Five steps from cancer genetics to treatment
Some unusual allies in defeating cancer
What will your legacy be?
Our mission is to make the discoveries that defeat cancer.
Welcome to the summer 2013 edition of Search. New technologies are revolutionising the face of cancer research, giving us greater insight into the genetic changes driving cancer development. With this knowledge we are able to fight cancer in far more effective and targeted ways. In this issue of Search we highlight the importance of these technologies and the positive impact they may have on cancer patients’ lives.

Our next ambition is to be able to profile all genetic mutations within a tumour, so doctors can provide patients with truly personalised treatment. We are aiming to raise £3.2 million in support of our new Tumour Profiling Unit, to accelerate this work. With your help, we believe that all patients in the UK could receive genetic profiling of their tumours within the next 10 years.

The ICR has some of the best minds in cancer research dedicated to its mission. But their success will be in no small part thanks to the help and commitment of friends and supporters like you. In this issue, you can read about our former Director, Professor Robin Weiss who has decided to remember the ICR in his Will, as well as this year’s intrepid London Marathon runners.

We are lucky enough to have many more donors and supporters like Robin and our runners, and I would like to say how grateful we are for your ongoing generosity and hard work on our behalf.

Thank you very much!

Lara Jukes
Director of Development
The Institute of Cancer Research, London

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Alliance to bring lung cancer trials to population of six million

The Institute of Cancer Research (ICR) is uniting with leading research institutions and hospitals across London to transform the care of lung cancer patients, with plans to invite patients over a population of six million into a pioneering new programme of clinical trials.

The London Lung Cancer Alliance aims to deliver dramatic benefits for patients in London initially, then nationally and worldwide.

Researchers will genetically profile tumours and test a panel of targeted therapies – many previously untried in lung cancer – in those with particular molecular defects. They will also develop ‘liquid biopsy’ blood tests for patients who are too ill to biopsy, or to monitor whether drugs are working and assess for signs of resistance.

The ICR’s Chief Executive, Professor Alan Ashworth, who is chairing the London Lung Cancer Alliance, said: “For far too long the prospects for patients with lung cancer have been bleak. But now we have an opportunity to change this as new genetic techniques for studying tumours open up the prospect of trialling novel targeted therapies for lung cancer.”

Drug target for incurable childhood brain cancer discovered

A team of ICR researchers have uncovered the genetic causes of a rare but lethal form of childhood brain cancer, known as glioblastoma. The research opens up the prospect of an effective treatment for the disease for the first time.

The study found that in some glioblastomas a chain of genetic activity triggers increases in the levels of a protein called MYCN, which is strongly linked to cancer.

Drugs which can block MYCN’s activity are currently in clinical trials for other types of cancer, and it is possible these could help extend the lives of young patients with glioblastoma too.

Study leader Dr Chris Jones, who heads the glioma team at the ICR, said: “We anticipate we will be able to quickly test our hypothesis in the clinic so paediatric glioblastoma patients with this specific mutation may benefit from receiving novel agents.”

Sadly, at present, children who develop glioblastoma currently only survive for a year on average, but Dr Jones has been inspired by families affected by the disease.

“A diagnosis of glioblastoma in a child is one of the most devastating pieces of news a parent can receive. We are lucky to receive research support from several parent-led foundations. Any progress which prevents other families facing such tragedy hugely motivates my team.”
Prostate cancer patients with BRCA2 mutations require urgent treatment

New research from the ICR and The Royal Marsden has found men who develop prostate cancer after inheriting a faulty BRCA2 gene need immediate surgery or radiotherapy rather than being placed under surveillance, as their disease is more aggressive than in men without the faulty gene.

These results could challenge current NHS guidelines for prostate cancer, under which BRCA2 mutation carriers are currently offered the same treatment options as non-carriers.

It is often difficult to tell at diagnosis whether prostate cancer will be life-threatening or not, and while treatment options for early-stage disease include surgery and radiotherapy, many men instead receive active surveillance to see if the disease starts to progress.

