck, Cambridge University and Addenbrooke's in relation to the clinical development of Merck's oncology pipeline.
- IS and property services functions have been devolved to the Institute, to allow greater autonomy.

#### Gray Institute for Radiation Oncology and Biology (8 Groups)

- A successful interim review of the Institute was jointly held with the MRC in 2009. The review concluded that the critical mass of researchers in radiation oncology, coupled with the state-of-the-art facilities had created the potential to allow the Institute to become a leading international radiation oncology centre.
- In 2009/10:
  - All equipment installation work was completed in 2009 with two CT-PET scanners and three MRIs fully operational.
  - A new clinical group leader started in 2009, bringing strength in translational bladder cancer research.
  - New DPhil and Masters courses were established in 2009 to build capacity in radiobiology in the UK.
- In 2010/11:
  - A new group leader, Andy Ryan, was recruited by the MRC from Astra Zeneca, and will lead work on lung cancer catalysing a grouping focused on lung cancer research.
- The funding to the Institute was restructured in 2010 into a single core award to the Director, Professor Gillies McKenna, which brings it into line with the other core funded Institutes. This will provide the Director with greater flexibility to manage the resources to the Institute to achieve its strategic goals.
- A tenure-track process has also been implemented at the GI-ROB to provide an increased commitment to the training and development of JGLs before they undergo a promotion review.
- Following a restructuring of the Medical Sciences Division at the University of Oxford, Professor Gillies McKenna has been appointed the Head of the Department of Oncology. Professor Tim Maughan has also been recruited from Cardiff to provide leadership in clinical oncology research in the Institute and in the Churchill NHS Trust.

### London Research Institute (45 Groups)

- In 2009/10:
  - Two SGLs within the Institute were reviewed, both scoring Forefront/Outstanding or above for future work.
  - Two JGLs were promoted to SGL.
  - Professor Adrian Hayday accepted a joint position working between LRI and Kings' College London, building strength in immunological research.
  - Core facilities were further developed following the transfer of Research Services, including restructuring of the Biological Resources Unit and Cell Services and the establishment of a clonal sequencing facility.
- In 2010/11:
  - Five SGLs in the Clare Hall Laboratories were reviewed, with scores ranging from F/O to O for past work. This review confirmed Clare Hall's reputation as one of the top international groupings investigating all aspects of genome integrity.
  - Two JGLs, Vincenzo Costanzo and Erik Sahai have been promoted to SGL.
  - Thomas Surrey started in January 2011 as an SGL (from EMBL) to work on the microtubule cytoskeleton.
  - Ilaria Malanchi is due to start as a JGL in summer 2011, working on tumour-host interactions in metastasis.
- IS and property services functions have been devolved to the Institute, to allow greater autonomy.
- Work is progressing on the UKCMRI project. Planning permission for the Institute has now been granted by Camden Council.
- During 2010, the first Director of the UKCMRI, Sir Paul Nurse, was appointed and the scientific vision document was published.

### Paterson Institute (17 groups)

- The Paterson Institute was reviewed in July 2009. As with the Beatson Institute in 2008, the review party praised the increasing strength of the fundamental research programmes as well as the greater integration of the Paterson with translational and clinical research in the Manchester Cancer Research Centre.
- In February 2011 Professor Nic Jones became CR-UK's Chief Scientist. Professor Jones will retain his position as Director of the Manchester Cancer Research Centre, but has stepped down from his position as Director of the Paterson Institute for Cancer Research. Recruitment for a new Director is now underway.
- In 2009/10:
  - Two JGLs were promoted to SGL.
  - One new JGL started, bringing strength in DNA damage response pathways.
  - Dr Donald Ogilvie was recruited to the Institute to establish a drug discovery programme.
- In 2010/11:
  - One JGL, Dr Angeliki Malliri, has been promoted to SGL.
  - One new JGL, Dr John Brognard, started with a focus on signalling networks in lung cancer.
- Laboratory research is underway in the new CR-UK Drug Discovery Centre. Drug discovery biologists and chemists have been recruited and the laboratory is now almost fully equipped. The Centre has been utilising its location to good effect by building relationships with researchers and clinicians for joint projects as well as accessing key technologies available at The University of Manchester and at CRT.
- Cancer Research UK provided £4.4m towards the development of the Derek Crowther clinical trials Unit (DCU), a chemotherapy delivery facility and part of a

major new Patient Treatment Centre at The Christie NHS Trust. The DCU opened in November 2010. This is the world's largest phase I clinical trials unit, with around 200 trials ongoing at any one time.

