

Issue 35 Spring 2017

search

For supporters of The Institute of Cancer Research, London



Structural biology: a scientific frontier
Focus on: myeloma
Mayor of London opens revolutionary radiotherapy machine

Our mission is to make the discoveries that defeat cancer.

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Contact us:

The Institute of Cancer Research
123 Old Brompton Road, London SW7 3RP

T 020 7153 5387

E supportercare@icr.ac.uk

W icr.ac.uk

 [facebook.com/theinstituteofcancerresearch](https://www.facebook.com/theinstituteofcancerresearch)

 [@ICR_London](https://twitter.com/ICR_London)

Editorial

A hot topic at the ICR over the past months has been our new research strategy. Developed with The Royal Marsden, this strategy will be at the heart of everything we do over the coming years, as we aim to outsmart cancer and transform routine healthcare for cancer patients.



It will be an exciting journey for the ICR as we aim to speed up our progress against cancer – and I hope you will join us every step of the way. Now more than ever, we need your support.

We hope you will continue to donate to the ICR. We want to take you on the journey with us and show you how your generosity makes a difference. This will include news of our discoveries, insightful blog posts from our scientists and videos from our labs.

Owing to changes in best practice, we need you to give us your permission to get in touch. Please go to icr.ac.uk/ subscribe to sign up today.

I do hope you enjoy reading this issue of Search.

Thank you.

Lara Jukes

Director of Development

The Institute of Cancer Research, London

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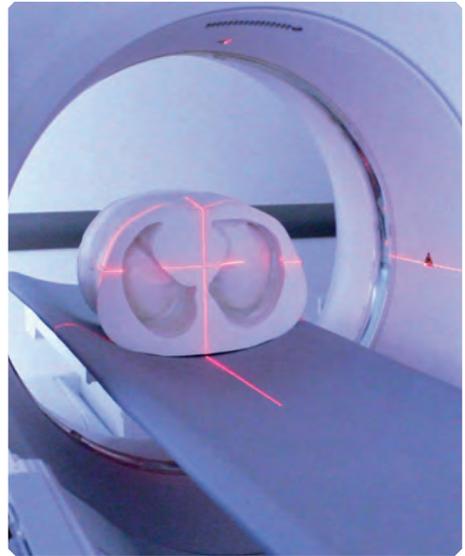
3D-printed 'AbdoMan' could transform radiotherapy

A 3D-printed human torso is helping doctors safely model internal radiation treatments for cancer.

AbdoMan, created by a team at the ICR and The Royal Marsden, is a replica of a human abdomen. It can be filled with a solution that replicates the radiation produced by a course of internal radiation therapy.

By scanning AbdoMan using CT technology, the team can see how radiation is distributed throughout the internal organs, and create computer models of how the therapy will affect real patients.

Internal radiation therapy is an innovative way to deliver radiation to the site of a tumour, and has been pioneered by



researchers at the ICR and The Royal Marsden. Rather than relying on an external source of radiation such as X-rays, the treatment uses unstable molecules that emit radiation as they decay. These are delivered into the bloodstream and are carried to the cancer cells, destroying the tumour from inside the body.

'Game-changing' immunotherapy doubles head and neck cancer survival

A major trial led by researchers including the ICR's Professor Kevin Harrington has found that immunotherapy drug nivolumab greatly improves survival for people with relapsed head and neck cancer – a disease that is notoriously difficult to treat.

In a phase III clinical trial for people in whom earlier treatment had failed, more

than double the number of patients taking nivolumab were alive after one year, compared with those treated with standard chemotherapy.

People treated with nivolumab were also less likely to experience serious side-effects than their counterparts given chemotherapy.

Scientists reveal ‘safety catch’ within all dividing cells

Our researchers have made a major discovery about how cells control when they divide.