Study leader Professor Ros Eeles, Professor of Oncogenetics at the ICR and Honorary Consultant in Clinical Oncology at The Royal Marsden, explains: “It is clear from our study that prostate cancers linked to inheritance of the BRCA2 cancer gene are more deadly than other types. Affected men need to be offered immediate surgery or radiotherapy, even for early-stage cases that would otherwise be classified as low-risk.”

Hidden potential of cutting-edge cancer drugs unlocked

A team of ICR researchers have made a new discovery into how a class of cancer drugs, known as kinase inhibitors, attack tumours. This step forward may help patients treated with these drugs live for much longer than they do now.

Kinase inhibitors are an effective treatment, but often only extend life by around three to six months. However, the team, in collaboration with the University of Sussex, believe they can unlock the true potential of the drugs by changing the way they are used – after uncovering a hidden mechanism of action.

Professor Paul Workman, Deputy Chief Executive of the ICR, said: “We already knew these drugs were very effective, but we now think they could be even better. We found that several clinically used kinase inhibitors could not only disable cancer-causing kinases but also cause their destruction. It’s an unexpected and exciting discovery, with major implications for how to dose these drugs to help patients live for longer.”

The researchers now plan to conduct clinical trials using kinase inhibitors at higher doses.
Cancer is a hugely complex genetic disease, with genes we inherit from our parents, and new mutations arising within our bodies, all playing a part in its development. Our scientists and clinicians are working to deliver personalised strategies for cancer treatment and prevention, tailored to the genetics of the individual patient – but that requires a thorough understanding of how genes cause cancer. Here is a step-by-step guide to the ICR’s work in moving from cancer genetics to targeted therapies.

1. Understanding our inherited genetics
Cancer is caused by mutations in our DNA. Sometimes we inherit mutations from our parents which can predispose us to cancer and it is crucial that we identify these and understand the risk they convey.

Professor Ros Eeles, Professor of Oncogenetics at the ICR, specialises in studying the genetic ‘hand of cards’ we are dealt, and is in pursuit of the genetic variants that increase men’s risk of prostate cancer. Results from the largest ever study into inherited risk factors for prostate cancer now make genetic screening for the disease a real possibility.

“The results from the study allow us, for the first time, to identify men who have a very high risk of developing prostate cancer during their lifetime through inheritance of multiple risk genetic variants,” she says.

“If we can show from further studies that such men benefit from regular screening, we could have a big impact on the number of people dying from the disease, which is still far too high.”

In families with a strong history of cancer, genetic testing is important in determining if an

“Advances in technology are rapidly transforming our understanding of the genetic causes of cancer. We are now able to pinpoint the precise set of genes that appear to be driving a cancer’s development, giving targets for the next generation of cancer drugs”

Professor Paul Workman, Deputy Chief Executive of the ICR
inherited cancer-causing gene is responsible. Relatives who have not inherited the gene mutation can be reassured that they are not at increased risk of cancer, while those who have the gene mutation can benefit from screening and strategies to reduce their risk.

Pinpointing mutations that kick-start cancer

Lots of genetic faults contribute to cancer, but researchers at the ICR are attempting to pinpoint the very earliest mutations responsible for the disease – in the belief that these will make ideal targets for treatment.

Professor Richard Houlston, Professor of Molecular and Population Genetics, and Professor Mel Greaves, Professor of Cell Biology, recently carried out a unique study sequencing the entire genomes of two pairs of identical twins with leukaemia. Their research uncovered clues to the genetic origins of the disease in the mother’s womb.

Professor Mel Greaves explains: “It’s unusual in cancer to be able to identify the mutation that kick starts the whole process. Twin children provide unique insight into the silent beginnings of leukaemia. One implication of these new findings is that the first or ‘founder’ mutation might provide an appropriate target for therapy as, unlike all subsequent changes, it is present in every cancer cell.”

Leukaemia is the most common cancer diagnosed in children, affecting a third of young cancer sufferers and killing 100 children a year in the UK.

Identifying the mutations driving cancer

Targeted drug development is dependent upon researchers understanding which of the many mutations in tumours are actually driving cancer and which are harmless.

Dr Rachael Natrajan, Team Leader in Functional Genomics, is searching for new mutations in genes which contribute to breast cancer development as a route to identifying more personalised cancer treatment.