### Future plans, challenges and opportunities

- CRI, GI-ROB and LRI will all undergo quinquennial reviews during 2011.
- Planning for the new Manchester Cancer Research Centre laboratories, which will encompass researchers from the Paterson Institute, the University of Manchester and the Christie Hospital, is now underway. The new laboratories are scheduled to open by autumn 2013. CR-UK will make a £10m capital contribution to this project.
- Target completion date for UKCMRI is 2015. Planning permission has been secured. Government funding for UKCMRI was safeguarded in the October 2010 spending review, although part of the budget is being met by the Department of Health.

### 3.2. Cancer Research UK Centres

Our strategy aims to establish a UK-wide network of up to 20 Cancer Research UK Centres across the UK. The aim of establishing the Centres is to create long-term, sustainable centres of excellence in cancer. A key element of Cancer Research UK Centres is that they will provide a stable environment for translational research and training through local training accounts. We also aim to improve local engagement through Centres.

#### Progress so far

- To date sixteen centres have been approved (with thirteen announced publicly). It is envisaged that the remaining Centres under consideration will be approved by Summer 2011.
- CR-UK has committed £21.3M *pa* to the Centres approved so far.
- As intended, the Centres initiative has led to excellent engagement and commitment from partners. To date NHS trusts have committed to significant investment (approximately £30m) in cancer research in the next few years;
- Universities and NHS trusts have so far agreed to provide support for nearly £4m of basic infrastructure posts and senior salaries previously funded by CR-UK.



Figure Twenty One: Approved CR-UK Centres

- 53 new senior academic appointments in cancer research have been committed by CR-UK and our partners so far.
- Liverpool, Edinburgh and Dundee have now received funding for Senior Research Nurses, in addition to those already in place in our other Centres.

- LEAD managers are now in place in the majority of our Centres. They are making good progress in linking their Centres into the local community, with many more researchers now getting involved in supporting fundraising events and a significant increase in the number of labs tours taking place for local donors. In addition, valuable contacts are being made with local health organisations and networks, helping to raise awareness of the early signs of cancer and the importance of healthy lifestyles.
- The Centres Governance Boards, with CR-UK representation, are driving change, for example through the integration of local research strategies.
- The NIHR has designated 6 locations as Academic Health Sciences Centres, each of which has a strong cancer theme (with the exception of Kings): Bart's and the London; Cambridge; Imperial; King's; Manchester; UCL. In addition, the Scottish Academic Health Sciences Collaboration has been established in Scotland.

	Cancer Research UK Centre															
	Barts	Belfast	Birmingham	Cambridge	Cardiff	Dundee	Edinburgh	Imperial	Leeds	Liverpool	Manchester	Newcastle	Oxford	Southampton	UCL	Glasgow
Area of strategic importance																
Epidemiology/Public Health																
Early Diagnosis																
Animal Models																
Drug Discovery																
Drug Development																
Biomarkers																
Tissue Resources																
Surgery																
Imaging																
Radiobiology/Radiotherapy																

**Table Five: List of CR-UK Centres vs areas of strategic importance**

### Future plans, challenges and opportunities

- We are continuing to work to implement the strategy recommendations in surgical oncology and pancreatic cancer through Centres.
- We are examining how we can best network the Centres.
- Recruitment to senior posts, particularly medical chairs, has been problematic in a significant number of Centres, reflecting a general shortage of high quality candidates
- A triennial review of individual Centres and of the Centres initiative as a whole will take place in 2013.
- CR-UK and the Department of Health will review all of the Experimental Cancer Medicine Centres in 2011; thereafter Centre and ECMC reviews will be aligned from 2016 onwards.

