ICR The Institute of Cancer Research

# search

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Remembering
Dame Deborah James

Inside this issue

# Our mission is to make the discoveries that defeat cancer.

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# Editorial

**This is my first editorial for Search magazine, and it coincides with my one-year anniversary as Chief Executive of The Institute of Cancer Research. It has been a busy and exciting year as we move on from the Covid-19 pandemic and look ahead to our exciting new research strategy.**

I have particularly enjoyed meeting many of you, our donors, who help to make our research possible.

Earlier this year our Director of Fundraising, Lara Jukes, left the ICR after almost 12 years. Lara was a driving force for our fundraising, and she will have been a familiar face to many of you. We are all very grateful for her tireless efforts to raise money for our research to improve the lives of cancer patients.

We were all deeply saddened by the death of cancer campaigner Dame Deborah James. It was amazing to see how she inspired so many people through her writing and podcast, and raised so much money for cancer research through her Bowelbabe Fund. In September we were proud to posthumously award her with an honorary doctorate for her outstanding contribution to raising awareness of living with cancer, and the importance of cancer research. Read more about her legacy on page 8.

In this edition you can also read about our cutting-edge new Centre for Protein Degradation, which will find brand new ways to target cancer, and was made possible thanks to the largest philanthropic gift we have ever received. Find out more on pages 12-13.

Finally, in May we found out that we were rated second in REF 2021 – the Government's evaluation of university research quality – among all higher education institutions in the UK. These results are recognition of our world-class research and the benefits it is having for people with cancer. Thank you so much again for supporting us and for being part of this success.

**Professor Kristian Helin**
Chief Executive
The Institute of Cancer Research

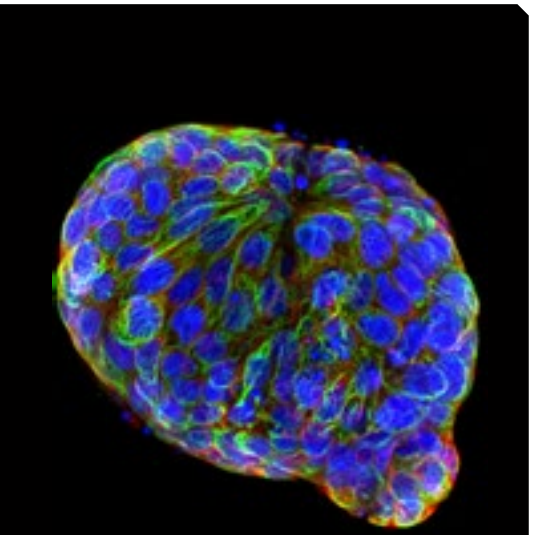
# Expanding reach of genetic testing could benefit patients

A new study has found that screening patients' genomes as part of routine GP care has the potential to significantly improve people's health.

The pilot study was led by Professor Ros Eeles, Professor of Oncogenetics at the ICR, in collaboration with a private GP practice and The Royal Marsden. The researchers screened healthy people for genetic changes that could increase their risk of various diseases using whole-genome sequencing. They found that a quarter of the participants had alterations that increased their risk of diseases such as cancer and heart disease, leading to changes in the way patients were managed by doctors.

Professor Eeles said: "We feel that this work could help to pave the way for a future where genomic screening is provided routinely to patients in primary care."

Professor Ros Eeles


A mini tumour grown from KRAS-mutated cancer cells

## Promising new drug combination to defeat cancer's 'death star'

Our scientists have discovered a new drug combination to target the KRAS protein, which drives one in four cancers and is known as cancer's 'death star'.

KRAS has a largely impenetrable, drug-resistant surface. But using a new approach, the team combined two drugs each targeting a different essential pathway. Results from a small, early-phase trial showed benefit in some patients with advanced lung, thyroid and ovarian cancers.

Professor Udai Banerji, Deputy Director of the Drug Development Unit at the ICR and The Royal Marsden, who led the study, said: "We are heartened that we've managed to slow cancer progression in several patients who had run out of treatment options."