“We are mining huge amounts of genomic data to look for recurrent changes associated with specific tumour types,” she says.

“We can then predict which mutations drive cancer development, and these become the focus of future targeted treatment.”

Driven by her passion for problem solving, Dr Natrajan aims to identify new treatments for breast cancer which will allow clinicians to choose the most suitable non-toxic drug for that particular patient.

“My ultimate motivation is witnessing my research translate into potential treatments for cancer patients”

Dr Rachael Natrajan, Team Leader in Functional Genomics
“It is essential that we continue to expand our knowledge of cancer genetics in order to improve treatment for breast cancer patients. It is exciting to find new genes which could be involved in causing and driving breast cancer, but my ultimate motivation is witnessing my research translate into potential treatments for cancer patients,” explains Dr Natrajan.

Profiling patients’ tumours
As we develop more therapies targeted to the gene mutations that drive cancer, it becomes critical that we can genetically profile individual patients’ tumours – so we can deliver truly personalised medicine.

That’s the ambition of the ICR’s newly opened Tumour Profiling Unit (TPU). It aims to change the way in which clinicians diagnose and monitor cancer, enabling doctors to develop treatment programmes tailored to the specific DNA mutations driving a cancer, at that particular point in time.

Professor Alan Ashworth, Chief Executive of the ICR, says: “Genome profiling opens up the possibility of using drugs in a context in which they were not originally developed. None of this is science fiction. It’s happening in a number of places around the world but we feel it will be absolutely routine within the next five to 10 years for every cancer patient.”
“Our new personalised drugs are having a positive impact on prostate and ovarian cancer patients. Giving the right drug to the right patient ensures they receive targeted treatment”

Professor Stan Kaye, Head of Clinical Studies at the ICR and Honorary Consultant at The Royal Marsden

The Discovery Club, a consortium of philanthropic investors, is helping to support this ground-breaking research to make personalised treatment day-to-day practice. With support from The Discovery Club, researchers at the TPU will be able to repeatedly test cancer samples to see how the tumour changes, as a means of understanding why drug resistance develops. The ICR is aiming to raise £3.2m to support the TPU in building up a picture of how cancer genes affect response to treatment.

**Discovering targeted cancer treatments**

One of the greatest advances in cancer care over the past decade has been the rise of targeted therapies and personalised medicine. Unlike traditional chemotherapy, targeted cancer drugs attack specific genetic abnormalities driving cancers. That specificity can not only make them more effective but also reduce the levels of side-effects.

Professor Stan Kaye, Head of Clinical Studies at the ICR and Honorary Consultant at The Royal Marsden, has been at the forefront of our attempt to discover and develop more targeted treatments.

“The ICR is one of the best places in the world to undertake clinical drug development. We have discovered 16 new cancer drug candidates since 2005 and progressed six to Phase I clinical trial,” he says.

The drug vemurafenib, now commercialised as Zelboraf, is a personalised medicine for melanoma patients with a mutation on the BRAF gene. The drug’s development was based on ICR research uncovering the key mutations to BRAF, and it has been shown to be nine times more effective than chemotherapy. It is now available for patients in the US and Europe.

If you are interested in joining our Discovery Club, or would like more information, please contact Caroline Totterdill on 020 7153 5304 or by email on caroline.totterdill@icr.ac.uk

If you would like more information about supporting ICR, please visit our Support Us pages on www.icr.ac.uk
The ICR is leading a new initiative, the Mainstreaming Cancer Genetics (MCG) programme, which aims to make genetic testing part of routine care for cancer patients.

Led by doctors at the ICR in collaboration with The Royal Marsden, the Wellcome Trust Centre for Human Genetics and Illumina Inc, the programme will implement a new patient pathway for cancer gene testing so that more genes can be tested in more people.

Mutations in some genes, known as cancer predisposition genes, greatly increase the likelihood that a person will get cancer. Recent advances in methods for reading the genetic code, known as sequencing, mean that looking for gene mutations is now faster and more affordable than ever before.

The programme aims to develop the laboratory, analytical, interpretative and NHS clinical capabilities required to make cancer predisposition gene testing information routinely available in the clinic. It will lay the foundations so every cancer patient can have access to genetic testing.