### 3.3. Working with industry<sup>9</sup>

Pharmaceutical and biotechnology companies have a key role to play in the improvement of cancer care. In order to deliver our Research Strategy we need to consider where there is greatest potential in interacting with industry beyond current arrangements and what the implications of such relationships might be for the Charity as a whole.

#### **Progress so far**

##### Further developing our relationship with industry

- This year the Stratified Medicines Initiative has been a major new focus for industry interaction, successfully developing partnerships with Pharma (Pfizer, AstraZeneca) and building strong relationships with a number of other companies in the Pharma, biotechnology and diagnostics sectors.
- The ECMC Network continues to be an important conduit for engaging with industry. During 2008/9 the ECMC Secretariat visited a number of pharma companies identifying key issues, educating industry on the ECMC initiative and discussing opportunities. The companies involved expressed a great deal of interest in the ECMC network and what it can offer to companies wanting to undertake trials in the UK. There was also a great deal of interest in the DDO, particularly around Clinical Development Partnerships (CDP). During 2009/10 ECMCs have reported using ECMC infrastructure support to strengthen and expand research efforts with industry partners. Centres have reported that ECMC funding has played a key role in securing a substantial body of translational research activity funded by industry.
- In 2008/09 industry funded trials represented 50% of the ECMC early phase trials portfolio. In 2009/10 this figure had increased to 60%.
- The ECMC Secretariat has been helping a number of pharma companies identify sites for early phase trials.
- Many CTAAC trials (and patients) benefit from industry via free drug and/or individual educational grants. Between October 2008 and September 2010, 23 different pharmaceutical companies contributed funding to 60 out of the 95 (63%) feasibility or late phase trials that CTAAC has supported. A total of 40 different agents (22 licensed and 18 unlicensed drugs) have been provided by industry.
- Following on from the success of the AstraZeneca/NCRN Pipeline Initiative, the AstraZeneca/CR-UK/ECMC combinations alliance has been established to encourage collaboration on early phase combination studies between AstraZeneca, CR-UK's Drug Development Office and the ECMC Network. Six potential combination studies were agreed with AZ and sent to ECMCs for expression of interest. Subsequently two of these combinations were approved at the NAC in November 2010 with plans to open the first study in Q3 2011. The next round of combination studies has already seen over 50 expressions of interest from ECMCs which led to a successful first combinations workshop in November 2010 between clinicians and AZ to discuss new proposals. 5 potential studies were identified to take forward and a second workshop is planned to take place jointly with NCRN in February 2011.

##### Increasing the Number of Anti-Cancer Drugs in our Pipeline

- The Clinical Development Partnerships (CDP) Initiative continues to make good progress. 6 CDP studies now make up 20% of the DDO portfolio, twice the level reported last year.

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<sup>9</sup> See case study on AstraZeneca-CR-UK interactions, Figure Twenty Two

- The NCRN/AstraZeneca initiative commenced in 2009 and continues to be successful with a total of 15 feasibility studies funded or endorsed investigating the use of 6 different novel agents across 13 different cancers. This is twice the level reported last year. Work continues to expand the initiative to other companies and there have been preliminary discussions with Eisai.

