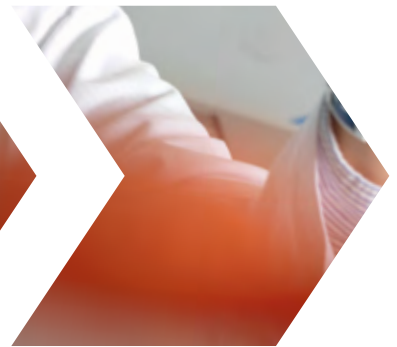


Making the discoveries

Our strategy
to defeat cancer





Our vision

We will overcome the challenges posed by cancer's complexity, adaptability and evolution through scientific and clinical excellence, innovation and partnership.

Our strategy to defeat cancer

Cancer is the UK's biggest killer. For all the dramatic progress against the disease in recent decades, it continues to claim around 160,000 lives every year. Survival rates have improved enormously in some types of cancer, but patients with other tumour types continue to do very poorly, and once the disease has spread round the body it is still often incurable.

We now know that the main reason cancer is so difficult to treat is that it is enormously complex, and can adapt and evolve as its environment changes – and in response to treatment. Not only are there more than 200 types of cancer, but each is genetically diverse, and there is variation even between the different cells of an individual patient's tumour. Cancer cells do not send and receive chemical signals through linear pathways, but via intricate and hugely complex webs. Patients will often respond initially to chemotherapy or new targeted drugs, only for the cancer to exploit this genetic diversity and complexity, and find a way to sidestep the effects of treatment.

The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust together form one of the world's top centres for cancer research and treatment, with a focus on taking research findings rapidly from the laboratory to the clinic, to improve outcomes for patients. We have worked together on a joint research strategy, *Making the discoveries: our strategy to defeat cancer*. The strategy covers the next five years, until 2021. We aim to

'We now know that the main reason cancer is so difficult to treat is that it is enormously complex'

accelerate progress against cancer by combating the disease's extraordinary complexity, and its enduring ability to adapt and become resistant to treatment. We will do so through scientific and clinical excellence, innovation and partnership.



Paul Workman

Professor Paul Workman
FMedSci, FRS
Chief Executive
The Institute of Cancer
Research, London



DSV

Professor David Cunningham
FRCP, FMedSci
Director of Clinical Research
The Royal Marsden and
The Institute of Cancer
Research, London



Our research pillars

Our research strategy is structured around four central pillars designed to overcome cancer's complexity and evolution. These are underpinned by strong foundations.



➤ **1**
Unravelling cancer's complexity

The first pillar of our joint research strategy is to gain a much fuller understanding of the complexity of cancer. We need to take an overview of cancer's complex ecosystems and communication networks – and yet also to drill down deep into the specific mechanisms that drive cancer development, growth and spread. In this way we can reveal the fundamental processes at work as cancers arise, change and evolve, and use this knowledge to outmanoeuvre cancer by opening up exciting new avenues for treatment.

➤ **2**
Innovative approaches

Scientific understanding on its own is not sufficient to defeat cancer – we need to innovate at every stage from the bench to the bedside. The second pillar of our research strategy is to discover novel and personalised approaches to cancer treatment, controlling tumours locally where possible, while also meeting the challenges of cancer evolution and drug resistance. We believe that drugs that target evolutionary mechanisms, adaptive therapy, precision radiotherapy and immunotherapy – often used together in innovative combinations – will all have a critical part to play in achieving long-term survival and cure.

➤ **3**
Smarter, kinder treatments

The ICR and The Royal Marsden will also work closely together to accelerate clinical development of innovative new treatments for the benefit of patients. The third pillar of our research strategy is to create and deliver innovative clinical trials assessing a range of personalised treatments: novel small-molecule drugs, biological agents including immunotherapy, precision radiotherapy, new surgical techniques, advanced cancer imaging and combination treatment. We need to use targeted treatment, based on accurate diagnosis, as early as possible in disease – and then to adapt therapy to the cancer's changing molecular and biological profile.

➤ **4**
Making it count

Finally, we recognise that our responsibility to cancer patients does not end with the delivery of excellent research, or even with the development of a new treatment. We need to take active steps to ensure our findings deliver real impact on the lives of cancer patients. So the fourth pillar of our strategy is a commitment to make our research count in embedding new treatments, technologies and strategies for prevention into routine healthcare, by building an evidence base to support their adoption, leading through national and international networks, and influencing health services. We want to ensure our results have the greatest possible beneficial impact on the lives of people with cancer – and people who may develop cancer in future.

Pillar 1

Unravelling cancer's complexity



We will comprehend the full complexity of cancer by harnessing the power of new technologies and Big Data.

1 >



Now



'We aim to take an overarching view across cancer's complexity and evolution'

The ICR has played a pioneering role in exposing the complexity and adaptability of cancer. We have driven forward understanding of how cancer cells signal through pathways and networks, revealed the three-dimensional structures of key cancer proteins and been world leaders in identifying cancer genes. We have also shown that cancers evolve and diversify in a way that can be explained by Charles Darwin's theory of evolution by natural selection.

We believe that gaining a much fuller picture of cancer's complexity, and its ability to adapt and evolve, is essential if we are to identify new, more effective approaches to cancer treatment, and to improve long-term survival and cure. We intend to apply advanced new techniques, such as computational approaches, gene-sequencing

technologies and innovative types of imaging, to provide a detailed insight into what makes cancer tick. Our approach will aim to take an overarching view across cancer's complexity and evolution, and also to dive down deep into the fundamental mechanisms at work in cancer's development and progression.



Read more about
cancer evolution at
www.icr.ac.uk/research



Professor Jon Pines



The fundamentals of cell division

In a normal cell cycle, the goal of cell division is to accurately duplicate genetic information and evenly divide it into two daughter cells. Complex cellular machinery makes sure the two daughter cells receive an identical set of chromosomes – ensuring cells remain genetically stable. The ICR's Professor Jon Pines has led research into how these fundamental mechanisms of cell division are regulated, helping to shed light on how errors in chromosomal segregation can lead to cancer.

Studying exactly how cells maintain the stability of the genome during normal cell division is critical to understand the development and evolution of cancer, and to open up new approaches to treatment. Our scientists are also producing detailed biological images of proteins, in unprecedented detail, to help us discern exactly how cells copy their chromosomes and divide. Visualising the structures of the key proteins involved in cancer allows us to design drugs to bind to them and block their activity.