Professor Nazneen Rahman, lead investigator of the programme and Head of Genetics at the ICR and the Cancer Genetics Clinical Unit at The Royal Marsden, explains:

“It is very important to know if a mutation in a person’s genetic blueprint has caused their cancer. It allows more personalised treatment, so for example such people are often at risk of getting another cancer and may choose to have more comprehensive surgery, or may need different medicines, or extra monitoring. Identifying people with cancer due to gene mutations and offering testing to their relatives is a very effective way of helping people at highest risk of cancer before they develop the disease.”

The MCG programme is funded by the Wellcome Trust and will run for three years from 2013-2016.

For more information please visit the website: www.mcgprogramme.com
Viruses are normally considered enemies of human health, but for one ICR researcher, they are a key weapon in the battle to defeat cancer.

Professor Kevin Harrington is a leader in the field of oncolytic virotherapy, which aims to manipulate viruses in order to destroy tumours.

“In effect, we are fighting fire with fire by giving cancer a virus,” explains Professor Harrington, who hopes these new treatments will improve prognosis for patients with hard-to-treat cancers such as head and neck tumours.

Professor Harrington has recently been appointed Joint Head of Radiotherapy and Imaging at the ICR, and is also an Honorary Consultant at The Royal Marsden. Professor Harrington is investigating whether viruses can be used to render tumours more sensitive to radiotherapy, as a means of delivering more targeted treatment with fewer side-effects.

His research has shown positive results in clinical trials. His team demonstrated the preclinical benefits of a unmodified reovirus in combination with two chemotherapy drugs, and took their research into Phase III clinical trials. Modified herpes simplex, the cold sore virus, has also delivered positive results in phase I and II clinical trials for patients with advanced malignant melanomas, and is now undergoing phase III clinical trials.

“My biggest achievement, without doubt, is being part of the research team for these two clinical trials. The results for herpes simplex virus indicate the first positive phase III clinical trial outside of China – this is an extremely exciting result.”

A leading ICR researcher has turned to some strange allies in the fight against cancer – viruses.

**Fighting fire with fire**

**CV**
- **Name:** Professor Kevin Harrington
- **Year joined the ICR:** 2001
- **Specialist subject:** Head and neck cancers
- **Research interests:** Oncolytic virotherapy and radiosensitiser drugs
- **Greatest achievement:** Achieving positive results in clinical trials for both virotherapy and radiosensitiser drugs
- **In his own words:** “The ICR is such an inspirational place to work. There is always someone who is brighter than you, or who tackles a problem in a different way! The best minds in the country really are working together to defeat cancer.”
Making a science career add up

For one ICR researcher, financial services provided an unconventional route to the laboratory

Dr Lauren Baker is a prize-winning postdoctoral training fellow in radiotherapy and imaging, whose work uses high-tech techniques to investigate whether a patient’s cancer has become resistant to treatment.

But Dr Baker’s route into academic science was not a conventional one. She grew up in south-east London and attended an all-girls school where science was not actively promoted as a career for women. After qualifying and working as a financial services advisor, Dr Baker decided that this career path was not for her.

“I wanted to feel like I was making a difference,” she reflects.

Remembering how much she had enjoyed science at school, she secured a new role as a laboratory assistant.

“The moment I looked down the microscope and saw chromosomes, I knew that I had made the right choice. I was hooked.”

After obtaining a degree, she moved to the ICR to do a PhD before gaining her current position. She considers that her unconventional route into science provided her with a valuable set of problem-solving skills and experiences which are useful for her chosen career path.

Dr Baker has recently been awarded a prestigious American Association for Cancer Research (AACR) Women in Cancer Research Scholar Award. The AACR hails the award winners as representing the best and brightest young female scientists.

Dr Baker is an active proponent of the promotion of science as a career path for
“The moment I looked down the microscope and saw chromosomes, I knew that I had made the right choice. I was hooked”

both men and women. She is an ambassador for a programme promoting the value of science, technology and engineering, and visits schools just like the one that she originally attended, to inspire young people to consider a scientific career.