## Light-activated 'photoimmunotherapy' could enhance brain cancer treatment

Our scientists have developed an innovative 'photoimmunotherapy' that could help detect and treat an aggressive form of brain cancer by forcing cancer cells to glow in the dark.

The study, led by Dr Gabriela Kramer-Marek, who heads our Preclinical Molecular Imaging Team, tested the therapy in mice with glioblastoma. The treatment improved the visibility of cancer cells during surgery and when activated by near-infrared light, also triggered an anti-tumour effect.

Dr Kramer-Marek said: "Our study shows that a novel photoimmunotherapy can both identify and treat leftover glioblastoma cells in mice. In the future, we hope this approach can be used to treat human glioblastoma and potentially other cancers too."

# Scientists discover how pancreatic cancer spread could be reversed

Our researchers have discovered how the spread of pancreatic cancer is controlled and could be prevented, paving the way for new cancer treatments.

The key is a protein called GREM1, which at high levels can reverse the process that changes cancer cells into a dangerous, invasive type. The findings could help to shift pancreatic cancer back into a less aggressive form that is easier to treat.

Professor Axel Behrens, who heads our Cancer Stem Cell Team and led this study, said: "This is a fundamental discovery that opens up a new avenue for uncovering pancreatic cancer treatments. We hope to now exploit this knowledge and identify ways to make pancreatic cancer more treatable."

Dr Gabriela Kramer-Marek

# From London to Paris: Son leads cycling challenge in memory of father who died of bowel cancer

**George Southgate and an 'unlikely' team of cyclists rode 310 miles from London to Paris in memory of his dad this June.**

George's dad Mike Southgate was diagnosed with stage 4 metastatic bowel cancer in April 2020. He underwent treatment for almost two years before dying aged 59, in January this year. George assembled a team to cycle from London to Paris this summer to raise money for our bowel cancer research.

George said, "We were an unlikely team of four to take on this challenge – one didn't own a bike and one hates cycling! Despite this, we made it unscathed. London to Dover was the toughest day and we started to think one member should have done more training. But we pulled together, the weather, scenery and company were fantastic, and despite the very sore knees at the end, it was all worth it to raise money for the ICR.

"The cycle was very poignant, allowing us all to share memories of my dad and take time to reflect whilst we peddled. Toasting to my dad and our achievement under the Eiffel Tower was definitely a high point.

The London to Paris team

Mike Southgate

"My dad tackled his cancer head on, and he maintained such positivity, optimism and humour throughout the whole period. Sadly he was ineligible for a clinical trial, but he wanted to help increase understanding of advanced bowel cancer. We decided to support the ICR in his memory, so they can develop smarter immunotherapy treatments for this disease to benefit future patients."

Many of Mike's former colleagues have also taken on fundraising challenges. Mike was the Director of the Marine, Energy and Specialty team at Hiscox, and his team embarked on a walk along London's 16 historic bridges. The Operations team completed the Surrey Three Peaks challenge and the Property team took on a 15-mile walk. In total, a fantastic £31,000 has been raised in Mike's name.

To find out more about how you can raise money in memory of a loved one, visit icr.ac.uk/inmemory

## Bob Willis Fund donates £75,000 to our prostate cancer research

We are delighted that our new charity partner, the Bob Willis Fund, has donated £75,000 to support Professor Ros Eeles's work in prostate cancer.

Regarded as one of the greatest fast bowlers of all time, Bob Willis was a former England Cricket Captain, International Cricket Council Hall of Fame member and Sky Sports broadcaster. Bob died of prostate cancer in 2019, aged 70. The Bob Willis Fund was set up to support critical research into prostate cancer, in the hope that a nationally accessible, accurate screening programme might be introduced to save the lives of men like Bob.

Professor Ros Eeles said: "The funding from the Bob Willis Fund will support our development of a targeted screening programme in the UK for prostate cancer. We believe that if our research is a success, we could have a programme up and running in the UK within three to five years. This will allow us to diagnose men at earlier stages of their disease, when their cancer is easier to treat and potentially cure."