To enable us to decipher these complex processes further we are investing in real-time cellular imaging. By live streaming of digital, microscopic images of dynamic cell division, we can understand precisely how the machinery that controls the process is regulated in space and time. Our researchers will be able to pinpoint exactly what goes wrong when cancer develops, helping us to find new ways to defeat cancer.



Future



- > We will understand in detail the critical mechanisms used by cells to grow, divide and spread – including how they copy, segregate and repair their DNA – and how these processes go wrong in cancer.
- > We will bring together analysis of germline and tumour genetics, to identify markers of prognosis or treatment response, and new diagnostics.
- > We will establish an overarching view of cancer's complex communication networks – so we can identify new targets for cancer drugs, new biomarkers for resistance and recurrence, and clues for how best to combine treatments.
- > We will develop innovative new imaging technologies designed to assess a tumour's behaviour and metabolism, and to predict or monitor the response to treatment.
- > We will reveal how cancers adapt and evolve in response to changes in their environment – including how they evade the immune system and develop resistance to drugs and radiotherapy.

How?



- ▶ We will recruit world-leading cell, molecular and structural biologists, and invest in cutting-edge forms of microscopy and other new technologies to support them.
- ▶ We will establish new strategic relationships with other academic organisations in areas such as genomic stability, cancer evolution and immunology.
- ▶ We will introduce new animal models and studies of human tissue from The Royal Marsden to explore how cancers interact with their tissue environments and the immune system as they grow and spread.
- ▶ We will establish long-term leadership for our Centre for Evolution and Cancer, and ensure it helps shape our future approach to discovery of new treatments by moving it alongside a new Centre for Cancer Drug Discovery.
- ▶ We will enhance the integration of all our genomics work across germline and tumour genetics, and spanning the ICR and The Royal Marsden.
- ▶ We will develop systems biology approaches and a new Knowledge Hub for analysis of Big Data so we can better understand cancer's complex communication networks.
- ▶ We will further invest in our new state-of-the-art building for imaging research – the Centre for Cancer Imaging – to ensure it is equipped with the latest technology and drives multidisciplinary collaboration.

Targets



Dr Andrea Sottoriva



Anticipating cancer's next steps

The ICR has pioneered research into cancer evolution and its discoveries are already informing practice on drug resistance in advanced disease. Our new Centre for Evolution and Cancer draws together researchers from evolutionary biology, ecology, bioinformatics, genomics and clinical oncology to provide better insights into the course of disease and find new avenues for treatment.

We will now seek to find ways to predict the path of disease in every person with cancer. The ICR's Dr Andrea Sottoriva has already shown that mathematical rules govern some elements of cancer evolution. He is using vast amounts of genetic data from human tumours to provide insights into how a given cancer will develop over time. Meanwhile, Dr Yinyin Yuan has shown that the course of ovarian cancer could be predicted by looking at how it interacts with its tissue environment. Her research has led to the development of an automated system that uses biopsy samples to predict a patient's chance of survival.

These new approaches to anticipate cancer's next steps will help us design drug regimens that are most likely to be effective, and least likely to drive resistance to treatment. We will co-locate our evolutionary scientists with our drug discovery teams so new insights into evolution can help shape the future of cancer treatment, and help us to prevent or overcome drug resistance.



To expand knowledge of how cancer cells develop and cope with genome instability, and apply our understanding to identify a new therapeutic target or drug.



To understand the complex ways in which cancer cells evolve and remodel their communication networks to adapt to the effects of treatment, and identify a new strategy for overcoming drug resistance.

Pillar 2

Innovative approaches



We will take on the challenge of cancer's complexity, evolution and drug resistance through the discovery of innovative new approaches to cancer treatment.

2 >





Dr Gert Attard



An early warning of drug resistance

Liquid biopsies have the potential to transform cancer treatment by providing a cheaper, faster, less invasive way of assessing genetic information from a tumour than a traditional tissue biopsy. Several research groups at the ICR and The Royal Marsden are developing liquid biopsy techniques that detect and sequence DNA released by cancer cells into the bloodstream. Dr Nicholas Turner has developed a blood test for breast cancer that picks up very early signs that a treatment is no longer working, eight months before tumours are visible on hospital scans. Dr Gert Attard found that a similar blood test in prostate cancer could predict in advance whether patients were likely to develop resistance to treatment.

Analysing circulating tumour DNA in this way could transform how we treat cancer patients. We can get a genetic profile of the cancer, non-invasively, and discover which mutations are driving it, and how the disease becomes resistant to treatment. We can then use this information to adapt treatment so we are giving patients the best drugs for their cancer at that point in time.

We are still at the early stages in the use of liquid biopsies. Over the next five years, researchers at the ICR and The Royal Marsden will devise new combinations or sequences of drugs designed to adapt to genetic changes within a cancer detected by blood tests over the course of treatment. We will select drugs to slow down cancer evolution, making it harder for the disease to evade the effects of treatment.

Read more about our drug discovery research at www.icr.ac.uk/research

Now



'We need to discover new approaches to treatment designed to overcome resistance'

The ICR discovers more new cancer drugs than any other academic centre in the world. Since 2005, it has identified 20 drug candidates – each designed to hit specific targets important for cancer – and nine have gone on to enter clinical trials at The Royal Marsden and elsewhere. The innovative drug abiraterone, also discovered at the ICR, has become a standard treatment for prostate cancer and is benefiting hundreds of thousands of men worldwide. The ICR and The Royal Marsden have also pioneered new forms of precision radiotherapy, through advances in physics research which have allowed radiation beams to be shaped to the contours of a tumour.

But for all the progress, cancers often remain very difficult to treat. Many of the new generation of targeted therapies are initially highly effective, only for cancers to adapt and evolve resistance to treatment. Over the

next five years, under the leadership of Professor Raj Chopra, the ICR will deliver a new programme of drug discovery designed to meet this major clinical challenge head on. We need to discover new approaches to treatment designed to prevent, anticipate or overcome the evolution of drug resistance. We will also aim to harness the adaptability of the immune system in new treatments capable of outpacing cancer evolution. And we will innovate in the delivery of radiotherapy to patients, so we can eradicate cancer locally before it gets the chance to evolve and spread.