She is also supporting the ICR’s bid to be recognised by the Athena Swan programme for promoting women’s roles in science.

Before the 1970s, fewer than one in 10 scientists were women. Now, only a single generation later, more than half of all qualifications in science are awarded to women, and they are establishing careers in many fields of research.

Dr Baker is one of many who is making her mark – and proving a career in science can add up.

CV

Name: Dr Lauren Baker
Year joined ICR: 2007
Areas of work: Testing markers of treatment resistance using non-invasive magnetic resonance imaging
Recent achievement: Awarded a prestigious AACR Women in Cancer Research Scholar Award. The winners are hailed as representing the best and brightest young female cancer scientists

In her own words: “The moment I looked down the microscope and saw chromosomes, I knew that I had made the right choice. I was hooked.”
MEET OUR SUPPORTERS

More than a lifetime dedicated to cancer research

Legacies are a vital part of the ICR’s funding. Professor Robin Weiss, a former Director of the ICR, explains why he decided to add a legacy into his Will to benefit us.

“I was Director from 1980 until 1989 after which I stayed on as Director of Research for a further nine years. During that time, I saw the ICR go from strength to strength and I am proud of the impact its research has had and will continue to have in the future.

“Cancer research is an international endeavour and it is difficult to tell where the next big advance will come from. But the track record of scientists is a very good guide to future success and I consider that the ICR houses some of the best scientists worldwide. It has the superb facilities and organisation to attract the brightest minds to continue this vital work. I have chosen not to specify where my legacy should be spent as I cannot foretell what the most pressing issues will be for the ICR at the time my legacy becomes available. But I do know I want to leave a monetary legacy to match my scientific one.”

“I want to leave a monetary legacy to match my scientific one”
What will your legacy be?

Past legacies have helped fund some of our most important breakthroughs to date and the legacies added to supporters’ Wills today could help us do so much in the future. They could help us train the next generation of world-leading scientists. They could help us further our understanding of the causes of cancer. And ultimately they could help us make the discoveries that defeat cancer.

There are four main steps to making a legacy in your Will to the ICR:

1. **Find a solicitor/Will writer**
   A qualified solicitor or Will writer will be able to help you ensure the legal formalities are followed and that your Will is valid. To find a solicitor or Will writer please go to:
   - The Law Society
     lawsoociety.org.uk/find-a-solicitor
   - The Institute of Professional Will Writers
     ipw.org.uk

2. **Choose the type of gift**
   There are three different types of legacies you could leave us, once you’ve provided for your loved ones:
   - A share in your estate (residuary) – a percentage of your estate once all other legacies and expenses have been settled.
   - A sum of money (pecuniary) – a specific cash gift
   - A specific gift – a non-cash gift such as a property, stocks and shares, a painting or an antique.

3. **Use the right wording**
   In order to make sure your legacy reaches us, please use our full name and registered address:
   The Institute of Cancer Research:
   Royal Cancer Hospital
   123 Old Brompton Rd
   London SW7 3RP

4. **Let us know!**
   Cancer research is an expensive business so we need to be able to plan our income long into the future. Please do let us know if you decide to leave us a legacy.

If you would like more information about leaving a legacy to the ICR, please contact the Legacy Team on 020 7153 5387, or by email on legacy@icr.ac.uk. They will be more than happy to answer any questions you might have.
Getting involved

If you want to get involved and support the ICR, we have some exciting events in the calendar. With everything from running the Berlin Marathon to singing hymns at our Carols from Chelsea, and trekking to ancient Petra, we’re sure you’ll be inspired to take part.

**Berlin Marathon | Sunday 29 September 2013**
Billed as a marathon party on the fastest course in the world, the Berlin Marathon attracts more than 40,000 runners with a million spectators cheering from the sidelines.

**Royal Parks Foundation Half Marathon | Sunday 6 October 2013**
Not sure about tackling a full marathon? Why not try this popular half marathon, which starts and ends in London’s picturesque Hyde Park, passing through Kensington Gardens, Green Park and St James’s Park and taking in many popular London landmarks along the way.

