How our pioneering drug research is changing lives.

Read Rob’s story – Page 16

Inspired by Alice
Kinder treatments for children with rhabdomyosarcoma

Inside this issue

12 | In profile: Dr Gideon Coster
How copying DNA offers cancer clues

14 | Focus on: Melanoma
Drug discovery and immunotherapy

19 | Inspired by Alice
Kinder treatments for children with rhabdomyosarcoma
Our mission is to make the discoveries that defeat cancer.
Welcome to our new-look Search magazine. Thank you to all those who sent in feedback on Search last year – we were touched by your kind words about the magazine and the ICR overall. I hope the refreshed magazine will give you an even greater insight into our wide-ranging cancer research, the people who make it happen, and the patients who are benefiting from our discoveries right now.

The beginning of January seems like a long time ago now, but we are still celebrating the news that our own Professor Mel Greaves was knighted in the New Year Honours list. Professor Greaves has spent decades researching childhood leukaemia and his discoveries have hugely increased our understanding of this disease.

We are very grateful to all those who supported our Christmas appeal to help progress the next stage of Professor Greaves’s research – to make childhood leukaemia preventable.

In this edition, I am delighted to introduce you to two PhD students who have been funded by different types of philanthropy – Harry Parr, who was the fortunate recipient of donations to our 2017 Christmas appeal, and Iona Black, who is funded by the Masonic Charitable Foundation.

Our PhD students are the next generation of cancer researchers, and we are excited to see where their research will lead.

I do hope you enjoy reading this edition of Search. Thank you so much for being a part of our journey to defeat cancer.

Lara Jukes
Director of Development
The Institute of Cancer Research
New ‘Trojan horse’ treatment shows promise in multiple tumour types

A brand new type of cancer drug that acts as a ‘Trojan horse’ to get inside tumour cells has shown promise in a global trial led by the ICR’s Professor Johann de Bono.

Over a quarter of patients with cervical and bladder tumours, and nearly 15 per cent with ovarian and lung tumours, responded to the new treatment.

The innovative new drug, called tisotumab vedotin (or TV for short), releases a toxic substance to kill cancer cells from within.

The results have been so positive the drug has now moved forward to phase II trials in cervical cancer and will be tested in a range of additional tumour types.

New AI test identifies women with very high risk ovarian cancer

ICR researchers led by Dr Yinyin Yuan have developed a new test that scans the shapes of tumour cells to pick out women with especially aggressive ovarian cancer, so treatment can be tailored to their needs.

The artificial intelligence (AI) tool looks for clusters of cells within tumours with misshapen nuclei – the control centres within each cell.

Women identified with these clusters had extremely aggressive disease – with only 15 per cent surviving for five years or more, compared with 53 per cent for other patients with the disease.

But these cancers also had hidden weaknesses in their ability to repair DNA, which could make them susceptible to drugs called PARP inhibitors or platinum chemotherapy.
Weight loss drug could help treat advanced ovarian cancer

A team of researchers led by the ICR’s Professor Nandita de Souza have found that a weight loss drug available over the counter in the UK could help women with treatment-resistant ovarian cancer respond to chemotherapy again.

The scientists treated chemotherapy-resistant ovarian cancer in mice with the obesity drug orlistat – the active ingredient in some slimming pills.

Orlistat made the ovarian cancers more sensitive to the chemotherapy treatment cisplatin and delayed tumour growth, compared with using either treatment alone.

Chemotherapy is one of the main treatment options for ovarian cancer, but once resistance develops it can be very difficult to treat the disease. The research shows that combining orlistat with cisplatin could potentially be an effective way to treat these women.

Immunotherapy extends lives of patients with head and neck cancer

A clinical trial led by the ICR’s Professor Kevin Harrington has found that a new immunotherapy can greatly extend the lives of some people with advanced head and neck cancer, with some living for three years or more.

Overall, 37 per cent of patients who received pembrolizumab survived for a year or more, compared with only 26.5 per cent of those on standard care.

But the results were particularly exciting among the group of people who did respond to pembrolizumab – with a median length of response of 18.4 months, compared with five months for standard care.