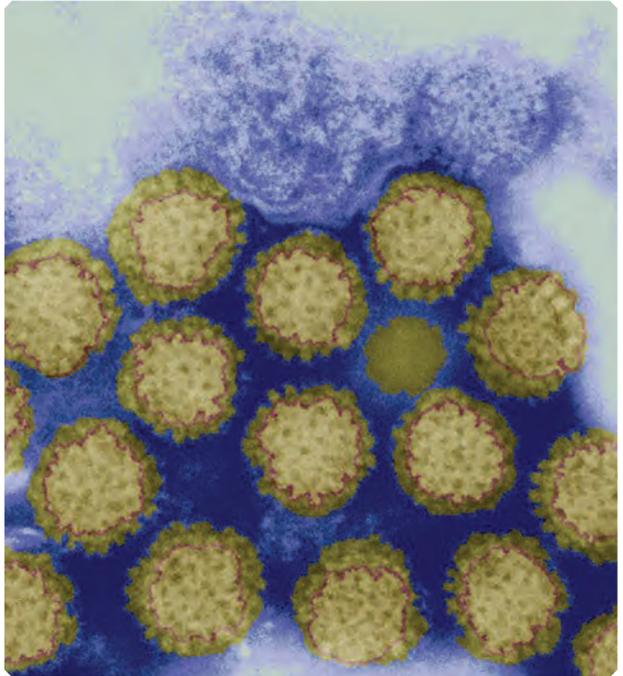
A new study led by Head of Cancer Biology, Professor Jon Pines, has revealed a ‘safety catch’ within cells that prevents them from dividing until DNA is allocated equally between its two daughter cells.

Cancer cells rely on this safety catch more than normal cells, because they often have more chromosomes and so need more time to divide.

The discovery could lead to new treatments that prevent cancer cells from dividing, or that kill them by forcing them to divide prematurely.



Professor Jon Pines



‘Cough virus’ kills liver cancer cells

A virus that causes childhood coughs and colds could help in the fight against liver cancer, a study led by the ICR’s Professor Alan Melcher has shown.

Reovirus stimulates the body’s own immune system to kill off the cancerous cells – and it is also able to kill off the hepatitis C virus, a common cause of liver cancer.

These early-stage findings are important because liver cancer is the third greatest cause of cancer deaths worldwide and if surgery is not an option, the prognosis is poor.

Study co-leader Professor Alan Melcher, Professor of Translational Immunotherapy at the ICR, said: “Our study establishes a completely new type of viral immunotherapy for the most common liver cancer type, hepatocellular carcinoma, which has a very poor prognosis in its advanced form.”



#GivingTuesday sees our colleague Jack going bald to help raise funds

Jack Walker, who works in the purchasing team at the ICR, bravely went under the clippers to raise money for our research.

Jack had his previously luxuriant locks shaved off on #GivingTuesday to support his friend and colleague Jennifer Herbert in her fundraising efforts.

He raised £200 towards Jennifer's fundraising for the ICR as she sets her sights on running the 2017 Virgin Money London Marathon.

Jennifer has already conquered the Inca Trail in Peru to raise money for the ICR's life-saving research.

Now on Sunday 23 April she will be joined by 25 other #teamICR runners, who between them are aiming to raise more than £70,000 to support our research.

You can watch a video of Jack's head shave online at icr.ac.uk/supportus.

Don't forget, if you would like to sign up to receive emails from the ICR, containing the latest news, videos and blogs, go to icr.ac.uk/subscribe.

Family aiming to raise £50k for brain cancer research

Elizabeth Waller was diagnosed with a type of low-grade brain tumour in 2010. Now she, her family and her friends are raising funds to support ICR research into low-grade brain tumours. They've raised more than £5,000 already and are aiming to reach £50,000.



Elizabeth Waller

Elizabeth is supporting research at the ICR led by Dr Igor Vivanco, who is seeking new treatments for people diagnosed with low-grade brain tumours. Currently, options are few and largely ineffective. Dr Vivanco's approach focuses on finding molecularly targeted cancer drugs that could treat tumours more effectively, and with fewer side-effects, than current treatments.