#### CRT – maintaining our excellence in technology transfer

- CRT has configured research consortia where different groups of CR-UK funded researchers work jointly with the results/intellectual property being housed in a Limited company providing a single point of collaboration for industry. One such collaboration company based on senescence (Senectus Therapeutics) involves 4 CR-UK groups funded by the Discovery Committee. Interest is being shown by industry in this model and two further collaboration companies are being formed around cancer stem cells and lipid metabolism.
- Within the CRT Discovery Labs in 2009, two major deals were completed, partnering with Cephalon and AstraZeneca.
- The CRT Discovery Labs are also working closely with academia both within CR-UK with the new discovery groups in the Beatson and Paterson but also more widely with Bill Denny In New Zealand, where 4 FTEs are being provided from Bill Denny's funding. Together these collaborations bring an extra 30 FTEs to develop CR-UK drug discovery projects.
- The CRT Discovery Labs have several small molecule inhibitor projects under evaluation with industry.
- CRT is continuing to explore the potential to establish partnerships with industry for discovery and pre-clinical development of therapeutic antibodies using platform technologies.
- CRT has implemented a 'key account' system, wherein 50 of the major Pharmaceutical and Biotechnology companies with an interest in oncology have been identified. For each, a key point of contact has been established to develop a two way dialogue to further understand
  - i. what specific types of opportunities are sought by commercial parties and as such direct CRT's strategy for project sourcing and development, and
  - ii. provide industry with a more direct access to the output of CR-UK funded science.

#### **Future plans, challenges and opportunities**

- Industry driven combination studies are an important avenue for future cancer drug development and we will continue to seek further collaborations with other partners.

**Figure Twenty Two: A Case Study of the coordinated interactions CR-UK has with one industrial partner – CR-UK and AstraZeneca partnerships**

### **3.4. Tissue banking**

The Research Strategy stated that CR-UK would cease providing funding for stand-alone tissue banks and that onCore UK should remain the only dedicated tissue banking mechanism. CR-UK would provide support for tissue collections through Centres or ECMCs in areas where existing collections were inadequate. CR-UK continues to support tissue banking activities through response mode mechanisms of BIDD and CTAAC and via infrastructural support provided by the ECMC Network and CR-UK Centres Initiative.

#### **Progress so far**

##### onCore UK

- Over the last four years, onCore UK has been successful in promoting biobanking activity and supporting the biobanking community in the UK. It has been instrumental in setting up the Confederation of Cancer Biobanks (CCB) and promoting an understanding of regulatory and governance issues.
- In January 2009, it was decided that onCore UK should cease biobanking activities and refocus its remit on advocacy, coordination and communication on behalf of the wider bio-banking community.
- The Funders will not provide further funding for onCore UK, which will not be maintained as an independent entity. Work on the following priority areas will we

supported as an NCRI workstream, which is expected to be ratified by the NCRI Board in March 2011:

- a. Maintenance and updating of the tissues portal
  - b. Development and support of the Confederation of Cancer Biobanks
  - c. Best practice and harmonisation
  - d. Accreditation scheme for UK biobanks
- Construction of a new Tissues Portal, building on the previous CR-UK Tissues Directory as part of a joint project between CR-UK, onCore UK and the NCRI Biomarker and Imaging CSG. Two new directories have been created: one for biosample collections associated with clinical trials and the other for more general biosample collections.
  - Following an external review of the CCLG Tumour bank to assess its quality and utility, opportunities for creating a unified leukaemia/solid tumour bank were (unsuccessfully) explored with Leukaemia and Lymphoma Research. Subsequently expressions of interest were invited from the CR-UK Centres to host the centralised CCLG Tumour Bank. Three candidate Centres were scored and ranked on their facilities and biobanking capability; expertise in paediatric oncology/ pathology and links with the CCLG Professional Body. Newcastle was selected by the review team as the preferred host Centre.

#### **Future plans, challenges and opportunities**

- We will monitor the dissolution of onCore UK as a charity. Unless there are any unanticipated developments, the charity will be brought to a formal closure on the 28<sup>th</sup> February 2011.
- The remaining onCore UK funds will be transferred to CR-UK for use by the NCRI to continue to support cancer biobanking activities. In addition, two members of onCore UK staff will transfer over formally to CR-UK employment from the 1<sup>st</sup> February 2011 and will report to Dr Jane Cope, Administrative Director of the NCRI.
- We will continue to monitor sample collections funded by BIDD and CTAAC to identify those which represent areas of unmet need.
- It is envisaged that the CR-UK Stratified Medicine Programme will harness the potential of patient samples for future research.