Dr James Larkin



Manipulating the immune system

Boosting a person's immune response against cancer is one of the most exciting advances in cancer therapy. The ICR and The Royal Marsden have already played an important role in developing immunotherapy for patients. Dr James Larkin helped lead a major international study demonstrating that the combination of two immunotherapy drugs – nivolumab and ipilimumab – could shrink tumours in almost 60 per cent of patients with advanced melanoma. We also led the UK arm of a phase III trial demonstrating the effectiveness of a viral immunotherapy called T-VEC. It was the first time an immunotherapy involving use of a virus had been definitively shown to benefit patients.

We plan to play a big role in creating the next wave of immunotherapies, by expanding our research into cancer immunology. Professor Raj Chopra, Head of Cancer Therapeutics, will lead a new focus on revealing how solid tumours directly and indirectly interact with cells of the human immune system. Understanding these interactions may allow us to manipulate the adaptive immune system at the molecular level to create new forms of cancer immunotherapy, including highly promising cellular therapy approaches as well as small-molecule drugs. We will also aim to identify key molecules within the tissue environment surrounding a tumour that could be targeted to enhance the immune response.



Future



- We will discover new treatments for adults' and children's cancers designed to prevent drug resistance by targeting key evolutionary mechanisms such as the ability to cope with genome instability.
- We will apply our understanding of cancer's complex signalling networks to create new ways of combining drugs, radiotherapy or immunotherapy, designed to block the paths to drug resistance.
- We will identify new biomarkers to detect or predict response to treatment, so we can select the best drug for a patient right from the outset, and use targeted therapies earlier in the course of treatment.
- We will lead advances in adaptive therapy by developing liquid biopsies and other rapid tests to assess treatment response and resistance, and applying these within innovative new treatment regimes.
- We will study how cancers interact with the immune system, and how these interactions can be exploited in the creation of new types of immunotherapy, including cellular therapy.
- We will target radiotherapy and therapeutic ultrasound more precisely at tumours, by solving physics-related problems and exploiting advances in imaging and computational science.

How?



- We will build a state-of-the-art Centre for Cancer Drug Discovery with cutting-edge chemistry and drug design facilities, and room for an extra 50 members of staff – so we can discover even more innovative cancer drugs.
- We will build capacity in cancer immunology and immunotherapy, by recruiting at least three new research teams and investing in the latest technologies.
- We will integrate the ICR's drug discovery teams with research on cancer evolution and immunology, so that researchers can collaborate to combat cancer's ability to adapt, evolve and evade the immune system.
- We will build new commercial and academic partnerships to support our drug discovery, including attracting companies and research teams to co-locate to our Sutton site as part of a major initiative called The London Cancer Hub.

- The ICR and The Royal Marsden will expand access to tumour samples and clinical imaging data for assessing the effectiveness of treatments by further integrating our activities through the Centre for Molecular Pathology.
- We will invest across the ICR and The Royal Marsden in facilities for storing and analysing liquid biopsy samples, so we can assess drug resistance and create new approaches to adaptive therapy.



Dr Udai Banerji



Exploiting stress in cancer cells

Cancer cells experience various forms of stress which create points of vulnerability that can be exploited by smart new targeted drugs. The ICR has led research revealing how cancers use the protein Hsp90 – known as a 'molecular chaperone' for its role in assembling other proteins – to protect themselves from stress and preserve cancer-causing signals. Based on this research, Professor Paul Workman led a multidisciplinary team that discovered the drug luminespib, which blocks the chaperone function of Hsp90, inhibits cancer cell growth and shrinks tumours. Dr Udai Banerji led the first clinical trial of luminespib that showed the drug effectively inhibits Hsp90 in cancer patients, and subsequent studies found it could also shrink tumours in patients with breast and lung cancer.

But our research also showed that use of Hsp90 inhibitors can trigger an adaptive stress response in cancers that limits the drugs' effectiveness. ICR scientists are now designing new approaches to targeting the stress response that also take into account how cancer cells evolve during treatment. They are creating inhibitors of particular forms of another stress response protein called Hsp70, which they found to be critical to blocking the cancer-killing effects of Hsp90 inhibitors. Our drug designers have also discovered highly potent and effective inhibitors of the stress response pathway controlled by a master regulator switch known as HSF1. And they are identifying further ways to exploit stress in cancer cells as well as to overcome resistance.

Targets



To bring forward a new image-guided therapeutic approach, involving precision radiotherapy or drug treatment.



To discover seven new cancer drugs over the five-year period, aiming to include:

- two drugs against especially challenging and novel targets
- one drug targeted against a novel evolutionary mechanism
- one new immunotherapy.

Pillar 3

Smarter, kinder treatments



We will move a step closer to cure by bringing personalised treatments into the clinic and developing them for patients.

3 >



Now



'We need to drive further innovations in the design of clinical trials'

The ICR and The Royal Marsden together run a world-leading programme of clinical trials – a mixture of pioneering, early-phase 'bench to bedside' trials of personalised cancer treatments, and larger, later-stage trials designed to change clinical practice. Together, we have developed a series of innovative new treatments for patients, including several in the last few years alone. We led critical clinical trials of the prostate cancer drug abiraterone, which was also discovered at the ICR, and olaparib, which exploits genetic principles revealed at the ICR, and has become the first drug targeted against an inherited mutation to reach the market. We have also changed practice through major trials demonstrating the effectiveness of precision radiotherapy.

But there remains an urgent need to develop better treatments for patients. Some cancers remain very hard to treat, as do most cancers once they have begun to spread round the body. And as we get better at treating cancer, more patients are living with the disease long

term – and often coping with serious side-effects from treatment. So we need more effective personalised therapies for cancer, with less severe side-effects than standard treatments.

We need to drive further innovations in the design of clinical trials, so we can better develop drugs that target genetic faults as they arise in a tumour, and scientifically select and assess combinations designed to overcome drug resistance. We also need to be creative in designing trials to evaluate biological agents including immunotherapy, precision radiotherapy, new surgical techniques and novel combination treatments. We need to improve our ability to get treatment right first time through development of molecular diagnostics, biomarkers and adaptive forms of therapy. The focus will be on taking new discoveries into the clinic more quickly and more smartly.



To find out more about clinical trials visit www.cancerbrc.org



Professor Johann de Bono



Combining drugs to improve outcomes

Combination treatment – where drugs or other therapies are used together – is a promising approach to cancer treatment. It has worked well in diseases such as HIV, and has the potential to cut off cancer's evolutionary escape routes and prevent it from becoming drug resistant. But combination treatments can have more severe side-effects than drugs used on their own, and drugs need to be carefully chosen to be complementary in their mechanisms of action, or cancers quickly find ways to evade their effects.

