Inspired by: TeamLuke Foundation funding research into childhood cancer

14 Advance: How digital pathology could transform cancer treatment

In profile: Professor Kristian Helin – introducing our new Chief Executive

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Issue 44 | Autumn 2021
Welcome

As coronavirus restrictions are lifted and life starts to look a little more like normal, I wanted to say thank you to you, our donors, for your unwavering support.

Although the past 18 months have been very difficult, we’ve seen so many fantastic examples of how during adversity, we come together to help those who need support the most. When times are tough, our values of kindness and generosity shine through.

It is a time of new beginnings for the ICR. This summer we welcomed our new Chair of our Board of Trustees, Professor Julia Buckingham CBE, and our new CEO, Professor Kristian Helin – two brilliant appointments who will drive forward our world-leading research to benefit cancer patients worldwide. You can read more about them on pages 10 and 12.

Though we had many challenges over the past year, it is heartening that we continue to see exciting progress from our labs. On pages 16-17 you can find out about how we are discovering innovative new treatment possibilities for patients with BRCA gene mutations.

And on page 8 you can read about the running events which are returning this autumn. We are delighted that #teamICR will once again be able to come together to run for research, and we are very much looking forward to cheering them on.

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

Lara Jukes
Director of Development
The Institute of Cancer Research
Genetic discovery could help manage and treat childhood cancer

Our researchers have led the biggest study to date of the childhood cancer rhabdomyosarcoma, which has linked key genetic changes in tumours to how the disease develops.

The team, headed by Professor Janet Shipley, analysed the DNA of more than 600 patients. Their study showed that errors in specific genes can lead to poorer response to treatment and worse survival prospects, and identified patients who might benefit from close monitoring or more intense treatment.

Less than 30 per cent of children with rhabdomyosarcoma who have relapsed or whose disease has spread will survive. This work could be incorporated into future clinical trial design to help better manage rhabdomyosarcoma and improve patients’ chances of survival.

Genetic forecasting reveals how bowel cancer evolves drug resistance

Our scientists have used a precise, long-term ‘weather forecasting’ approach to predict how people with bowel cancer will respond to drugs, before they even start treatment.

The team, led by Dr Marco Gerlinger, found that by applying principles similar to those in meteorology, they could forecast how new mutations might arise in patients’ tumours to develop resistance to a drug called cetuximab.

Our researchers detected a specific ‘footprint’ before treatment called SBS17b which leads to gene mutations that cause drug resistance.

Bowel cancer drugs can have short-lived benefits, with tumours often developing resistance, so knowing when a drug will stop working can help clinicians to prepare the next treatment steps for patients.
Manchester father releases EP to fundraise in son’s honour

The father of a young boy who died of brain cancer has released a recording of evocative spoken word poems and music to raise money for research into the disease.

Chris Nelson, from Manchester, was inspired by the bravery of his son, Blaise, who was diagnosed with a glioma brain tumour in 2018 at the age of six. Blaise underwent major surgery, chemotherapy and several rounds of radiotherapy — but ultimately the treatments were unsuccessful and he died a year later.

There are various types of glioma, each of which may need different treatments. Funds raised by Chris’ EP will support our life-changing studies to classify children’s brain tumours into different types and find new ways of treating each one.

Chris says, “Blaise was such a bright and sensitive boy. He was hugely popular at school, and was just so full of joy and light that everyone warmed to him. Much more research into brain tumours needs to be done. There is an urgent need for better treatments and for better diagnoses. We were never able to find out exactly what cancer Blaise had — maybe if we’d been able to, it would have helped him.”

To listen to the EP, visit: www.chrisjammcr.bandcamp.com

Star fundraiser completes 19th charity trek

Rosemary Dunstan, a librarian from Oxfordshire, has completed her 19th fundraising trek — and her 11th for the ICR. She hasn’t let the coronavirus pandemic hold her back and has raised almost £1,800 for our vital research.