Our researchers hope that pembrolizumab could be a much needed smarter, kinder treatment option for people with advanced head and neck cancer.
In the autumn we were delighted to welcome 30 of the ICR’s legacy pledgers and other close supporters for an afternoon tea at Church House, by Westminster Abbey.

Guests heard from Professor Alan Melcher, Professor of Translational Immunotherapy at the ICR, who talked about the exciting potential of immunotherapy to revolutionise cancer research.

Guests were able to chat to our scientists over tea and find out more about their areas of research. One attendee, John Freeman, said, “It’s a pleasure and a privilege to meet some of the ICR’s scientists. Their enthusiasm for their work just shines through the conversation – it makes me feel, in a small and humble way, part of the team.”

If you have left the ICR a gift in your Will, thank you for making such a generous commitment to the future of cancer research. Legacy gifts make up around one third of our overall donations each year, so they are critically important to funding our life-changing research. We would be grateful if you could let us know of your intentions, so we can invite you to future events.

Don’t forget, the ICR offers a Will for Free programme all year round, which enables people 60 and over to make or update their Will for no charge.

Find out if we have a participating solicitor near you at ICR.ac.uk/wff or call 020 7153 5387.
We are incredibly grateful to all those donors whose generosity has helped make our Christmas appeal the most successful in the ICR’s history. More than £90,000 has been raised to support Professor Sir Mel Greaves’s work to eradicate childhood leukaemia. Professor Greaves published momentous research in 2018 which set out the likely cause of the most common type of childhood leukaemia, acute lymphoblastic leukaemia (ALL). You can watch him explain this research at icr.ac.uk/ALL.

Thanks to the incredible generosity of thousands of donors, Professor Greaves will now start on the next phase of his research – exploring how we could use simple and safe interventions to stop ALL ever occurring in the first place, and finally make this a disease of the past.

Professor Greaves received yet more good news at the end of 2018, when it was announced that he was to be knighted in the New Year Honours list for his services to children’s leukaemia research.

The ICR’s Christmas appeal has raised more than £130,000 for research into childhood leukaemia, immunotherapy and a rare form of cancer called rhabdomyosarcoma.

ICR supporter raising £21k before 21st birthday

ICR fundraiser Amy Elvidge has given herself quite the task – to raise £21,000 by the time she turns 21 in September. Amy is already one of our dedicated London Marathon runners, but she has also signed up to several difficult challenges throughout 2018 and 2019 to help meet her huge target.

Amy’s challenges include:

— a parachute jump at 10,000ft
— running the London Marathon in April
— running and walking 100km from London to Brighton in May
— hiking the UK’s Three Peaks.

Amy took on this monster challenge to support the ICR after her Dad, Mark, was diagnosed with cancer. Amy says that this challenge is “a way to support the scientists who are working every day to make sure more people survive cancer.”

Mark has since received the good news that his treatment worked and has even signed up to run this year’s London Marathon with Amy. The father and daughter team are looking forward to crossing that iconic finish line together for the ICR come April.

If you would like to support Amy and Mark, please visit Amy’s fundraising page justgiving.com/amy-elvo
Foundation funds project to probe cell growth

We are delighted that the Masonic Charitable Foundation (MCF) has chosen to generously support PhD student Iona Black over the next four years.

Iona joined the ICR in October 2018 after studying chemistry at the University of Glasgow. Her supervisors are Professor Ian Collins in Cancer Therapeutics and Dr Sebastian Guettler in Structural Biology.

Iona’s project will involve designing chemical probes to help identify new ways to target the molecule Tankyrase – which plays a role in the growth of cancer cells. Tankyrase is involved in a process known as scaffolding, where two or more cellular signals are brought together in a stable structure.

She plans to use a variety of structural biology and drug discovery techniques to find probes that could stop the scaffolding ability of Tankyrase – preventing signals being sent out that can promote cell growth.

These chemical probes will then be tested in cancer cells grown in the lab, to see what effect blocking the Tankyrase scaffolding functions has. This is a crucial step towards the design of drugs that could one day be used in cancer patients.

“...”

My first few months at the ICR have been intense but very exciting, as I realise how wide the field of drug discovery is. I look forward to seeing where this project leads me!