Bob Willis in his bowling heyday

## Spring appeal raises more than £100,000 for innovative combination therapies

Karen O'Malley, 60, pictured with her grandsons

We are hugely grateful to all of you who so kindly supported our spring appeal. Thanks to your generosity, we have raised £107,000 to help overcome cancer drug resistance with new and better treatment combinations.

Our appeal featured Karen, who has been living well with cancer for more than six years thanks to a combination of chemotherapy and the targeted drug cetuximab.

You can watch her story and donate to the appeal at icr.ac.uk/helpfinishcancer

# Carols from Chelsea marks its 20th year

**This year we celebrate the 20th anniversary of the ICR's annual Carols from Chelsea. Committee Chair, Diana MacKenzie-Charrington, reflects on two decades of our flagship fundraising event.**

Since our first event, we have raised more than £1.8 million towards the ICR's research, helping its world-leading scientists to make discoveries that improve outcomes for cancer patients. The evening of carols from the stunning

Diana MacKenzie-Charrington
Committee Chair, Carols from Chelsea

Wren Chapel at the Royal Hospital in Chelsea is full of beautiful music, with popular carols and readings.

The Carol Service marks the start of the Christmas season and is so popular that it sells out every year. Covid-19 restrictions didn't stop Carols continuing virtually in 2020, before returning to Chelsea in 2021, and we raised a fantastic amount of money during those challenging times.

I have been involved in the committee since 2012 and during that time I have never ceased to be amazed at how people come together to make this event so successful. Thank you so much to everyone who plays their part, especially the team at the Royal Hospital which includes the music department and the In-Pensioners. I am so grateful to the committee who work hard to make the evening a success and to the high-profile readers who give their time for the ICR.

Plans are already under way for our special 20th anniversary celebration, and we do hope to see many of you there.

If you would like to buy tickets, please visit **carolsfromchelsea.com**

## Events calendar

Are you ready for a challenge? If you would like to join #teamICR and raise money for our vital research, we have places available in the following events next year. For more information visit icr.ac.uk/sports or email sports@icr.ac.uk

### Upcoming events

London Landmarks Half Marathon
Sunday 2 April 2023

TCS London Marathon
Sunday 23 April 2023

Edinburgh Marathon Festival
Saturday 27 and
Sunday 28 May 2023

# Dame Deborah James celebrated with an honorary ICR degree

**We paid tribute to the incredible contributions of Dame Deborah James at this year's graduation ceremony as we posthumously awarded an honorary doctorate to the inspirational campaigner.**

As well as documenting her journey on social media, and in a regular newspaper column, the former deputy headteacher co-founded the You, Me and the Big C podcast, where she and her co-presenters candidly discussed all things cancer.

Earlier this year, Deborah and her co-presenters, Lauren Mahon and Steve Bland, graciously accepted honorary doctorates from us in recognition of the impact they have had in raising awareness of cancer through the podcast.

Dame Deborah James.
Credit: Sophie Mayanne
commissioned for
Bowel Cancer UK

Sadly, in May this year, Deborah announced that she was entering into end-of-life hospice care at home. She then launched a fundraiser, which raised more than £7 million. Her Bowelbabe Fund will be allocated, with the support of Cancer Research UK, to causes close to her heart – including precision medicine projects here at the ICR and The Royal Marsden, and awareness-raising programmes at Bowel Cancer UK. Before her death in late June, Deborah was awarded a Damehood by Prince William for her 'tireless' work in raising awareness of bowel cancer.

Dame Deborah leaves behind an incredible legacy. At our graduation ceremony, we posthumously awarded the honour to Deborah, and celebrated her extraordinary achievements with some of her loved ones.

Dame Deborah James's family with Lauren Mahon and Steve Bland at the graduation ceremony

# Professor Trevor Graham

**Professor Trevor Graham joined us in March 2022 as the new Director of our Centre for Evolution and Cancer. His research uses evolutionary principles and computational modelling to reveal how cancer develops, with the aim of improving cancer diagnosis, treatment and prevention.**

**Joined the ICR**
March 2022

**Specialist subjects**
Evolutionary theory, mathematical modelling and genomics

**Interests**
Outside of the lab, Trevor spends a lot of time with his young children. When they fall asleep and he has a moment to himself, he likes to play with their Lego.