Rosemary’s fundraising treks have previously taken her across the world, to destinations including Bhutan, India, Jordan, Zambia, Mongolia and Cambodia. Though far-flung travel was restricted, Rosemary did not let that put her off. Instead, she hiked 35 miles in three days along the Cornish coast.

Rosemary said: “I usually do some sort of charity event each year and I was thinking about going to Ecuador, but then the pandemic happened. This year I thought I had better still do something as I am getting older and I want to keep doing things while I can — so I decided to do something in this country instead. It was more challenging than I expected, and my legs really felt the strain!”

Spring appeal raises £130,000 for bowel cancer research

Thank you so much to all those readers who kindly supported our spring appeal. So far you have donated £130,000 to help us develop more effective immunotherapy treatments for bowel cancer.

Overall bowel cancer survival has improved, but it is still the second most common cause of cancer death in the UK — and the frequency of bowel cancers is increasing in patients under the age of 50. Dr Marco Gerlinger, who leads our Translational Oncogenomics Team, has discovered that people with bowel cancer who have stopped responding to existing treatments could benefit from innovative immunotherapies.

Dr Gerlinger said, “I am very grateful to everyone who has donated to our vital research. Your support will bring us a step closer to personalised treatments and give patients a better chance of surviving their cancer.”

There is still time to donate to our appeal. Visit www.icr.ac.uk/helpfinishcancer

The Chris Lucas Trust celebrates 20th annual flagship bike ride

The Chris Lucas Trust held its 20th annual Great North Bike Ride in August. The fundraising event took 862 participants 60 miles along the beautiful north Northumberland coastline.

Lynn and Lynn Lucas set up the Chris Lucas Trust as a legacy for their son, who died aged 18 from rhabdomyosarcoma — a cancer resembling muscle tissue. The trust has been supporting Professor Janet Shipley’s research at the ICR for over a decade. Their generosity is enabling her laboratory to make great strides in its work to identify new ways to treat young patients with particularly aggressive disease.

862 participants

Stuart Lamb, one of Chris’ close friends who has completed the bike ride every year, with his son Harrison.
In focus

#teamICR celebrates a return to running

As coronavirus restrictions across the UK are lifted, #teamICR is excited to run together again in fundraising events this autumn.

After many months of cancelled events and virtual runs, we are delighted that in-person events are returning this autumn. The London Marathon and the Royal Parks Half Marathon will both take place in October.

For those who cannot attend the main event, the London Marathon will also include 50,000 virtual participants, making it the biggest and most inclusive marathon ever.

One person who is looking forward to returning to the London Marathon is Susan Farrow. Last year Susan was supposed to take on the mass participation event, but when the pandemic hit she switched to the virtual event instead. She is still keen to run the 26.2-mile course through the streets of London in memory of her mum, and will return this October. Not content with just one event, she has already run the London Landmarks Half Marathon and the Great North Run this year.

We are also excited to be holding the first ever Terry Fox Run UK in Battersea Park, London, on 2 October 2021, which will also be available virtually. Last year we joined runners from all over the world in virtual Terry Fox Runs to celebrate 40 years of Terry’s ‘Marathon of Hope’ — and UK runners raised a fantastic £75,000 for our research. This year hundreds of participants of all abilities will come together in Battersea and beyond, to run in memory of Terry and all he achieved.

Our new Supporter Events Manager Robyn Plowman, a keen runner herself who will be taking part in the Terry Fox Run, said: “I’ve been very impressed with the enthusiasm from #teamICR to get back to real-life running events, and I can’t wait to meet our runners this autumn.”

Events calendar

Are you ready to return to running? 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 3 April 2022
- Edinburgh Marathon Festival
  Saturday 28 and Sunday 29 May 2022
- TCS London Marathon
  Sunday 2 October 2022

The Rawhides’ Ride 4 Artemis

Artemis Alice Wood was three years old when she was diagnosed with juvenile myelomonocytic leukaemia (JMML). Despite the best efforts of the doctors and nurses at The Royal Marsden and St George’s hospitals, she died just a few months later from complications caused by chemotherapy and a bone marrow transplant.