Events calendar

Whether you like to cycle or trek, we have an event for you. By joining #teamICR this year, you’ll be helping us make the discoveries that defeat cancer.

See our website for our full events calendar at icr.ac.uk/challenge or contact the team on 020 7153 5375 or sports@icr.ac.uk

May

Vitality London 10,000
Monday 27 May 2019

Take part for #teamICR in London’s most inspiring 10K race. It features a spectacular route in the heart of the capital, starting on The Mall and finishing in front of Buckingham Palace.

August

Prudential RideLondon-Surrey 100
Sunday 4 August 2019

Start in Queen Elizabeth Olympic Park, follow a 100-mile route on closed roads through the capital and into Surrey’s stunning countryside, and cycle back into London for a spectacular finish on The Mall.
Annual ICR mountain trek surpasses £1 million

The ICR’s annual Lake District mountain trek, the Climb of Life, passed the £1 million mark at November’s event for the amount raised since it was set up.

The event, created by ICR fundraiser Graeme Chapman MBE and supported by the stationery industry, has been run on behalf of the ICR for the last 12 years. Each year the event beats the previous year’s total and has in the last five years raised more than £100,000 each time.

This year we hit a big milestone, with the overall combined fundraising total for the 12 years surpassing the magical £1 million mark.

The ICR’s Cumbrian-born Chief Executive, Professor Paul Workman, who together with his wife, Liz, regularly takes part in the event, said: “The £1 million raised so far from the Climb of Life continues to make a huge difference at the ICR as we work to achieve our mission of making the discoveries that defeat cancer.”

Last year also saw the launch of the very first Ride of Life, a sister event which focuses on cycling. The riders started at the ICR’s Sutton campus, and the 100km route took in the rolling Surrey countryside and the challenging ascents of Box and Leith Hills before returning home to the ICR. In its inaugural year, participants raised more than £15,000 for the ICR.

Graeme Chapman MBE presents the £1 million cheque to the ICR

Graeme has recently announced that he will be stepping down as chief showrunner of the Climb of Life for the 2019 event. The position will be taken up by the recently retired Chief Executive of the BOSS Federation, Philip Lawson.

Graeme had this to say about his departure: “I have thought about stepping down for some time, but I wanted Climb of Life to continue and I couldn’t leave until I had the right successor in place. Having worked with Phil for the last three years I’m delighted that he and his wife Heather will be in charge.”

The ICR would like to extend our sincerest thanks to Graeme for all his hard work and dedication to bringing this event to life year after year.

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**September**

**Great North Run**

**Sunday 8 September 2019**

Join in the celebration of what makes the North East great by running the UK’s biggest half marathon for #teamICR.

**October**

**Great Wall of China Trek**

**11 - 19 October 2019**

Take on a majestic nine-day trekking adventure for the ICR and conquer the twists, turns, steps and slopes of the formidable and famous Great Wall.

**October**

**Royal Parks Half Marathon**

**13 October 2019**

Join #teamICR and run this stunning 13.1-mile route which takes in the capital’s world-famous landmarks on closed roads, and four of London’s eight Royal Parks – Hyde Park, Green Park, St James’s Park and Kensington Gardens.
Harry’s research is helping us to better predict whether prostate cancer will recur following radiotherapy.

Using data from a major clinical trial called CHHiP, he is devising statistical models that can predict a patient’s prognosis after treatment. The CHHiP trial, led by the ICR and The Royal Marsden, assessed the effectiveness of fewer, more targeted doses of radiotherapy on more than 3,000 men with prostate cancer.

He says: “The CHHiP trial found that giving fewer, higher doses of radiotherapy can be as effective as the standard treatment – and could save each patient on average 17 trips to the hospital, and the NHS tens of millions of pounds per year.

“We now that the trial is in its follow-up stage, we are collecting a wealth of information from participants. Tracking these changes provides us with vital information about when a cancer is likely to recur.”

Key to this research is carrying out blood tests that measure levels of a protein called PSA, which can rise in men who have developing prostate cancer, or whose cancer is becoming more aggressive.

By modelling the trial participants’ PSA levels, Harry should get a better understanding of the underlying biological mechanisms linking a patient’s response to treatment and the likelihood of their cancer returning.