Professor Johann de Bono leads teams of researchers in combining drugs that inhibit different targets critical to cancer's growth and survival. He and colleagues have, for example, assessed several paired drug combinations including the PARP inhibitor olaparib, and shown remissions in ovarian, breast and prostate cancers that have defects in their systems for repairing damage to DNA. The combination of olaparib with the AKT inhibitor AZD5363, a drug discovered by Professor Ian Collins and colleagues at the ICR in collaboration with two pharmaceutical companies, has achieved impressive tumour responses in multiple patients.

Researchers at the ICR and The Royal Marsden are now developing multiple-drug combinations that target many of the different faults present within patients' tumours, and that can be adapted during the course of treatment to overcome drug resistance. They are scientifically selecting combinations using computational algorithms, and putting molecularly targeted drugs together with other treatments including immunotherapy and radiotherapy. Innovative clinical trial designs are helping overcome the challenges of trialling such combinations in patients.



Future



- We will match patients to the best targeted treatment using biomarkers, and carry out innovative clinical trials of smarter, kinder personalised therapies.
- We will enhance precision targeting of radiation at tumours using advanced imaging and biological markers, to create new, more effective forms of radiotherapy with fewer side-effects.
- We will design clinical trials of novel treatment schedules aimed at anticipating and adapting to the emergence of drug resistance.
- We will bring the advances in personalised medicine that we have seen already in adult cancers to children through new paediatric cancer trials.
- We will devise novel clinical trials to accelerate the development of innovative combination treatments, such as use of targeted drugs together with immunotherapy or radiotherapy.
- We will develop new precision forms of surgery designed to be more effective and less invasive than current treatments, and aim to reduce post-operative complications.

How?



- ▶ We will create innovative designs for clinical trials to assess combination treatments – including dose escalation in individual patients, and new statistical design approaches for testing hypotheses.
- ▶ We will develop genetic and imaging biomarkers predicting response to treatment with targeted drugs, radiotherapy and immunotherapy, and incorporate these within novel clinical trial designs.
- ▶ We will build a national co-operative group drawn from UK centres of excellence to lead on the development, assessment and clinical implementation of new radiotherapy technologies.
- ▶ We will grow our expertise in medical physics, and apply this expertise to the creation of new forms of precision radiotherapy.
- ▶ We will play a leading role in a major, nationwide matrix trial for children, in which patients are directed by genetic testing to one of a range of targeted therapies.
- ▶ We will apply use of cancer biomarkers to surgery, as a means of selecting patients for treatment and judging excision margins during operations.

Targets



To deliver practice-changing clinical trial evidence of improved survival or quality of life involving innovative small-molecule drugs, immunotherapy, precision radiotherapy, surgical techniques or new combinations.



To demonstrate the benefits for patients of image-guided precision radiotherapy by completing the first phase of clinical evaluation of the MR Linac – the world's most advanced radiotherapy machine.



Professor Uwe Oelfke



Tracking tumour movement in real time

The ICR and The Royal Marsden have made great advances in the development of precision radiotherapy, which targets tumours more effectively while reducing damage to healthy tissue. Intensity-modulated radiotherapy can shape radiation beams to closely fit the tumour, while image-guided therapy uses frequent imaging during a course of radiation to improve the accuracy of treatment. We have developed ways of giving radiation in fewer but higher doses, reducing the number of hospital appointments for patients and avoiding serious side-effects.

Professor Uwe Oelfke is now pioneering new-generation treatments that use sophisticated imaging to target radiotherapy at tumours in real time, even as they move in the body as patients breathe. He has developed software that tracks tumour movement to within one hundredth of a second. The software could be incorporated into current high-tech forms of radiotherapy to further improve their accuracy.

But we have even greater ambitions. The ICR and The Royal Marsden will be the first organisations in the UK to gain access to the MR Linac, a state-of-the-art radiotherapy system, after entering into a pioneering research collaboration with manufacturer Elekta. This offers the potential to combine two advanced technologies: magnetic resonance imaging (MRI) and a linear accelerator.

Professor Oelfke and colleagues will use the MR Linac to develop the next generation of image-guided radiotherapy by replacing conventional X-ray-guidance with MRI. Using MRI's superior soft-tissue contrast in real time during treatment has the potential to revolutionise radiotherapy practice.

Pillar 4

Making it count



We will deliver better outcomes and improved quality of life for patients by establishing innovative treatments, diagnostics and strategies for prevention as part of routine healthcare.



Now



'It is essential that advances in treatment or prevention are embedded into routine healthcare'

It is not enough to make important discoveries, or even to develop new treatments. If the ICR and The Royal Marsden are to have a real impact on patients' lives, it is essential that advances in treatment or prevention are embedded into routine healthcare. These advances need to be implemented in the best possible way, so the most people benefit with the least unnecessary treatment and side-effects.

We have already successfully driven many of our research findings into patient care. The landmark START trials, for example, changed the scheduling of radiotherapy for breast cancer in the UK and worldwide – allowing patients to benefit from fewer hospital appointments, and saving money for the NHS. The MAGIC trial, led by Professor David Cunningham, established chemotherapy before and after surgery as standard of care for stomach and oesophageal cancer, and increased cure rates.

In cancer genetics, we have been instrumental in embedding testing of cancer genes into mainstream healthcare, and in establishing how best to manage patients who are identified as being at high cancer risk. And Professor Mitch Dowsett's TransATAC study helped usher in a new era where molecular profiling is now used routinely on the NHS to predict outcomes in breast cancer.

Over the next five years, we will put even greater emphasis on ensuring our research is made to count for patients. We will lead moves to establish treatments as part of routine healthcare – by studying cost-benefit and driving adoption through networks. We will determine who will respond best to treatment, how to minimise side-effects and how best to tailor treatment for older patients. And we will go beyond an understanding of cancer risk to assess new strategies for prevention.



Find out more about patient involvement at www.cancerbrc.org



Dr Anna Kirby

Reducing the risk of heart problems

The ICR and The Royal Marsden have always been committed to easing the impact of cancer treatment on quality of life. We have discovered genetic markers that identify patients with less aggressive cancers who can avoid harsher treatments. We have fine-tuned radiotherapy to reduce the impact on healthy tissue. And we have launched the first clinical study to examine the impact of radiotherapy on gut bacteria to try to ease gut symptoms.