Elizabeth says: "Despite the poor outcomes associated with brain tumours, this area of research receives proportionately less funding compared with other tumours with better prognoses. This is why we are so determined to raise a significant sum to support research at the ICR. Dr Vivanco's research is urgently needed, and has the potential to restore many years of life to patients and their families."

Record-breaking Christmas appeal raises more than £90,000

We are hugely grateful to all those who donated to our 2016 Christmas appeal. Our supporters gave a record-breaking £90,000 to support our research into breast cancer and a rare type of sarcoma cancer.

Our Christmas appeal focused on two vital research projects. The first is using cutting-edge 3D 'organoid' models to study hormone receptor-positive breast cancer – the most common kind. The second involves learning

more about a rare form of sarcoma that affects young people.

More than 2,500 people generously supported our fundraising appeal this Christmas – a wonderful show of support for the vital work we do. We were especially delighted to see so many people donating to the ICR for the first time. We're looking forward to keeping you updated on our progress in future issues of Search.

Profile:

Professor Jessica Downs

Professor Jessica Downs recently joined the ICR as a Team Leader, from the University of Sussex. She joins our Division of Cancer Biology, where our researchers make discoveries about the fundamental biological make-up of cancer cells.

Professor Downs's work focuses on how cells package up and organise their DNA, and how errors in these normal functions can lead to cancer. Her team aims to make important new discoveries about the complexities of cancer, and these discoveries could lead to new types of treatment.

In particular, Professor Downs's work could lead to the development of new drugs.

In normal cells, DNA is carefully wound up into bundles. This packaging is important for keeping the DNA safe and protected from the changes that can lead to cancer.

"Several of our big projects revolve around the tightly regulated processes of winding and unwinding DNA," says Professor Downs. "We have a particular focus on a major complex of proteins, which is inactivated in roughly 20 per cent of cancers, and has an important role in preventing and repairing wear and tear to DNA.

"I'm enthusiastic about joining the ICR because of the fantastic colleagues, world-leading research, proximity to people doing translational and clinical research, and great support."



Name

Professor Jessica Downs

Joined the ICR

November 2016

Specialist subject

DNA instability, damage responses, the biology of chromosomes – bundled-up DNA – and epigenetics, which is the study of how information is coded into the bundling of DNA.

Interests

Outside work, Professor Downs likes to spend time with family and be outdoors – and can often be found running. She has completed the Marathon des Sables, a 150-mile ultra-marathon in the Sahara desert.

Profile:

Dr Jumi Popoola

Dr Jumi Popoola is a Higher Scientific Officer at the ICR. She joined in 2009, and is part of our Division of Cancer Therapeutics, where researchers discover new, more personalised cancer treatments.

Dr Popoola is trying to understand how cancers respond to drugs, to pave the way for new treatments that can overcome drug resistance.

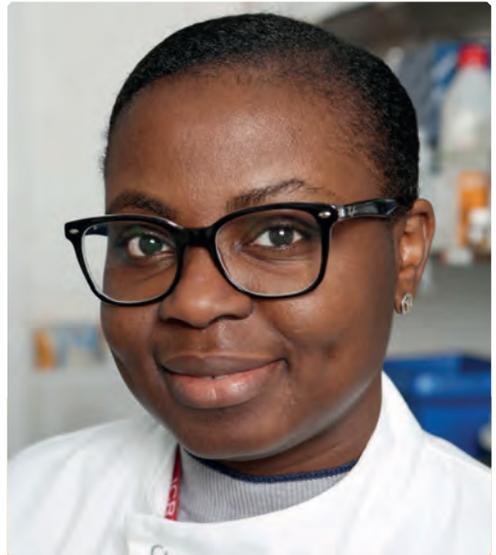
Part of this work focuses on learning how cells send and receive signals. In the development of cancer, these signalling mechanisms can go wrong, causing uncontrolled cell growth and division, and eventually leading to a tumour. Understanding how these signalling networks work can help scientists to find new ways to get them under control.