With this information, Harry aims to develop a web-based clinical risk calculator that could help clinicians create a tailored treatment plan for each patient.
Dr Gideon Coster

Dr Gideon Coster joined the ICR last year to lead the Genome Replication Team. His research is helping to explain how DNA is copied – a crucial step towards understanding how cancer begins and develops.

Dr Coster began his research career at the Hebrew University of Jerusalem where, during his PhD, he discovered new links between the immune system and the way the body responds to DNA damage.

He later spent time at the London Research Institute looking in more detail at the way DNA is copied, a process known as DNA replication.

DNA replication is a vital process that allows our cells to divide, and our bodies to grow and repair themselves. But if it goes wrong, and errors are introduced that allow cells to divide and grow uncontrollably, the result can be cancer.

Now at the ICR, Dr Coster’s research uses a variety of methods to understand how DNA replication works and what happens when it goes wrong.

His work could lead to a better understanding of how cancers can arise from replication errors.

It could also tell us more about the way cancers grow and evolve – since cancer cells are prone to developing further errors in their DNA. The result could be the discovery of new approaches to treating cancer.

Look out for more information about Dr Coster’s work in our upcoming spring appeal.

In profile

Joined the ICR
October 2018

Specialist subject
Investigating how our DNA is accurately copied and how this process goes wrong in cancer

Interests
Spending quality time with his family (including three boys), watching movies, reading and going on holiday to warm places.

“Our work will help us unravel the mechanisms that dictate how DNA is replicated accurately. It will contribute to our understanding of how cancer arises, and may also uncover exciting new approaches and targets for cancer therapy.”
Looking down a large, state-of-the-art microscope in the ICR’s Chelsea laboratories, Dr Chris Bakal explains how technology is giving his team an unprecedented understanding of how cancer cells grow and spread.

Dr Bakal works on a skin cancer called melanoma – the fifth most common cancer in the UK, with around 16,000 newly diagnosed cases each year.

Scientists at the ICR have long been at the forefront of research to better understand melanoma, and our research is behind the discovery of some of the most important new treatments for the disease.

Dr Bakal is using a sophisticated ‘lattice light sheet’ microscope – purchased thanks to generous donations from our supporters – to illuminate melanoma cells in ultra-fine detail, and to generate many images at very high speed.

It is one of Dr Bakal’s instruments of choice in his latest research to understand how the shape of cancer cells influences their ability to spread round the body.

Dr Bakal explains: “The difference between a fatal and non-fatal cancer is usually its ability to spread around the body – a process called metastasis. We’re aiming to understand what makes some cancer cells, including melanomas, leave their original site and make that journey to other tissues and other parts of the body.”

Recent discoveries by Dr Bakal’s team include uncovering how melanoma cells ‘shape-shift’ by using a set of genes to change rapidly between two configurations, and developing a ‘postcode’ system to map proteins in cells that has shone more light on melanoma metastasis.

We know a melanoma cell’s ability to change shape is a crucial factor in its ability to spread. Metastatic cells can take on many shapes, squeezing through tissues and finding their way into places they should not naturally be, using a complex system of adhesion molecules on their surfaces to move around.

“We know a melanoma cell’s ability to change shape is a crucial factor in its ability to spread.”
Drug discovery
Our researchers have also made breakthroughs that have helped transform treatment of melanoma. One of the ICR’s most high-profile successes of recent years was research to understand how mutations in a gene called BRAF could help cause the disease.

Our work in the laboratory led to the discovery of the BRAF-inhibiting drugs vemurafenib and dabrafenib, which are now mainstays of treatment for advanced melanoma, buying extra months or years for many thousands of patients around the world.

One of these drugs, dabrafenib, was discovered by a team in pharmaceutical company GlaxoSmithKline which included Dr Olivia Rossanese – who is now the Head of Biology in our Division of Cancer Therapeutics, working to find the next generation of cancer drugs.

Our success in discovering new drugs is underpinned by gaining a deeper understanding of the biological processes at work in cancer, as Dr Rossanese explains.