A recent project to reduce side-effects in breast cancer was so successful it has been rolled out across the UK. Dr Anna Kirby led the UK HeartSpare study, asking patients with localised, left-sided breast cancer to hold their breath during radiotherapy for 20 seconds to pull the heart away from the radiation beam. The technique helped reduce the risk of heart problems later in life, and has become standard practice on the NHS. Dr Kirby has since extended the research to include patients with cancer that has spread to the lymph nodes.

Studies like this are increasingly important, because as patients live longer after cancer treatment, the long-term side-effects of drugs and radiotherapy are becoming more apparent. We plan to look more closely at cancer survivors to assess the long-term effects of treatments on quality of life. We will identify biomarkers assessing whether a drug is likely to be toxic to a particular patient. We will find ways of predicting in advance whether different groups of patients will benefit from a therapy and what side-effects they will experience – to help guide personalised healthcare.



Future



- ▶ We will work collaboratively across the UK and internationally to build evidence of the effectiveness of new treatments and technologies, and will lead efforts to embed them into healthcare.
- ▶ We will take cancer genetics further into mainstream healthcare so that many more patients and their families can benefit from testing.
- ▶ We will carry out health economic assessments to evaluate the cost-effectiveness of new treatments and technologies, and the overall cost to the NHS, as a means of supporting adoption across the UK.
- ▶ We will put our research into the genetic, environmental and behavioural risks of cancer into practice by evaluating new cancer prevention programmes – and by helping others to do so.
- ▶ We will reduce the potential harms of treatment by assessing long-term adverse effects, finding ways to ease side-effects, and developing better ways of deciding whether patients will benefit from treatment.

How?



▶ We will co-ordinate methodological developments in clinical trials to provide evidence of patient benefit that can support uptake of new treatments or technologies by health systems.

▶ We will collaborate with academic partners to produce detailed economic modelling of cost and cost-effectiveness.

▶ We will use biomarkers to predict patients' response to treatment and side-effects, and analyse long-term data on adverse effects, to guide decisions on care and improve survivorship from cancer.

▶ The Royal Marsden will drive moves to develop and spread best practice in cancer care and diagnose patients earlier through its lead role in the Vanguard New Care Models Programme for reshaping the NHS.

▶ We will develop new care models extending access to genetic testing on the NHS, and assess novel ways of preventing cancers or detecting them early in high-risk patients.

▶ We will make our huge reservoir of data on cancer genetics and epidemiology publicly available, so academics and health organisations can use it to develop new public health and prevention programmes.

▶ We will engage extensively with patients and their families, to make sure their voice is heard and that research is designed to meet their needs.

Targets



To help implement wider use of genetic testing on the NHS, enabling more effective treatment and earlier detection or prevention of cancers in high-risk groups.



To bring about the adoption of innovative approaches to treatment, early diagnosis and prevention by providing evidence of cost-effectiveness, redesigning care pathways and influencing health services.



Professor Nazneen Rahman



Taking cancer genetics into the mainstream

The ICR is a world leader in the genetics and epidemiology of cancer risk. We have identified many cancer genes, including the BRCA2 breast cancer gene, and helped to tease out how genetic, environmental and lifestyle factors come together to shape cancer risk.

We believe it is time to increase the impact of our research by putting more information about cancer risk into action. We have already begun to collate information on genetics and cancer risk to find ways of stratifying patients. For example, inherited genetic mutations can now identify the 0.7 per cent of women who have a three-fold increased risk of breast cancer and the 1 per cent of men with a six-fold increased risk of prostate cancer.

The ICR and The Royal Marsden will now start to put to use our knowledge of cancer risk to identify people who have inherited cancer genes, support those individuals in prevention or active surveillance programmes, and provide appropriate counselling for family members.

Professor Nazneen Rahman wants to increase access to genetic testing, by making it part of routine care for cancer patients. Her ambitious Mainstreaming Cancer Genetics programme is developing new care pathways and technologies to test for cancer predisposition genes. The idea is to widen access to testing by providing rapid tests at reduced cost. Knowledge of a person's genetic make-up can be vitally helpful when treating cancer, and genetic tests can provide information about the cause of the cancer and the best treatments to use.

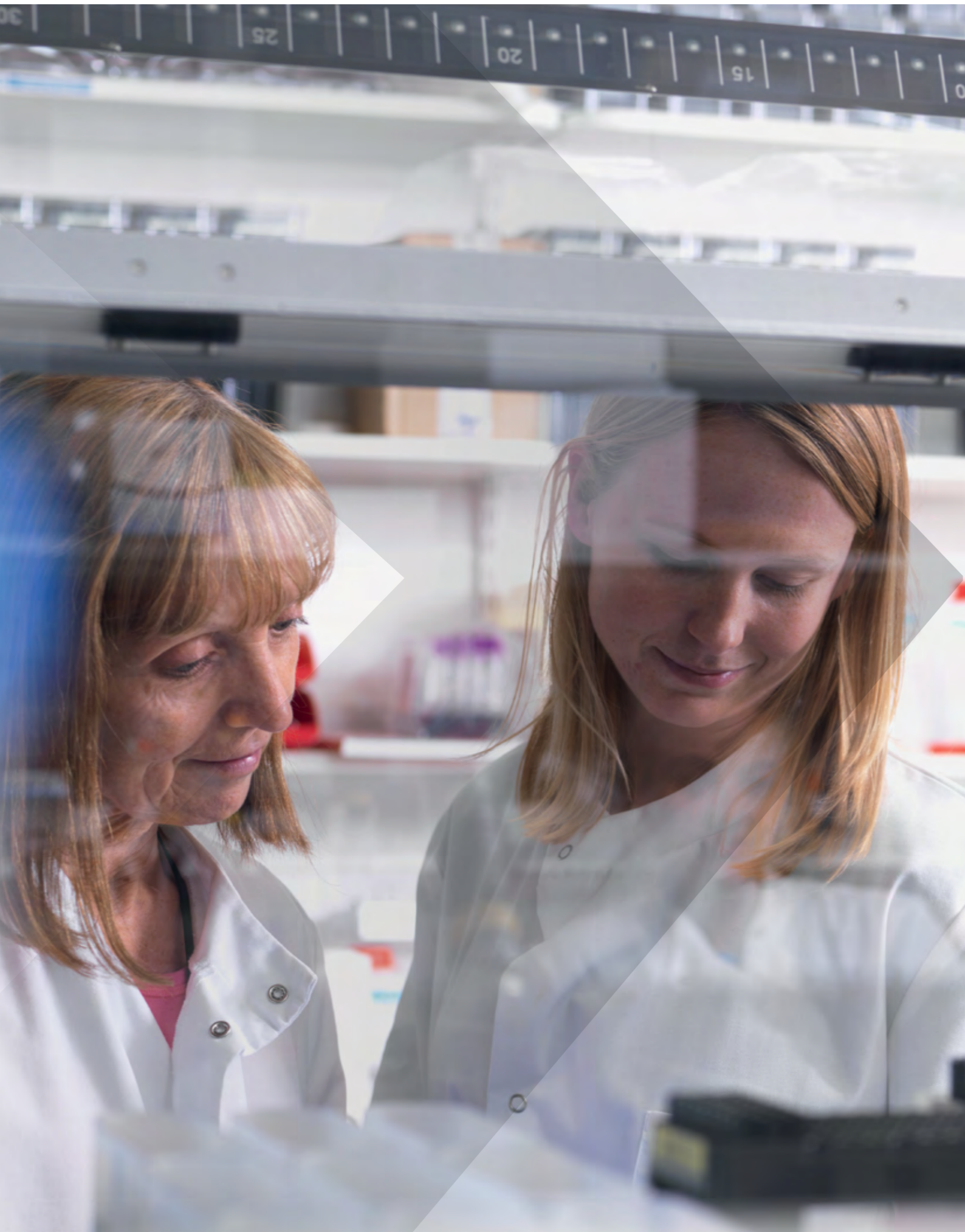
Benefiting a wider range of cancer patients