JMML is a very rare type of slowly developing blood cancer that occurs in young children. Artemis underwent chemotherapy and a stem cell transplant, which is currently the only way of treating the disease. Matilda, her brave big sister, provided the stem cells. While the transplant was successful, the side effects of the chemotherapy and transplant were too much for Artemis to bear. She died on 27 November 2019.

Artemis’ father, Jody, is a member of an amateur cycling group known as the Rawhides. In Artemis’ memory, the Rawhides rode 829 miles in eight days in July, raising an incredible £165,000 for the ICR and The Royal Marsden Cancer Charity.

The ‘Riding 4 Artemis’ challenge took the team on a punishing route from Durness to Wiltshire, via the Yorkshire Dales and the Peak District. In the end, the cyclists climbed the equivalent of Mount Everest — twice! Jody said: “Artemis showed courage and resilience right until the very end, and she was the bravest of little girls. We wanted a tough challenge and to endure some pain in solidarity with her. We were in awe of the generosity shown by everybody who supported the ride and delighted by the total amount raised.”

The money raised will help fund research by the ICR’s Professor Sir Mel Greaves into the biology of childhood leukaemia. He said: “Everyone here at the ICR is honoured that the Rawhides have chosen to support our research in Artemis’ name and memory. We are humbled to be part of her legacy, and we would like to create an enduring link between Artemis and the research advances we will be making for years to come.”
Professor Kristian Helin

Professor Kristian Helin joined the ICR in September as our Chief Executive. He is a world-leading cancer researcher with exceptional leadership experience across three countries. He is known internationally for his pioneering scientific discoveries in cancer ‘epigenetics’ – showing how regulation of the way the DNA code is read can play an important role in the development of cancer.

Professor Helin shares our passion for advancing the scientific understanding of cancer biology, and using that knowledge to drive the discovery and development of innovative cancer treatments.

He discovered the first members of a family of proteins called the E2F transcription factors, which play an important role in helping control whether cells divide. He has also worked on understanding the proteins which help control how the DNA code is read – the field of epigenetics – and their importance in cancer. He has made pioneering discoveries in this area, advancing our knowledge of how cancers develop.

In 2003 Professor Helin was appointed as the first Director of a new institute in Copenhagen, the Biotech Research and Innovation Centre (BRIC), which he developed into a world-class research institute. Following this success, he became Chair of Cell Biology and Director of the Center for Epigenetics Research at the prestigious Memorial Sloan Kettering Cancer Center in the US.

In addition to his groundbreaking science, Professor Helin co-founded the biotech company EpiTherapeutics ApS which has discovered new prototype drugs targeted at the regulation of DNA transcription in cancer.

We will benefit enormously from Professor Helin’s extensive international leadership experience, and his world-class scientific expertise. His appointment is a sign of the strength of our ambition to remain at the cutting edge of cancer research and treatment, by doing innovative science that is focused on the needs of patients.

“...My job as CEO is to ensure that we can continue to pursue our vision of making a difference for cancer patients. This requires the continued recruitment of talented colleagues, being at the forefront of new research technologies and having the required resources to follow our mission.”

Joined the ICR
September 2021

Specialist subject
Epigenetics and cancer biology

Interests
Professor Helin enjoys playing and watching football, as well as travelling with his family. He is also planning to learn how to make his own wine and olive oil.
Professor Julia Buckingham joins us as Chair of our Board of Trustees with an exceptional track record of leadership across the UK higher education and academic research sector. She will provide robust governance, leadership and support for our new Chief Executive Professor Kristian Helin as he makes his transition to the ICR.

Our new Chair, Professor Julia Buckingham takes over from Luke Johnson after his eight successful years in the role.