She is also investigating how cancer cells respond to inhibitors – small molecules that disrupt the cells' biological processes. This knowledge could point to ways in which inhibitors could be developed into targeted treatments.

Seeing it through

Dr Popoola's interest in inhibitors of cancer began during her PhD, and this inspired her to begin a career investigating the causes and treatment of cancer.

After graduating, she joined the ICR in her current role: "I saw that the ICR was one of the most prestigious research institutes in the UK, so I applied straight away. I'm incredibly proud to be part of an organisation that produces such excellent research."



Name

Dr Jumi Popoola

Joined the ICR
September 2009

Specialist subject

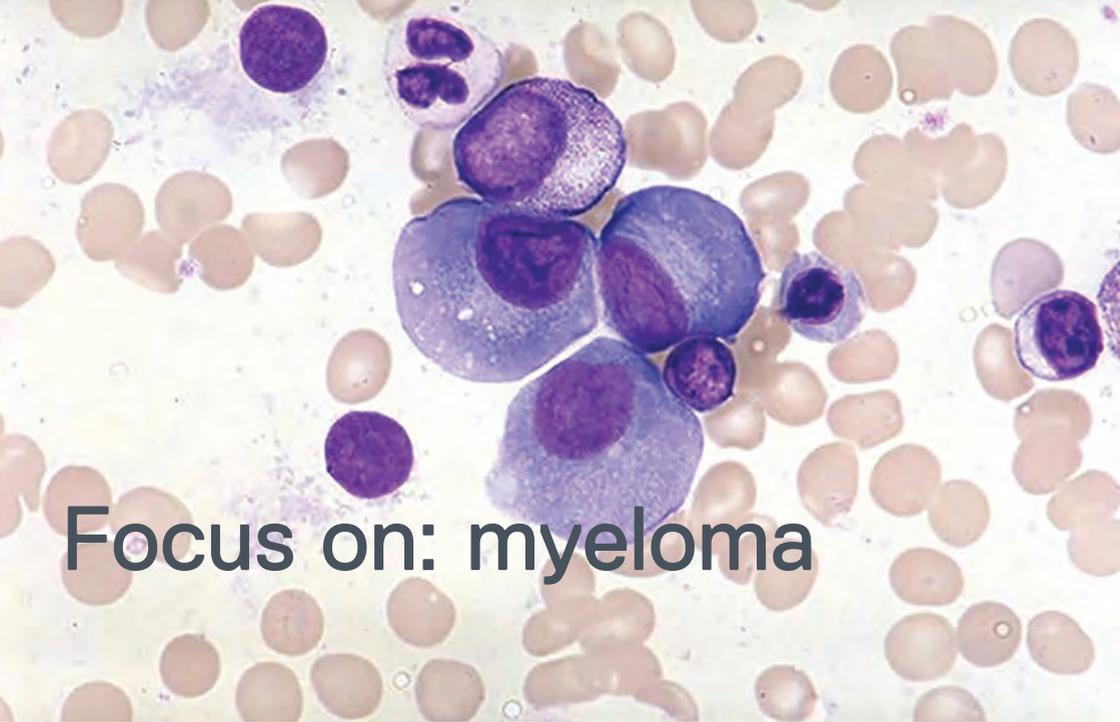
Characterising cancer cells' response to inhibitors, to aid the development of more effective, targeted cancer drugs.

Interests

Outside her work at the ICR, Dr Popoola is also a talented musician, and is able to play six musical instruments.

Of course, excellent research is only part of the story – it's important to make sure that results in the lab make it into the clinic as quickly as possible. This is something that Dr Popoola is enthusiastic about: "The favourite part of my job is seeing a project start from small beginnings and build up into the successful development of a drug."

She adds that the benefits of working at the ICR extend beyond the research expertise: "I love the rich culture and diversity here. The overwhelming support the ICR provides for women in science is very empowering and has helped my dream of a research career become reality."