### **3.5. Informatics**

#### **Progress so far**

- Initial scoping work has been carried out for a review of CR-UK's investment in informatics.
- The informatics work stream of the Stratified Medicine project was initiated in March 2010. An advisory group of experts was convened and the design and governance for the informatics requirements for the project were delivered as part of the overall Stratified Medicine design phase.

#### **Future plans, challenges and opportunities**

- The informatics work stream of the Stratified Medicine Initiative will continue as part of the overall initiative.
- We are currently exploring the strategic implications of our increasing investment in genetics and genomics in terms of data gathering, storage, curation and access.

### **3.6. Organisational effectiveness**

In the Research Strategy we committed to simplify and streamline our processes, for example our grants management and finance systems. Our aim is to create more effective, efficient and user friendly systems that also allow us to capture data on our research more effectively.

#### **Streamlining research management and administration**

- The research operations and funding Directorates were restructured in October 2009, and an Operations Team was created to support funding streams across both Directorates. This new team is already improving the skill base, resource flexibility and business continuity in our administrative staff, and driving simplification and consistency in all of our processes.
- The restructure also ensured that staff were in the roles required for the introduction of the new electronic Grant Management System (eGMS).
- The Research Operations and Funding (ROF) Directorate was created in October 2010, bringing together Science Operations and Funding (SOF) and Clinical and Translational Operations and Funding (CTOF). The new directorate includes the Science Funding, Clinical Research, Translational Research, Drug Development Office, Centres and Operations teams and will promote a consistent and efficient approach across all funding areas.
- The eGMS went live in October 2010. The Operations Team will now manage delivery of full benefit. This will involve process review and a governance structure to ensure Research Operations and Funding employ simplified and consistent processes within the new system.
- The policies and procedures team is at full capacity and is working across Research Operations and Funding to ensure we are clear and consistent in the delivery of our work.
- A communications role has been developed to improve and promote internal, inter-directorate and external communications.
- The changes brought by eGMS should provide the scientific teams with more time for face to face interactions with the research community.

#### **Creating greater financial flexibility for Principal Investigators**

- We aim to reduce bureaucracy for our principal investigators and allow them greater financial flexibility. This has in part been achieved through the new CR-UK Terms and Conditions implemented in February 2009. Changes include:
  - introduction of a standard rate of indexation for the duration of the award, clarifying the value of the award and supporting financial planning;
  - introducing multi-year award letters and reconciling awards less frequently – reducing routine paperwork by >50% and increasing flexibility to vire funds between grant years;
  - an open virement policy which allows the PI to manage salary and running expense budgets as per project requirements.

#### **Implementation of Programme Review Panels**

- In early 2011, the process for assessment of Programme grant applications will change, with all applicants attending a face to face interview with a panel of Committee members and expert reviewers in advance of a funding decision.
- Programme review panels will assess all new and renewing programmes across all committees from the new financial year.

- Benefits of this change include:
  - Rigorous review process that ensures parity in treatment for all programme awards within the CR-UK portfolio.
  - Increased interaction with programme applicants and grant holders.
  - An opportunity to showcase CR-UK programmes to international experts sitting on the review panels.

**Future plans, challenges and opportunities**

- Through a comprehensive set of measures we will monitor if these changes are having the desired effect and will review after the new systems have been fully operational for a suitable period.
- During Q1 FY2011-12, a review of the role of our funding committees will be conducted to ensure they are configured to accomplish relevant CR-UK strategic objectives.

## 4. Provide the right people for research

### 4.1. Training in Institutes and Cancer Research UK Centres

Cancer Research UK provides opportunities for career progression and development through the Training Accounts in our Cancer Research UK Centres, Fellowship and Career Establishment schemes, and also through our Institutes.

#### Recent highlights

- In 2010 we appointed three new Clinician Scientists, three Career Development Fellows and two Senior Cancer Research Fellows.
- Disappointingly, because of the quality of the candidates at the interviews, we were not able to spend all of the funds available for fellows.
- Over the past year we have increased our advertising about our fellowship funding and worked with the Centres to promote these opportunities to their staff. As a result, we received 97 preliminary applications for the 2011 New Investigator awards (Career Development Fellowships, Senior Cancer Research Fellowships and Career Establishment Awards). This is an increase of about 50% compared to 2010. 31 were invited to submit full applications, of which three are current Career Development Fellows, four are clinicians and one is in the area of population research.
- We will be able to support 10 New Investigator awards each year for the next 5 years.