Professor Buckingham is one of the highest-profile figures in the UK higher education sector, having held positions as President of Universities UK, Vice-Chancellor and President of Brunel University London, as well as senior leadership roles at Imperial College London, and Charing Cross and Westminster Medical School.

Throughout her career, Julia has combined research and education with supporting the broader aspects of academic life through work with UK research councils, medical charities and learned societies.

She has published widely in her research field of pharmacology, served on national and international review panels and received prestigious awards and honours for her work. In 2018, she was awarded a CBE for services to biology and education, and in 2019 she was elected as a Fellow of the Academy of Medical Sciences.

Her first priority is to support our new CEO, Professor Kristian Helin, as he settles into his new role. Her experience as both an executive and non-executive leader of academic institutions means she understands the demands and differences of both roles, which will help to ensure a smooth transition.

With decades of experience in the research sector, Professor Buckingham appreciates our strengths in areas such as drug discovery and our unique ‘bench-to-bedside’ approach.

As Chair, she understands the importance of securing the funding our researchers need, and the important role our supporters play in this. And as the cost and the complexity of science increases, Professor Buckingham also recognises the importance of forging partnerships to increase the scope and impact of our research.

Above all, she wants to help foster an environment at the ICR where fantastic science can thrive. Her appointment as Chair will help build on our status as a world-leading cancer research institute by strengthening our position within the UK’s academic research and higher education sectors.

“...I’m looking forward to learning more about the amazing science being done by our researchers and being a great ambassador for the ICR.
A new field called digital pathology is set to transform the way cancer is diagnosed and treated, using sophisticated computing tools and artificial intelligence to uncover crucial clues about tumours.

The field of pathology is one of the oldest in medicine and it is vitally important to treating cancer. Doctors specialise in evaluating cells, tissues, organs and test results to help diagnose patients and determine what type of cancer they have.

Advances in microscopy, imaging and DNA sequencing are uncovering more information about tumours than ever before. Now a new, high-tech specialism called digital pathology promises to make sense of all this data, and to make it easier and faster to diagnose cancer.

### Building digital pathology

We are building our expertise in digital pathology under the leadership of Professor Yinyin Yuan and Professor Manuel Salto-Tellez.

Professor Yuan leads the Computational Pathology and Integrative Genomics Team, which aims to train powerful computers to automatically identify cancer cells in pathology samples from the clinic. Professor Salto-Tellez joined us in the summer of 2020.

Their teams are leading efforts with colleagues at The Royal Marsden to ensure all our pathology images are captured digitally and that diagnosticians and scientists can make the most of cancer tissue analysis to enhance cancer diagnosis and treatment.

Digital imaging will allow doctors to extract new information from existing images, or look at multiple biological markers of cancer at the same time, while information can be accessed and analysed remotely.

### Going digital

Around the world, pathology departments are starting to digitise pathology images and information, so that researchers and clinicians can analyse them using computational tools.

New tumour imaging systems can scan slides of tissue samples taken from patients, so that they can be shared with colleagues, and assessed alongside molecular, radiology and pathology data.

Increasingly, digital pathology aims to integrate data from different sources using AI-driven analytical tools, to help spot patterns and crucial clues that would not be visible to the naked eye. Digital pathology offers the chance to make a huge difference to the way we understand, diagnose and characterise cancer, and to help transform how cancer is treated.

### AI and machine learning

Computers are excellent at finding patterns in data and by using tools like AI and machine learning, they can be taught how to identify features in digital pathology images that are linked with cancer.

Professor Yuan, Professor Salto-Tellez and their colleagues at the ICR and elsewhere are building a range of laboratory and computer tools to process and classify images of tumour tissue, to increase our knowledge about the biology of cancer and help pathologists make more accurate cancer diagnoses.