The ICR and The Royal Marsden have always sought to benefit patients with many different kinds of cancer. Often the best way to do this has been to carry out world-leading research in particular cancer types – especially breast cancer and prostate cancer – and then to find ways of applying our findings to other forms of cancer too. These days, what matters most is often a cancer's specific molecular profile, rather than its site of origin, and much of our research will be relevant across the field of cancer.

But some cancer types continue to have much better survival rates than others. Our research has helped to deliver dramatic improvements in treatment and care for breast cancer, prostate cancer, blood cancers and children's cancers – but in other areas, such as lung cancer and pancreatic cancer, death rates remain very high. Our strategy will aim to deliver benefits for a wider range of cancer patients, including helping to improve survival for cancers where outcomes are particularly poor.

We will continue to build on our success in those cancer types where we have been traditionally strong, working particularly with Breast Cancer Now on breast cancer, Prostate Cancer UK and Movember on prostate cancer, Bloodwise on leukaemia and lymphoma, and Myeloma UK on myeloma. We will also create new areas of strength in cancers of unmet need, such as lung cancer, pancreatic cancer, and cancers of the stomach and oesophagus. We will continue to do research into children's cancer and other rare tumour types too. The ICR and The Royal Marsden will use a matrix-like approach to bring together scientists and clinicians who work in particular tumour types, and ensure each type of cancer benefits from advances in research more broadly.





Foundations

Our strategy is an ambitious attempt to turn scientific discovery into real benefits for cancer patients. To achieve our aims, we need to put down strong foundations in the way we organise and support our research.

The following section sets out four foundations to underpin the pillars of our research strategy: putting in place the people and skills we need, establishing world-class digital infrastructure and research facilities, delivering a culture that promotes talent and collaboration, and working in close partnership with other organisations. Each of these foundations supports every aspect of our research across the ICR and The Royal Marsden.

In science, ambition costs money. We will only deliver on our research priorities by putting in place significant investment and organisational support. The ICR's new organisational strategy will set out how we will build the foundations outlined here by generating and allocating the resources needed to support our science and teaching.

- **1**
People and skills
- **2**
Digital and infrastructure
- **3**
Culture and team science
- **4**
Partnership

People and skills

Talented, brilliant, passionate people lie at the heart of our research strategy. Our plans are ambitious and wide ranging – and we will need to recruit and train the brightest and best scientists and clinicians to deliver them.

We plan to increase the number of researchers working at the ICR, so we can build on our existing strengths while also expanding into promising new areas of research. We will for example need world-class cancer immunologists, medicinal chemists, cancer biologists and clinical researchers. We will also be recruiting a new cadre of 'integrated' research staff, in areas such as computational science, bioinformatics and molecular pathology, to work across disciplines and be focal points for multidisciplinary collaboration.

We will not always be able to recruit people with the right skills – in which case we will develop them instead. We will train staff members and PhD students in the latest technical areas, and in high-demand disciplines such as Big Data.

➤ We will expand the overall number of Faculty at the ICR so we have the capacity and skills we need to build on our existing strengths and move into new areas of research.

➤ We are recruiting a new wave of senior leaders in scientific and clinical research to drive forward our strategy, including specialists in cancer therapeutics, cancer biology, evolutionary biology and paediatrics.

- We will recruit new specialists in areas of science where we will be expanding our work, including immunology, cell and structural biology, and molecular pathology.
- We will be recruiting or training new 'integrated' research staff in computational science and bioinformatics, designed to work across multiple areas of science, and with flexible skills so they can adapt to new technologies.
- We will design the ICR's PhD programmes with the aim of equipping scientists with multidisciplinary research skills, including in molecular pathology and bioinformatics.
- The ICR and The Royal Marsden will work together on formal succession planning for senior researchers – in particular for clinical academics, where there is fierce competition for the best people.
- We will nurture NHS clinicians who are growing their interest in research by expanding the pool of honorary Faculty members at the ICR.



To find out more about careers at the ICR visit www.icr.ac.uk/careers



Dr Carmen Rodriguez Gonzalez

From astrophysics to a career in cancer research

To defeat cancer we need the very best minds from across the spectrum of science. The ICR recruits researchers from a wide range of disciplines to drive forward our science – including people from well outside the traditional boundaries of medical research. Using vast amounts of scientific and clinical data is relatively new in cancer research – but in astrophysics, the analysis of big, complex datasets has been a longstanding challenge.

Dr Carmen Rodriguez Gonzalez was previously an astrophysics research scholar, with a strong background in the analysis of data. She has now joined the ICR as a leading data scientist applying analytical and statistical techniques developed over decades by the astrophysics community to biological challenges. Career transitions like this can be powerful catalysts for scientific innovation and will help us unravel cancer data to open new avenues for treatment or prevention.