**Carols from Chelsea | Tuesday 3 December 2013**
Held in Wren’s stunning chapel of the Royal Hospital Chelsea, this wonderful carol service is a must in anyone’s events calendar.
Virgin London Marathon | 14 April 2014
As one of the most iconic and popular marathons in the world, the Virgin London Marathon is an essential experience for all marathon runners. If you have your own ballot place, we’d be delighted for you to run for the ICR. Get in touch to join our team.

London to Paris Cycle | 23–27 April 2014
A bike ride challenge connecting two of the world’s most chic capital cities.

Three Cities Cycle (London, Amsterdam and Brussels) | 28 May–1 June 2014
An epic cycle ride through beautiful English villages and into the Dutch lowlands via Amsterdam and finishing in Brussels.

Great Wall of China Trek | 4–13 September 2014
Trek through woodland, terraced farmland and the beautiful mountains north of Beijing; a once-in-a-lifetime experience.

Petra Trek | 8–12 October 2014
Beginning in the ancient city of Petra, this trek provides the opportunity to visit some of the world’s most historical sites.

For more information about any of these events, or to get involved, please contact the Events Team on 020 7153 5375 or by email on sports@icr.ac.uk.
Our PhD students are encouraged to develop their intellectual curiosity, creativity and talent under the guidance of our distinguished scientists.

Fiona Rowan is among our current crop of PhD students. She is researching how proteins called kinases, which are over-active in many types of cancer, can be controlled by chemical modifications. This will help provide a better understanding of how drugs can be designed to block the activity of kinases.

Fiona’s day tends to be busy and varied: “I know it is clichéd, but I don’t really have a typical day. I could be in the lab purifying a protein I want to use, performing chemical reactions on the protein in a test tube, testing the activity of the modified versions, or trying to grow microscopic crystals of the protein so I can study its shape.

“During breaks from experiments I analyse results and make sure my lab notebook is up to date. I’m currently writing up some results to publish in an academic journal, so it’s really important to keep a record of what I’ve done, and attention to detail is essential.”

PhD students meet regularly with their supervisors to discuss their research and which avenues to explore next.

“A PhD is excellent as it gives you the freedom to experiment and see where your research takes you. The ICR provides a stimulating environment where I am surrounded by world-class scientists, and this motivates me to be persistent and keep going. Realising the real impact on the lives of patients is truly motivating.”

You could help us to train the cancer research leaders of the future. If you or your organisation is interested in helping support a student, please contact Caroline Totterdill on 020 7153 5304 or by email on caroline.totterdill@icr.ac.uk.
ICR secures significant donation from Rosetrees Trust

The ICR has secured an extremely generous £36,000 donation from The Rosetrees Trust to support our research into pancreatic cancer. Dr Claus Jørgensen is carrying out research into pancreatic tumour progression by studying how cells communicate. His work aims to identify substances known as biomarkers – indicators of a biological state – to help develop better treatments.

He says: “We have identified several novel signalling molecules that could be used by tumour cells to co-opt normal pancreatic support cells into promoting tumour progression. Support from The Rosetrees Trust will enable us to test which of these signals are critical to pancreatic tumour progression.”

The Rosetrees Trustees are longstanding supporters of the ICR’s work, and have donated in total nearly half a million pounds. We are very grateful for their support.

Team ICR take on the London Marathon

A team of intrepid runners took part in the Virgin London Marathon and raised £50,000 for the ICR. Fantastic support from the ICR cheer station at the 12-mile point really helped to spur on our athletes.

The runners and their families joined us for a post-race reception at The Farmers’ Club in Whitehall, where they were offered a welcome shower and massage, and shared their race tales with fellow runners.

Spring Appeal supports lung cancer therapy

Our recent Spring Fundraising Appeal has raised an amazing £30,000 to support our work. The appeal featured the exciting research we are undertaking into combined drug therapy that could give hope to lung cancer patients. It has been a while since we last carried out an appeal like this and we are thrilled by the response we have received.

“The Spring Appeal has been a huge success and I want to thank everyone for their generosity. It’s only because of you that we can continue to make the discoveries that defeat cancer. Thank you so much,” says Russel Caulfield, Head of Legacies and Appeals at the ICR.