Focus on: myeloma

Our researchers are pioneering a new understanding of the genetic complexities of myeloma, and the innovative use of existing drugs as treatments.

Myeloma, also called multiple myeloma, is one of three main categories of blood cancer that affect white blood cells. The other types of blood cancer are leukaemias and lymphomas.

Myeloma is a cancer of the plasma cells. Plasma cells, along with other types of white blood cells, are produced by the bone marrow. White blood cells form a vital part of our immune system.

Our researchers are studying myeloma to understand more about how it develops. Research led by Dr Martin Kaiser, a Senior Clinical Research Fellow at the ICR, is looking at the effect of switching genes on and off, and using this understanding to design and trial new treatments.

Dr Kaiser explains: “When myeloma develops, too many abnormal plasma cells are produced in the bone marrow. These myeloma cells can cause painful lesions and bone fractures, and produce antibodies that can harm the kidneys.

“At the same time, the body produces fewer of the other types of white blood cell, meaning people with myeloma can get severe infections out of the blue.”

In your genes

When viewed through a microscope all myeloma cells look alike. But at the genetic level, myeloma cells are highly variable.

Our researchers, including Dr Kaiser, have played leading roles in demonstrating the genetic variability in myeloma cells. They are also using this knowledge to test treatments in large-scale clinical trials. These trials have helped to establish the best treatments for myeloma, including the use of a drug called lenalidomide in patients who still have the disease after initial treatment. The success of lenalidomide in the trials has led to related



Left: Myeloma lesion affecting the radius bone in the arm. Above: Dr Nandita deSouza in front of an MRI machine used to diagnose the spread of myeloma.

drugs like pomalidomide also being developed as treatments for myeloma.

Recent trial results have shown that 90 per cent of patients with the worst prognoses can be identified using a test for mutations in nine key genes. Researchers are now examining how to use this ability to spot those at highest risk to plan treatments that extend life more effectively – as well as delving into more complex questions, such as how genes are switched on or off in myeloma.

Vital insights

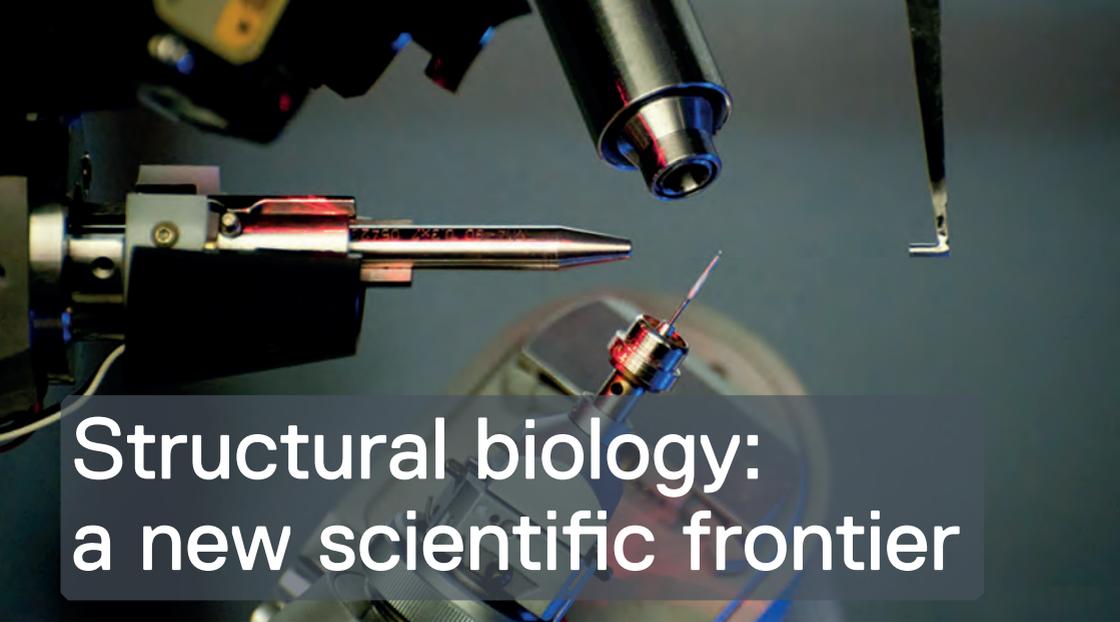
We are also examining myeloma from different angles. Dr Nandita deSouza's group has established whole-body scans using magnetic resonance imaging (MRI) as a tool to help doctors diagnose how far the disease has spread in individual patients. Their research will free doctors from having to rely on repeat X-rays of individual bones or repeat bone marrow biopsies, which are less precise and can be painful.