> “There’s a real opportunity here to be able to harness ideas from evolution to improve outcomes for patients.

Professor Graham originally trained as a mathematician before doing an interdisciplinary PhD in Mathematical Biology. He joins us from the Cancer Research UK Barts Cancer Institute within Queen Mary University of London, where he led the Evolution and Cancer laboratory – the first in the Institute to be led by mathematical theory – for nearly nine years.

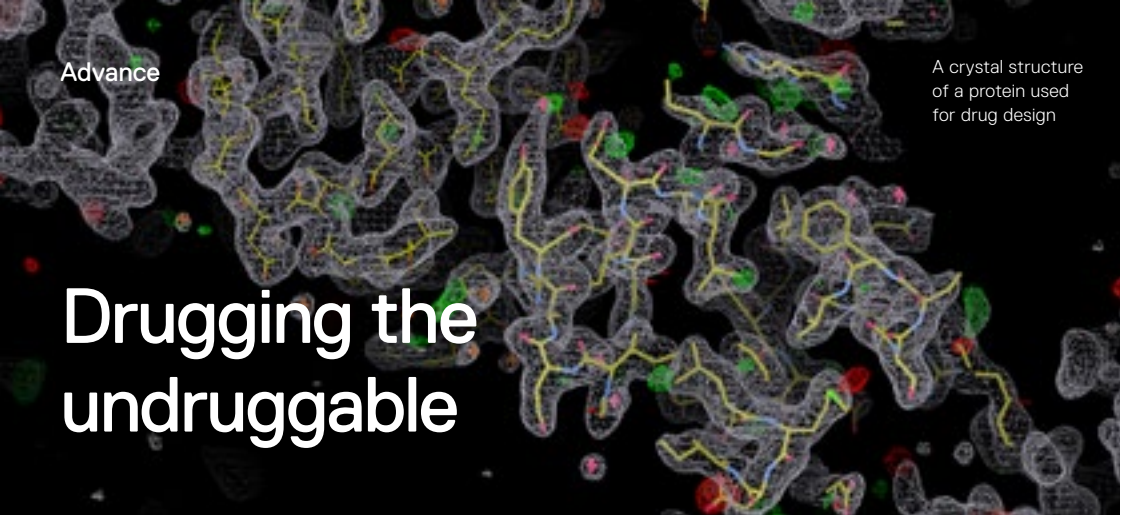
“I feel very passionate about trying to use our understanding of evolution to make a difference for people affected by cancer. Harnessing big data and mathematical models of evolutionary theory will be crucial to making progress in discovering new treatments – as well as using the treatments we already have more effectively and detecting cancer earlier.”

Professor Graham was recently awarded a prestigious Fellowship by the Academy of Medical Sciences. The award recognises scientific excellence and ability to advance understanding and improve health around the world.

He will bring his expertise in evolutionary theory and computation to his role as new Director of our Centre for Evolution and Cancer.

His centre is based within the Centre for Cancer Drug Discovery – a state-of-the-art building made possible with the generous support of donors. It hosts the world’s first ‘Darwinian’ drug discovery programme, designed to tackle cancer’s lethal ability to evolve resistance to treatment.

Professor Graham says, “I’m excited to be at an institute where cancer evolution is at the fore of so many scientists' minds. It means that there’s a real opportunity here to be able to harness ideas from evolution to improve outcomes for patients.”



A crystal structure of a protein used for drug design

# Drugging the undruggable

**For decades, some cancer proteins have been considered undruggable. But as a new field of research comes of age, our scientists are redefining what's possible and creating the cancer drugs of the future.**

Over the last couple of decades, new types of targeted drugs have improved the lives of cancer patients by precisely treating their tumours. Many of these drugs work like a key fitting into a lock – latching on to the active site of a cancer protein and stopping it from causing disease. But there are some cancer patients who have remained impossible to treat with these new kinds of precision medicine – those whose disease is caused by so-called 'undruggable' proteins.