#### Governance and oversight

- The Training and Career Development Board is an advisory group for Cancer Research UK to advise on all aspects of career development and training, particularly with respect to new investigators. We have recently reconstituted the Board and the membership now comprises Professors Ron Laskey, Jane Wardle, Adrian Hayday, Margaret Frame and Philip Johnson, and Dr Sally Leever from the London Research Institute.
- The TCDB delegates the authority to review applications and appoint fellows to a number of fellowship panels. Over the past few years, in response to recommendations from the SEB and the CRSC, we have made some changes to the structure of the selection panels and their funding streams.
- The non-clinical fellowships interview panel considers applications for Career Development Fellowships and Senior Cancer Research Fellowships and has now taken over the allocation of Career Establishment Awards from the Biological Sciences Committee. The Panel is chaired by Professor Margaret Frame.
- The Clinical Fellowships Panel reviews the Clinician Scientist Fellowships, and has recently taken on the task of assessing the Research Bursaries for Clinicians. The panel is chaired by Professor Philip Johnson.

#### New investigators

- We currently have 43 new investigators running their own research group, as well as 20 Clinician Scientists and 5 other early-career fellows funded on other schemes.
- The five core-funded Institutes currently support a further 29 Junior Group Leaders.
- Until 2010, Career Establishment Awards were only available to non-clinical researchers working in disciplines within the remit of the Biological Sciences Committee. As a result of the amalgamation of the New Investigator funding

streams, these awards will be available to researchers in basic, translational and clinical research, and to those working in population science.

- We have increased the opportunities for networking and collaboration between our junior researchers. We expanded the remit of the Senior Fellows' Meeting to include Institute Junior Group Leaders and Career Establishment Award holders. 39 researchers attended the most recent meeting in September 2010.
- We continue to provide funding to allow fellows to attend management training courses such as the EMBO laboratory management course held in Germany. Cancer Research UK worked with other funding bodies to run the EMBO course in Cambridge in 2008.

#### **Post-doctoral research staff**

- We have adjusted the remit of our existing bursary schemes to increase the support provided to post-doctoral research fellows. The bursaries will give Cancer Research UK-funded post-docs an opportunity to spend some time in a different research group.
- As part of a wider analysis of the state of cancer epidemiology research, we will review the training needs in this area. In 2011 we plan to offer up to 4 new Post-doctoral Fellowships in Population Research.

#### **Students and graduate clinical fellows**

- The former separate funding streams for graduate students have now been combined to form clinical and non-clinical training accounts in the Centres. The first students and fellows were appointed in autumn 2010.
- We currently fund just over 400 PhD students, of which 55% are in our Institutes.
- We will be introducing a new meeting for final year PhD students in March 2011. The focus will be on their future careers. We will include talks from senior researchers, as well as contributions from employers that recruit graduate students.
- We will continue to hold annual meetings for our PhD students and for our clinical fellows. We have adjusted the agendas for these meetings to include more information and advice about career opportunities after graduation.
- We will continue to run our Graduate student Public Engagement with Science and Technology (GradPEST) course, to give our PhD students and clinical fellows the skills needed to present their work to the public. We will work with LEAD managers and Centre staff to ensure that the students and fellows have a chance to get involved in local engagement and put their skills into practice after they complete the course.

#### **Support for clinicians**

- In 2008 we ended the Senior Clinical Research Fellowship, and increased the funding for the post-doctoral Clinician Scientist Fellowship.
- New Investigator awards are now open to clinicians, and in 2010 we awarded Dr Faith Davies, a haematologist at the Institute of Cancer Research, a Senior Cancer Research Fellowship.
- This year we received 8 preliminary New Investigator applications from clinicians, of which 4 have submitted full applications.
- This year we received 28 applications for Clinician Scientist Fellowships, which is more than twice the number received in 2010.
- There is an effort across several parts of Cancer Research UK to promote careers in academic surgery, and as part of this we will continue our Joint Fellowship with the Royal College of Surgeons of England for a further five

years. It was encouraging to see that 9 of the 28 Clinician Scientist Fellowship applications were from surgeons.