“What’s really important for us is to understand the underlying mechanisms and genetic alterations in cancer that lead to uncontrolled tumour growth and spread. And when we begin to understand those mechanisms, we really have a good idea of what the targets are for therapeutics.” That’s true for melanoma and other cancers.

Immuno+therapy
Regular readers of Search will be familiar with another area in which ICR researchers are leaders in their field: immunotherapy. Recent clinical trials involving our researchers alongside our hospital partner, The Royal Marsden, have led to the approval of new immunotherapies for patients on the NHS and worldwide to treat advanced melanoma and other cancers. These treatments have included talimogene laherparapvec (T-Vec), which is a highly innovative viral immunotherapy.

Professor Kevin Harrington, Professor of Biological Cancer Therapies at the ICR and Consultant Clinical Oncologist at The Royal Marsden, was the UK leader of the definitive trial that showed the benefits of this drug, which uses a genetically altered virus to burst cancer cells and attract the immune system to tumours.

Research at the ICR has led to vital new drugs to treat melanoma, and a better understanding of its biology than ever before. Our scientists are determined to keep on building on what is known about this disease, and find more new ways to treat it.

This image, winner of the ICR’s annual science photography competition, shows metastatic melanoma cells as they feel their way through their environment, changing their shape to suit the tissue they are invading.

Dr Bakal took this image using a new ‘total internal reflection fluorescence’ microscope, which allows us to see cells at the point where they are making contact with their environment, and capture structures that would otherwise be difficult to see.
Patient focus

How the ICR’s pioneering drug research is changing lives
The ICR has discovered more new cancer drugs than any other academic institution globally, and led the underpinning science for many more cancer treatments. We have helped lead clinical trials of these drugs and many others – taking them to cancer patients as quickly as possible.

Our work has transformed the lives of cancer patients across the world, helping many live longer, better lives and giving them precious time with their loved ones.

We spoke to three people who have benefitted from our research, about what it means to them.

‘I hope to live 10 years’

The prostate cancer drug abiraterone is one of the ICR’s biggest success stories. Discovered and jointly developed by our researchers, it was the first treatment shown to be effective in men with advanced prostate cancer.

It’s now used as standard treatment for advanced prostate cancer, and has helped extend the lives of more than 400,000 men with advanced prostate cancer across the world.

Rob has benefited from abiraterone for more than six years.

“Abiraterone has given me hope. When I was first diagnosed with prostate cancer, I hoped I would survive for five years. I have now survived six.

Not only have I survived, I have been living and enjoying life, and having a great quality of life. I am now hoping I will survive 10 years, and if I am really lucky, 15 years.”

At the time of Rob’s diagnosis, abiraterone was still a very new drug. It was approved for use on the NHS in 2012, but work on it began in the 1990s when scientists at the ICR were looking for ways to shut off production of male sex hormones, which drive prostate cancer.

The ICR team discovered that abiraterone was particularly good at switching off testosterone production. Later clinical trials, led by the ICR and The Royal Marsden, showed that up to 70 per cent of men responded to abiraterone – with scans showing their tumours decreased in size, and their PSA levels dropped substantially. PSA is a protein whose levels can rise in men if the cancer is becoming more aggressive.

“I would call myself a lucky man,” says Rob. “The drug brought down my testosterone level very quickly, and also my PSA. It is less than 0.1 at the moment and has been so for six years, which is unbelievable.”

‘Keeping me chemo free’

The ICR’s science also underpinned the development of olaparib, a groundbreaking treatment for women with ovarian cancer.

Our researchers discovered how to genetically target olaparib – showing that it could attack a vulnerability in ovarian cancer in women with inherited BRCA mutations.

In 2004 it became the first licensed cancer drug directed against an inherited genetic fault – and since then 20,000 women with ovarian cancer worldwide who carry these BRCA mutations have received olaparib to treat their cancer.

Anne was diagnosed with ovarian cancer in 2015. She received surgery and chemotherapy, but two years later her cancer returned. Genetic testing identified that she carried a BRCA mutation, and she started taking olaparib in March 2018.

She now feels better than she has in years.
“Olaparib worked amazingly for me, and really quickly,” she says. “The fact it worked immediately put my mind at rest that it would extend my life. I’m hopeful that I’ll have a few years chemo free and feeling good with fewer side effects.”