Back in the early 2000s, bone marrow cancer, or myeloma, was one type of cancer that was often considered undruggable. But then an exciting new treatment, called lenalidomide, was approved after giving long-lasting benefits for patients with the disease in clinical trials. It worked not by blocking the function of proteins, but by wiping them out completely.

Now our scientists aim to take forward the exciting approach that made that possible – called protein degradation – as a treatment option for a much wider range of cancers.

Dr Olivia Rossanese

## The power of protein degraders

Targeted drugs are a very successful way of treating cancer, but to work they need an active part of a cancer protein to bind onto. Some cancer proteins have a relatively smooth outer surface with no obvious active element to latch onto – which is why they have been considered undruggable.

That's where protein degradation comes in. It doesn't need to inactivate a cancer protein – instead it just attaches a label to the protein to tag it for destruction, which is conducted by cells' natural system for disposal of proteins.

Dr Olivia Rossanese is Director of the Cancer Therapeutics Unit at the ICR – the largest academic cancer drug discovery group in the world.

She explains: "Protein degradation drugs, also known as degraders, can bind to a protein and cause them to be destroyed. Not only are degraders a new way to target important and 'undruggable' proteins, but they are also potentially a more powerful way."

By removing all the target proteins from a cell, protein degradation drugs not only block the function of the protein, but also stop it interacting with other proteins in the cell.

## A visionary research centre

This year, we launched a new Centre for Protein Degradation which brings together researchers working in drug discovery, cancer biology and artificial intelligence. The Centre will be based within our Centre for Cancer Drug Discovery, and will form part of our pioneering drug discovery programme dedicated to overcoming cancer evolution and drug resistance.

The Centre for Protein Degradation was made possible by a £9 million donation by David and Ruth Hill, supporters of the ICR.

Mr Hill says: "The programme is focused on delivering treatments for as yet untreatable cancers and is likely to benefit research into other diseases. We have a shared common goal, to maximise the research benefits to improve the lives of all humankind."

## From the lab to the clinic

It's a pivotal time for this field of research as new protein degraders move from the lab towards the clinic.

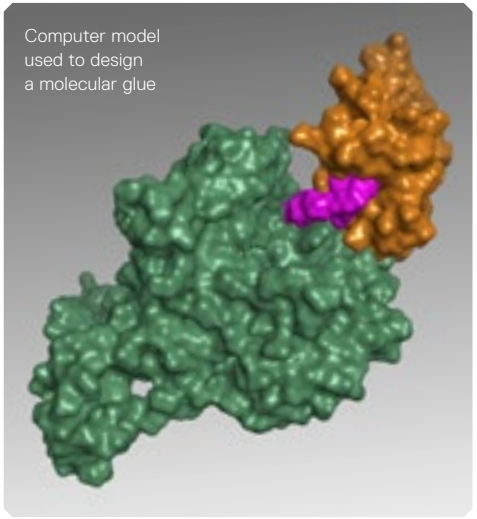
One type of degrader is known as the proteolysis targeting chimera, or PROTAC.

The first PROTACs are currently being evaluated for early clinical trials. They are designed to target the receptors for hormones like oestrogen and testosterone and bring them to the cell's removal machinery for disposal.

Dr Rossanese says: "This could be a whole new way to treat hormone-driven cancers, such as breast or prostate cancer. The trials will deepen our understanding of how degraders work which we can translate into benefits for patients."

## Molecular glues

Our scientists contributed to early research into another type of protein degradation drug called 'molecular glues'. These work in a different way, pointing the body's natural degradation enzymes towards cancer-causing proteins.



Computer model used to design a molecular glue

"This is an exciting time for the clinical development of protein degraders," says Dr Rossanese. "Our researchers are using this exciting area of drug discovery to make the so-called 'undruggable' druggable, one protein at a time."