Digital and infrastructure

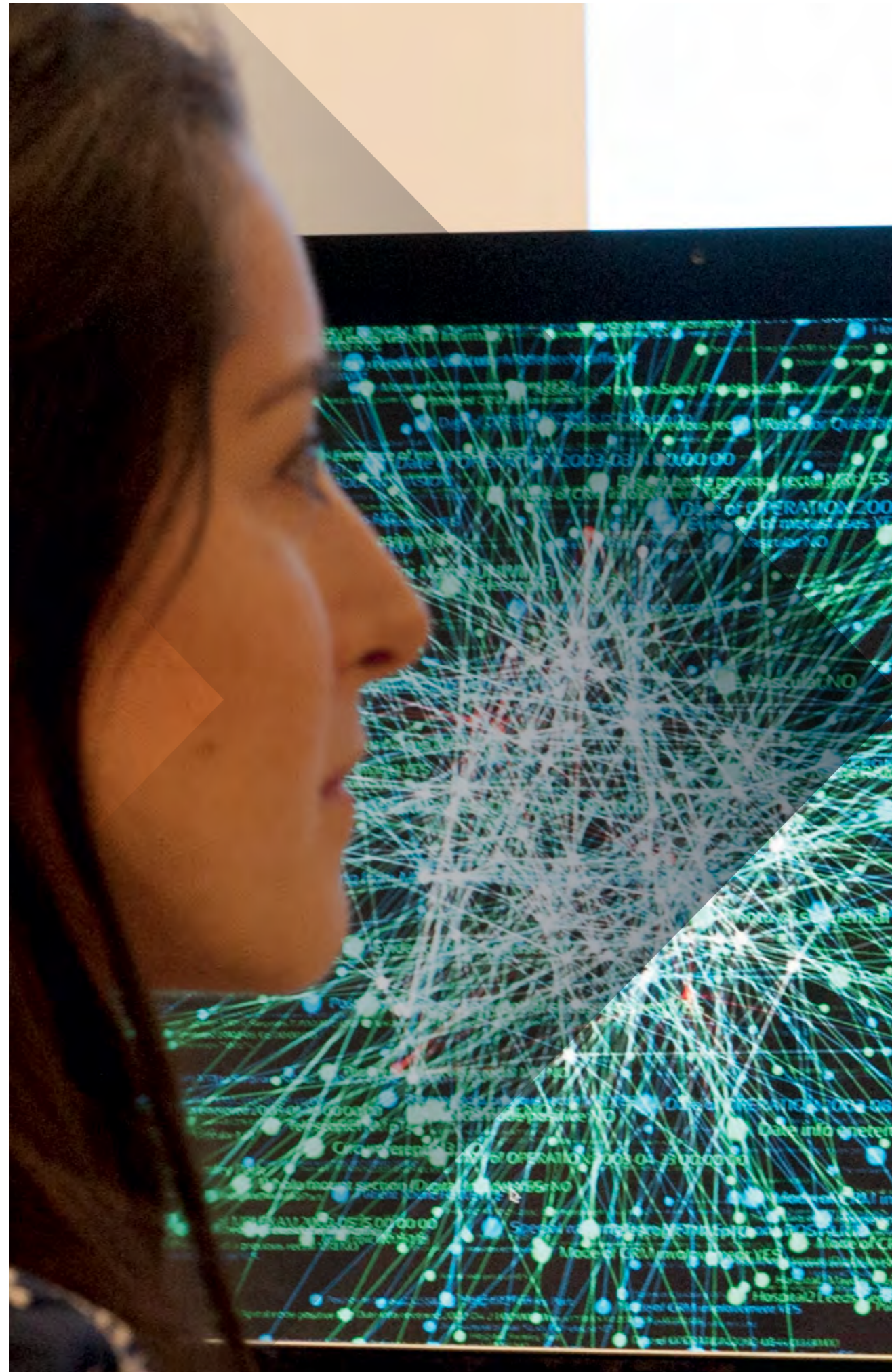
We are in exciting times for cancer research, with huge advances in computing and technology opening an opportunity for rapid progress in our understanding of cancer. It is essential that the ICR and The Royal Marsden take full advantage of these new technologies in delivering our research strategy.

We are now living in an era of Big Data, with the ability to collect and mine huge amounts of information from the laboratory and from patients, including genomic information, imaging and clinical data. We need a step change across both organisations in our ability to navigate Big Data, and store, share, integrate and analyse it effectively.

The ICR and The Royal Marsden also need to invest in other aspects of our research infrastructure to support the priorities identified in our joint strategy. We will enhance our facilities across a range of areas including cancer biology, immunology, genomics and clinical research, and will introduce more advanced animal models to study metastasis and the microenvironment. We will also create physical spaces that bring researchers together and encourage multidisciplinary collaboration.

➤ We are investing substantially in new digital infrastructure for the storage, transfer and analysis of Big Data, and launching a new Digital Programme to coordinate investment, and ensure it meets the needs of scientists.

- We are creating a Knowledge Hub for sharing and analysis of data across the ICR and The Royal Marsden, and developing our advanced CanSAR database to enhance knowledge sharing across the wider research community.
- We will harness developments in e-health, for example through remote monitoring of patients and self-reporting of outcomes, to improve data collection on clinical trials.
- We will use applications for major grants such as the Biomedical Research Centre and Cancer Research UK Centre to enhance clinical research and bioinformatics facilities.
- The ICR will build a new Centre for Cancer Drug Discovery to greatly enhance our capacity and facilities for drug discovery, and integrate it with evolutionary biology.
- We will conduct a review of all our research infrastructure requirements, with the aim of finding more effective and efficient ways of delivering scientific services.
- We will create state-of-the-art scientific facilities to support our expansion into new areas of research such as immunology and the study of genome instability.



Dr Bissan Al-Lazikani

Navigating the Big Data landscape

Scientists and clinicians are generating data like never before. Thanks to an explosion in technology, it is now possible to collect huge amounts of data in areas such as genomics and cancer imaging, alongside clinical data collected from patients throughout diagnosis, treatment and follow-up. Navigating this Big Data landscape is key to understanding the complex interplay between a patient, a cancer and its treatment and, consequently, to delivering better outcomes for patients.

Dr Bissan Al-Lazikani is leading on an important initiative within the ICR and The Royal Marsden to develop The Knowledge Hub as a way of meeting the Big Data challenge. The aim is to create a sophisticated platform for sharing, standardising and analysing huge amounts of scientific and clinical data. It will bring researchers together, and help them to collaborate on analysis of complex datasets, as a means of identifying new approaches to combination or adaptive cancer treatment.