Olaparib’s origins lie in ICR research into the BRCA genes in the 1990s, when our scientists tracked down the gene BRCA2.

ICR researchers then found that targeting a DNA repair protein called PARP was a potential way to kill cancer cells with a faulty BRCA gene. This helped lead to the development of olaparib, and other so-called PARP inhibitors.

The same ICR team also contributed to the refinement of PARP inhibitors, working with The Royal Marsden on early clinical trials of olaparib, with subsequent larger trials leading to the drug’s authorisation.

Innovative drugs like olaparib can make a huge difference to women who, like Anne, no longer respond to traditional chemotherapy: “My tumour markers had gone down by a third within the first month of treatment,” she says. “They’re now the lowest they have been in 18 months.

“I feel very lucky to have been able to get olaparib.”

‘I can get on with my life’

The ICR’s experience in clinical trials also helped the innovative breast cancer drug palbociclib to reach patients.

Palbociclib is known as a first-in-class drug, because it’s the first drug to work in the way that it does – blocking two proteins, called CDK4 and CDK6, that help cancer cells divide and spread.

This innovation is already changing lives – more than 90,000 patients have been prescribed the drug.

Christine has been treated with palbociclib and hormone therapy since early 2018, and has seen the difference a targeted treatment can make: “I take my pill every morning, and I get on with my life,” she says. “It’s just a much more manageable, softer drug.”

Christine was initially diagnosed with breast cancer in 2012 but, nearly five years after surgery and chemotherapy left her cancer free, she found the disease had returned, and spread to her brain.

Following radiotherapy, she needed a targeted treatment to keep her cancer at bay. Fortunately, palbociclib had been approved for use on the NHS just months before, thanks to clinical trials that showed how palbociclib could benefit patients.

Researchers at the ICR and The Royal Marsden led a key clinical trial of palbociclib, showing that it could slow the progression of advanced breast cancer in conjunction with standard treatments, and substantially extended the lives of patients.

Christine is doing well on palbociclib: “I’m on the ninth cycle and my cancer is currently stable,” she says. “I’m able to work part-time, and I can keep up my cycling, which I could never have done had I been on conventional therapy.”

Smarter, kinder treatments

All these stories demonstrate how well people can live with cancer thanks to new, innovative treatments that are both smarter and kinder.

That is why our researchers are dedicated to getting our discoveries into the clinic and to patients as quickly as possible, so that more people have stories like those of Rob, Anne and Christine.
The charity Alice’s Arc is funding ICR research to find more targeted and kinder treatments for children with rhabdomyosarcoma.

Sara and David Wakeling set up Alice’s Arc, inspired by their little girl Alice who, at the age of three, was diagnosed with stage 4 alveolar rhabdomyosarcoma in March 2015. She was given a 50/50 chance of survival. Alice relapsed in February 2018. In the four years since her diagnosis, Alice has been treated with a combination of chemotherapy, proton radiation, surgery and brachytherapy. She has undergone treatments in the UK, US and Amsterdam. She is now seven years old and is currently cancer free.

Rhabdomyosarcomas are the most common soft tissue sarcomas that occur in children. The tumours tend to look like developing muscle or fibrous tissue, which can make diagnosis hard. There are around 70 new cases in the UK each year.

Throughout the family’s experiences of cancer, they became aware of the lack of funding for research into children’s cancers and especially the shortage of clinical trials for children offering the latest treatments. And so Alice’s Arc was born with a commitment to help find a cure for rhabdomyosarcoma with less toxic treatment options than are available to children today.

The charity has already donated more than £200,000 to drive the ICR’s rhabdomyosarcoma research forward, with plans to continue its support for years to come: “The money we raise now and in the future for the ICR will contribute to better treatments and, one day, a cure for children diagnosed with rhabdomyosarcoma.”

The charity’s generosity is supporting research in Professor Janet Shipley’s laboratory to study the molecular biology of rhabdomyosarcomas and discover more targeted treatments. The charity is funding two research roles within the sarcoma team, along with the consumables needed for those scientists to undertake their vital work.

For more information about Alice’s Arc, visit alicesarc.org