## “Abiraterone has saved my life”

**In 2011 I was a fit and healthy 54-year-old at the top of my game. I’d worked in the entertainment industry for nearly 30 years providing security for celebrities like Beyoncé and Bob Dylan.**

But my career finished instantaneously when I was diagnosed with advanced prostate cancer.

My prognosis was not good, and I was told to only plan for the short term. Telling my five children was so hard. I promised them I would fight, but in reality I went downhill really quickly.

Then in March 2012 I was introduced to the STAMPEDE trial and I started on hormone injections and a treatment called abiraterone. Doctors do a blood test to measure levels of a molecule called PSA to look for signs of prostate cancer. When I started, my levels were at 509, when a normal reading should have been between two and four. Over the next six months I was amazed to see it reduce to 480, then 325, and finally to less than 0.1. In between there were side effects, mental anguish, and financial worries. I went through a lot, and I have to be honest about that.

I’m still being treated with abiraterone, and another medication called zoladex. I live differently now. My work is focused on being a patient advocate. I try to help men come to terms with their diagnoses and the effects of long-term treatment on their bodies.

Abiraterone has saved my life and I am grateful for that. But not everyone is as fortunate as I was to get on that trial and respond to the drug as well as I did. We need more treatments like abiraterone, drugs that enable people to live their lives with cancer – and live them well. It’s not just about surviving, it’s about so much more.

Alfred Samuels with his daughter and granddaughter

Alfred Samuels with his wife Grace

> “We need more treatments like abiraterone, drugs that enable people to live their lives with cancer – and live them well. It’s not just about surviving, it’s about so much more.

Alfred Samuels has published two books based on his experiences and the diaries he has kept of his journey. *Invincibility in the Face of Prostate Cancer: Coming Out the Other Side* charts his time in the clinical trial and *Motivated to Inspire* focuses on the post-treatment period. His film *A survivor amongst survivors* has won 23 international awards.

## “Cracking on for Tom”

**Ten years ago, 18-year-old Tom Bowdidge was diagnosed with desmoplastic small round cell tumour – an aggressive and rare type of sarcoma that affects soft tissues in the body.**

His parents Richard and Nikki, and sister Emma, will always remember Tom for his kindness. “He loved animals,” Nikki says, “and was a keen sportsman and an excellent goalkeeper.

“He’d been planning to go to university. But six months after his diagnosis, on the way back from one of our many hospital appointments, he said he was going to set up a charity instead and told us exactly what he wanted to achieve.”

Tom wanted the charity to fill the gaps for teenagers going through cancer. A crucial part of that was research.

Shortly before he died, he told his mum she would need to ‘crack on without him’ and continue his work.

Six months later his parents launched the Tom Bowdidge Youth Cancer Foundation and it’s gone from strength to strength, raising its first million pounds in February 2020.

The Foundation has partnered with us to support scientists led by Professor Janet Shipley, one of the world's leading authorities on research into soft tissue sarcomas. Her team aims to find more effective and kinder treatments that target the specific molecular defects that drive the growth of these deadly tumours.

Tom Bowdidge with his mother, Nikki

Tom Bowdidge with his family

> “Research is so desperately needed. The treatment regime was so brutal and debilitating that Tom was never well enough to have a bucket list.
>
> When we were told there were no treatment options left, we just fell through the floor.
>
> That’s now the drive for us. We don't ever want another mum or dad to have to sit there and hear that news. I know there are so many out there still having to hear it, and we’ve got to stop this. Nobody should go through that.
>
> **Nikki Bowdidge**

# Giving in memory

Making a donation in memory of a loved one is a wonderful way to celebrate their life, while also helping to fund our life-changing cancer research.

We have teamed up with MuchLoved, the leading tribute website service. The MuchLoved tribute service is quick and simple to set up and use. It provides you with the very best way to record and share your memories and stories. You can add pictures, music and video, as well as light virtual candles to help you create a truly special and unique tribute site.

Setting up a MuchLoved online tribute fund is also an easy way for your friends and family across the world to make in-memory donations. You can share the page on your social media channels and by email.

**Visit icr.muchloved.org to find out more.**