And Professor Richard Houlston's team – who are experts in large-scale population studies

of genetics – has made several important discoveries about the fundamental causes of myeloma. His team has found 17 genetic variants – slight changes to the DNA sequence – that seem to put a person at higher risk of developing myeloma. In 2016 they made two new findings.

They discovered that one genetic variant helps to increase the production of a protein that raises the risk of myeloma, and they found that the gene that produces osteoprogesterin – usually associated with regulating bone density – could be involved in causing bone disease in patients with myeloma.

Our research programme in myeloma is allowing us to identify which patients are most at risk, and which treatments are most likely to help them. Not only are our studies providing new clues that could lead to completely new treatments in the future but, importantly, we are providing new tests and clinical tools that clinicians can use right now to maximise the benefits that patients get from current treatments.



Structural biology: a new scientific frontier

Several research teams at the ICR are devoted to structural biology – a crucial discipline in cancer research that is shedding light on some of life’s most fundamental processes.

Every cancer drug is a molecule – a collection of atoms put together in a particular shape. Modern drugs are meticulously designed with a particular target in mind, either within a cancer cell or on its surface.

These targets are proteins, the drivers of all our biological processes, which are co-opted in cancer to drive cell growth and spread.

Our structural biologists explore the shapes of these proteins in detail, down to the individual atom, and work out how they interlock with other proteins and potential drugs.

As Laura Mariotti, a PhD student in the ICR’s Division of Structural Biology, explains: “We’re interested in finding out what a protein looks like in three dimensions, to better understand its function and how, in cancer cells, it can go wrong.

“If we can determine which parts of the protein are important for its role in normal cells and cancer cells, then chemists might be able to design drugs that turn the protein on or off.”

To do this, researchers use two main techniques: protein X-ray crystallography and electron microscopy.

“For protein X-ray crystallography, we make a crystal containing millions of copies of our protein of interest, all slotting together in a highly ordered way,” Laura explains. “Then we irradiate the crystal with X-rays to create a map of the atoms’ positions.

“In electron microscopy, we image our protein at around 50,000 times magnification using a beam of electrons, rather than light.”

This enables structural biologists to make two-dimensional projections of protein shapes in many orientations, and use these different views to re-construct a model of the 3D object.

Making maps

Several ICR-led research programmes are using these two techniques to improve our knowledge of key cancer-causing proteins, and are sharing their discoveries with the whole field.

One focus is cell division – normally a highly regulated process, but hijacked by cancer to drive its continued growth. Recent studies from the ICR’s Division of Structural Biology have produced detailed maps of two major players in this process: the proteasome and the anaphase-promoting complex.

These maps have advanced our understanding of how the various parts of both complexes weave together and pull apart during cell division – not only in humans, but in all animals and plants.



Drug discovery

Our structural biologists also work closely with our drug discoverers, exploring how prototype drugs interact with proteins to block signalling pathways. They often focus on cancer targets that no current drugs are effective against.

For example, Dr Rob von Montfort led a recent study that explored how tiny fragment molecules could be used to block a protein called Hsp70 – a ‘master controller’ that oversees several cancer-driving signals. Because of its shape, Hsp70 is a challenging target – but our research has shown how it might be possible to make drugs that block its action.