#### **Future plans, challenges and opportunities**

- We will continue to develop the support that we provide for research careers, including exploring ideas for research funding opportunities and career skills training for post-doctoral research fellows.

### **4.2 Increase the number of international leaders in cancer research working in the UK**

#### **Progress to date**

In last year's report we noted that progress against our strategic aim to increase the number of international leaders in cancer research working in the UK had been slow. We also noted that the current financial constraints meant that this is an area of our strategy that could not be prioritised at this time and would need to be re-visited in the future. These observations remain true today, and activity has been limited to recruitment within standard budgets for our Institutes (section 3.1) and new posts in CR-UK Centres (section 3.2).

#### **Future plans, challenges and opportunities**

- During 2010 the UKCMRI published its scientific vision and research strategy, including a scientific career structure designed to develop world-class researchers, and a recruitment policy for long-term group leaders based on the principle of worldwide competition for places. In the medium term UKCMRI will provide a significant opportunity to focus international recruitment.
- Many Centres have found it difficult to recruit to senior positions, particularly medical Chairs
- The impact of the enactment of new employment law affecting retirement is not yet clear, but may affect employment patterns.
- Opportunities to engage the expertise of late career and retired scientists are being explored.
- The immigration cap implemented by the Government has presented difficulties for a number of research institutions. Our Policy and Public Affairs team is working to make the case for relaxing restrictions on employment of non-EU scientists.

**Appendix: Glossary of Acronyms**

BIDD	Biomarker and Imaging Discovery and Development Committee
BSC	Biological Sciences Committee
CCLG	Children's Cancer and Leukaemia Group
CDP	Clinical Development Partnerships
CRI	Cambridge Research Institute
CRT	Cancer Research Technology
CTAAC	Clinical Trials Advisory and Awards Committee
CTRad	Clinical and Translational Radiotherapy Research Working Group
CTRC	Clinical and Translational Research Committee
CSO	Common Scientific Outline
CSP	Coordinated System for gaining Permission
DCC	Discovery Coordinating Committee
DDAG	Drug Discovery Advisory Group
DDL	Drug Discovery Leadership
DDO	Drug Development Office
DL	Discovery Laboratory
EORTC	European Organisation for Research and Treatment of Cancer
ECMC	Experimental Cancer Medicine Centre
EPSRC	Engineering and Physical Sciences Research Council
ESRC	Economic and Social Research Council
FSC	Feasibility Studies Committee
FTE	Full Time Equivalent
GI-ROB	Gray Institute for Radiation Oncology and Biology
GWAS	Genome wide association study
ICR	Institute of Cancer Research
ICGC	International Cancer Genome Consortium
IMI	Innovative Medicines Initiative
IMRT	Intensity Modulated Radiotherapy
JGL	Junior Group Leader
MCCC	Marie Curie Cancer Care
MRC	Medical Research Council
NAC	New Agents Committee
NAEDI	National Awareness and Early Diagnosis Initiative
NCI	National Cancer Institute
NCRI	National Cancer Research Institute
NCRN	National Cancer Research Network
NICE	National Institute for Health and Clinical Excellence
NIHR	National Institute for Health Research
NIMR	National Institute for Medical Research
NPRI	National Prevention Research Initiative
PRC	Population Research Committee
PET	Positron Emission Tomography
PRC	Population Research Committee
RT/RB	Radiotherapy / Radiobiology
SEB	Scientific Executive Board
TAG	Tobacco Advisory Group
TRICC	Translational Research in Clinical Trials Committee
SGL	Senior Group Leader
SSAG	Science Strategy Advisory Group
UKCRC	UK Clinical Research Collaboration