Culture and team science

We want to create the best possible culture at the ICR and The Royal Marsden – open, equal and collaborative. If we are to defeat cancer, we must make use of all the talents available to us, and harness their skills and expertise by encouraging them to work together in multidisciplinary teams.

We have been working hard to deliver an organisational culture where men and women with a wide variety of backgrounds and skills can thrive. We have introduced a range of initiatives designed to ensure that everyone is given the same chance to progress to leadership positions in science, as part of a more general commitment to equal opportunity for all.

We are also determined that our organisational culture should strongly encourage researchers from different disciplines to work together in collaboration. We believe that many of the biggest challenges in cancer research will only be met by adopting a multidisciplinary ‘team science’ approach, with for example various types of scientists, clinicians, mathematicians and computational experts working closely together. We need to recognise, incentivise and reward effective teamwork, so that scientists and clinicians from different fields are actively encouraged to work together.

➤ We will pioneer new ways of working that maximise the opportunities for all our scientists, and particularly women, as part

of our application for an Athena SWAN Gold Award.

- We will ensure all researchers are given the same opportunity to flourish and progress through a strong commitment to equality in everything we do.
- We are developing new leadership programmes for researchers at all levels, as a means of distributing leadership and responsibility across the organisation.
- We will actively promote collaboration across the ICR, through a new prize for the best team science project, and by exploring the rotation of postdocs around laboratories to forge stronger links between teams.
- We will link scientists to multidisciplinary clinical teams on appointment, as a means of promoting team working across the ICR and The Royal Marsden.
- We will be open and transparent in our communication about our science with the public, and will seek the views of patients in shaping our research priorities.
- We will learn from other fields where excellence is achieved through collaboration, such as the re-engineering of team working in Formula 1 and British Cycling.



Professor Paul Workman

Driving efforts for multidisciplinary team science

Much of modern-day science is a team game, and the ICR and The Royal Marsden have worked hard to build strong connections between scientists and clinicians, and across disciplines. Together, we have established structures, cultures and systems that recognise and promote team science.

It's this kind of cultural drive that led to a multidisciplinary team from the ICR and The Royal Marsden winning a prestigious global Team Science Award for its success in taking new cancer drugs from concept to patients. It was the first time that the award, from the American Association for Cancer Research, had been won outside the US.

Professor Paul Workman, the ICR's Chief Executive and a member of the winning team, has personally driven efforts to promote collaboration. He co-hosted the Horizons in Cancer Drug Discovery conference, which gathered together academia, industry, charities and investors to share ideas and build relationships. More recently, Professor Workman launched a Team Science Competition to reward the best multidisciplinary collaboration across the ICR and The Royal Marsden.

Partnership

Neither the ICR nor The Royal Marsden can achieve all our ambitions in isolation. The modern world of cancer research is underpinned by strong partnerships between organisations – sharing knowledge, and pooling complementary expertise and resources. The ICR and The Royal Marsden have worked together in partnership for more than a century, and our relationship is a crucial ingredient in our successes – one that we will strengthen even further over the next five years. To deliver on our ambitious strategy, we will also seek to build upon our many other existing partnerships, such as our relationships with Cancer Research UK, Breast Cancer Now and the National Institute for Health Research. We will need to create fresh partnerships too, in London, across the UK and globally, and with a wide range of public and private bodies. We will need to expand our range of commercial partnerships with biotech, pharma, technology and software companies, as a means of translating our discoveries into medical advances.

➤ We will apply for new funding streams open to research institutions working in collaboration with partners, such as the Cancer Research UK Centres Network Accelerator Awards and other multidisciplinary funding.

- We will build partnerships with academic institutions across London, including Imperial College London and the Francis Crick Institute, as a means of strengthening our research and expanding into new areas such as bioengineering.
- The ICR is working with the London Borough of Sutton, with the support of The Royal Marsden and the Greater London Authority, on a major new initiative to establish The London Cancer Hub on our Sutton site.
- The Royal Marsden is working with The Christie NHS Foundation Trust and University College London Hospitals NHS Foundation Trust on a national programme to improve cancer care, as part of NHS England's Vanguard programme.
- The Royal Marsden will work in partnership with patient representative organisations to help redesign care pathways for cancer and ensure research is focused on patients' needs and priorities.



To find out more about our industry partnerships visit www.icr.ac.uk/enterprise



Professor Kevin Harrington

A UK partnership for radiotherapy

Researchers at the ICR and The Royal Marsden are establishing a new UK collaboration to accelerate the assessment, development and clinical implementation of new radiotherapy technologies. The network will involve world-leading researchers and state-of-the-art equipment from centres of excellence across the UK to ensure that scientific advances quickly benefit patients.

Professor Kevin Harrington will lead the network and will work closely with colleagues in University College London Hospitals, Manchester Cancer Research Centre, The Christie NHS Foundation Trust, Leeds Cancer Centre and the University of Oxford. The network will assess new technologies in phase I and II trials to provide the rationale for subsequent phase III evaluations. It will also develop expertise in medical physics specifically for new types of radiotherapy and will help to design clinical trials to streamline health technology assessments of new technologies in specific tumour types. Research from the network will generate the evidence base required to guide investment in these technologies across the NHS and will help to make policy on their provision throughout the UK.

Assessing progress

The ICR and The Royal Marsden will do all we can to ensure our strategy delivers excellent cancer research, faster progress and real impact on the lives of patients.

We will closely monitor our performance against the targets set in this strategy document, so we can make sure we are meeting our commitments, and can respond quickly to any challenges as they emerge.

We will report our progress against the strategy on an annual basis, and will publish a report at the three-year mark, in 2019, assessing our performance in each of the four pillars quantitatively and qualitatively.

We will also make sure that this is a living strategy document, which is used as the basis for a rolling programme of events, discussions and communications.

At the end of the five-year period, we would expect to have delivered concrete progress in understanding cancer's complexity, discovering innovative new treatments, developing treatments for patients, and establishing practice-changing advances in cancer care.



Working together to defeat cancer

Cancer research is a team effort. The ICR and The Royal Marsden work together with funders, donors, supporters and collaborators to make our research happen, and to take our findings to patients. We would like to take this opportunity to thank all of our valued partners for their continuing support, as we put our new research strategy into action. While we can only highlight some of our funders and collaborators here, we are indebted to all of those who work with us to defeat cancer.



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