Cool tech

Some of our researchers are also using a developing technology that is sparking much excitement in the field, called cryo-electron microscopy. This involves freezing and imaging samples at -180°C to preserve the finest details of the protein shapes.

Dr Ed Morris’s team used the technique to image the proteasome, a protein complex important for cell division and protein degradation, at ultra-low temperatures. The team revealed a target site for potential drugs – and even showed an inhibitor molecule bound in place, blocking the protein’s action.

Dr Morris says: “Cryo-electron microscopy is an emerging and tremendously exciting approach in cancer drug design. As well as offering much greater detail than it did even a few years ago, it provides the opportunity to study protein complexes in conditions closer to those in the human body – which should make it much easier to design entirely new cancer drugs.”

Our structural biologists are helping to answer some of the big unknown questions in biology – as well as helping to discover new treatments for cancer.

Mayor of London opens revolutionary radiotherapy machine

Mayor of London Sadiq Khan has hailed our new radiotherapy machine as ‘groundbreaking’ on a visit to the ICR and our hospital partner, The Royal Marsden.

Mr Khan joined leading researchers and clinicians, funders, local MPs and councillors, and commercial partners on a visit to open our new machine, called an MR Linac.

“It’s a great honour to be involved in officially opening the MR Linac radiotherapy system,” Mr Khan said. “This truly groundbreaking device is the first of its kind anywhere in the UK and has the potential to transform the care that cancer patients receive. The MR Linac will give patients access to the most cutting-edge treatment available, which could help to save lives.”

The MR Linac machine is the first technology that can perform an MRI scan of a patient while simultaneously delivering X-rays for radiotherapy. Its purchase and installation has been funded by a major grant from the Medical Research Council.

The device directs the radiation beam in real time, even at tumours that move during treatment – for example, as the patient breathes. The better targeting should make radiotherapy more effective, and reduce the risk of side-effects.

The first patients are due to be treated in the second half of 2017, initially through clinical studies in hard-to-treat cancer types.



Our research strategy is unveiled with pledge to turn ‘weeks into years, and years into cures’

Our new research strategy, which we developed jointly with The Royal Marsden, lays out the vision for our research over the next five years. We are aiming to address what we believe is the single biggest problem in treating cancer patients – cancer’s ability to adapt and evolve. It is this adaptability that allows cancers to become drug resistant and stop responding to treatment.

Launching our ambitious new plan, Professor Paul Workman, Chief Executive at the ICR, said: “With such a complex challenge, we need to raise our game even higher and focus on anticipating, outpacing and overcoming cancer evolution and treatment resistance.”

We want to unravel cancer’s complexity, to better understand the processes that cause cancers to change and evolve. We can then use this knowledge to come up with new ways of attacking cancer, and develop smarter, kinder treatments for patients by running innovative clinical trials. An important part of the strategy is to make sure our discoveries are embedded into routine healthcare, so they can make a real difference to the lives of cancer patients and their families.

Professor Workman said: “In the difficult to treat cancers, our previous treatment advances have commonly delivered extra months of valuable life. Now we want to turn months into years, and

years into cures. But we won’t be able to achieve our goals without you, our supporters, who make possible everything we do.”

We look forward to keeping you updated on our progress in future issues of Search.





“If my wife
can fight,
then so
can I”

Fundraiser Dave Griffiths is set to complete 10 full marathons and one ultra-marathon between March and October this year – all to raise money for our research.

Dave was motivated to take on this incredible series of challenges by his wife Michelle, who is currently undergoing treatment for thyroid cancer.

“I made the decision to run 10 marathons this year for the ICR because their relentless research means that people like my wife and many more can continue in their fights against cancer.

Dave's events:

ASICS Greater Manchester Marathon	2 April
Brighton Marathon	9 April
Virgin Money London Marathon	23 April
Belfast City Marathon	1 May
Shakespeare Marathon	7 May
Rock 'n' Roll Liverpool Marathon	28 May
Hadrian's Wall 'The Wall' 70 mile Ultramarathon	17 June
Ely 'Monster' Marathon	24 September
Plusnet Yorkshire Marathon	8 October
Birmingham International Marathon	15 October
Snowdonia Brooks Marathon Eryri	28 October

"I have run three marathons before, but training for 10 in six months has taken my training, but more importantly my mind, to a whole new level. Many miles have been run during training already and many more will be run before my challenges come to an end at the Snowdon Brooks Marathon in late October.

"Any time I feel tired or pain during these runs I will think of all those people, including my wife, who are fighting cancer and who could benefit from the discoveries taking place in the ICR's labs. I'll use their strength and heart to help me keep putting one foot in front of the other. I can't and won't let them or this wonderful organisation down."



Have you been inspired by Dave and our amazing fundraisers? You can apply for any of our events by visiting www.icr.ac.uk/sports or going to page 19 for our full events calendar. Doing your own event? Let us know by emailing sports@icr.ac.uk.

Fundraiser recognised by Prime Minister

Lynn Lucas has raised millions for the ICR

Prime Minister Theresa May has praised fundraiser Lynn Lucas, who set up a trust to fund research into a rare form of cancer in memory of her son Chris. Chris was diagnosed with a rare sarcoma called rhabdomyosarcoma in 1997. He twice battled back after treatment before his death in 2000.

In Chris's memory his parents, both called Lynn, set up the Chris Lucas Trust – and have since raised more than £2 million towards our research into the disease.

In recognition of these incredible efforts, Lynn was chosen for a Points of Light Award, which recognises outstanding volunteers who are making a change in their community.

“I was very shocked to get the call,” says Lynn. “Things like this don’t happen in Newcastle!

“It’s an honour I want to share with my husband – we’ve dedicated our lives to this cause. It started during Christopher’s illness when we raised money for the local hospital and, since he died, we’ve raised money for research that offers hope for others with this rare cancer.”

In a personal letter to Lynn, Prime Minister May wrote: “Your fundraising efforts are making a vital contribution to research into sarcoma. Your important work through the Chris Lucas memorial fund is a wonderful tribute to the memory of your son.”



The Trust has already contributed to important research at the ICR. One study it helped to fund showed that combining two targeted therapies could slow cancer growth more effectively than either therapy alone.

In addition, a recent pledge by the Trust enabled us to employ two scientists to work exclusively on rhabdomyosarcoma, supervised by Professor Janet Shipley – a world leader in researching the disease.

Professor Shipley is hugely grateful for their support: “The Lucases and the supporters of their charity have tirelessly raised funds for our research for many years.

“Lynn is hugely deserving of this award – her support has been tremendous and so important to my research, as well as to future rhabdomyosarcoma patients.”

Events calendar

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

Run

British 10k London Run

9 July 2017

See some of London's most iconic sights when you take on this 10k run, one of the world's greatest road race routes.

Great North Run

10 September 2017

Take on the challenge of the UK's biggest half marathon, which starts in Newcastle-upon-Tyne and ends at the coast.

Cycle

Prudential RideLondon – Surrey 100

30 July 2017

Join #teamICR and cycle 100 miles past London landmarks and the beautiful Surrey countryside – perfect for every cycling enthusiast.

Vietnam to Cambodia cycle ride

November 2017 and March 2018

If you're looking for something a little more demanding, sign up now for this 10-day, 400km ride from bustling Ho Chi Minh City to the ancient temples of Angkor Wat.

Trek

TrekFest

June and September 2017

The ICR is charity partner of this challenging event and we still have a few places available. You can choose to trek in the Brecon Beacons or the Peak District.



Social

Carols from Chelsea

5 December 2017

We invite you to join us in Christopher Wren's beautiful chapel at the Royal Hospital, Chelsea, for an evening of traditional Christmas carols and readings.

If you are already taking part in an event, get in touch and use your own place to raise funds for us.

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

www.icr.ac.uk