Computers can mark areas with similar features within tumour samples to quickly identify cancer cells and other tissue types. These can be compared with other samples and assessments by pathologists to fine-tune the results, and to spot patterns that can’t be seen by doctors. This could help to detect cancer before symptoms occur or make earlier assessments of whether treatment is working.

By drawing on the rich information contained in these images, and combining it with other types of information such as DNA sequencing data from cancer cells, the researchers can visualise cancer and its surrounding tissues in new ways. These new tools could help us understand how cancers interact with their environment as they develop and spread, diagnose patients more quickly or precisely, and predict how they might respond to a treatment.

Using the multitude of digital information produced when a person is scanned and tested for cancer, digital pathology could uncover amazing new information about the disease, and transform its diagnosis and treatment.
BRCA1 and BRCA2 are genes that we all carry. They encode for proteins that help guard our cells by repairing DNA breaks. But when there is a mutation in a BRCA gene, cells can no longer defend themselves against DNA damage – and the result can be cancer. Our researchers discovered the BRCA2 gene in the mid 1990s, and a decade later found that it was possible to exploit cancer’s weaknesses at repairing DNA with new targeted treatments.

In the early 2000s, our researchers conducted key lab experiments which showed that drugs called PARP inhibitors were particularly good at killing cancer cells with mutations in their BRCA genes. PARP is a protein involved in another process for repairing DNA – and it is essential for the survival of cancer cells with BRCA mutations. Our experiments were an early example of ‘synthetic lethality’, in which a drug is lethal for cancer cells with particular mutations, but leaves healthy cells relatively unscathed. Over the past two decades, we have developed PARP inhibitors in clinical trials as treatments for patients with BRCA mutations who have ovarian, breast and prostate cancer.

One of our researchers who did the crucial initial experiments on PARP inhibitors was Professor Chris Lord. He says: “As a scientist, you dream that some of the experiments you do in the lab eventually change the way people who have cancer are treated. Seeing that happen with the development of PARP inhibitors is the reason why we are scientists.”

**OlympiA trial: a major breakthrough**

Recently, research on PARP inhibitors took another major step forward with the release of results from the international OlympiA trial, led globally by Professor Andrew Tutt of the ICR and King’s College London. OlympiA found that women with inherited BRCA mutations who had early-stage breast cancer and took olaparib for one year following standard treatment such as surgery, chemotherapy, hormonal therapies or radiotherapy had a 42 per cent reduced risk of their cancer returning.

The findings establish olaparib as the first drug that targets the specific biology of the BRCA genes with success in treating early-stage breast cancer.

**POLQ inhibitors: a new class of drugs**

PARP inhibitors are now becoming standard of care for many BRCA-mutated cancers. But like many other cancer drugs they do eventually lose effectiveness over time as tumours can become resistant to treatment.

A new study, led by Professor Lord, suggests new drugs called POLQ inhibitors could help. These drugs target the protein POLQ which is also involved in DNA repair and could provide an alternative for patients whose cancers are resistant to PARP inhibitors.

Researchers believe that using both a POLQ inhibitor and PARP inhibitor in combination to treat patients with BRCA mutations could prevent resistance from emerging in the first place.

Professor Lord says: “It’s incredible how those early discoveries of how BRCA mutations left weaknesses in cancer cells are now leading to an increasing number of different treatments being taken forward, many of them based on that scientific principle we discovered of synthetic lethality. Our ambition is now that we can cure patients with BRCA-mutant cancers.”

**“This treatment could be there to help my children”**

“I was 38 when I was diagnosed with triple-negative breast cancer – when I got the news, my world fell apart. The cancer hadn’t spread, so I was booked in for a lumpectomy, but I knew straight away that I wanted a mastectomy to reduce the risk of the cancer returning.

Although I’m the first person in my family to have cancer, I was referred for genetic testing because I was so young, and because of the type of cancer that I had. That was when I discovered I had the BRCA2 gene mutation. I’d already been pushing for a double mastectomy and, after getting the results back, it was a no-brainer for me to have further preventative surgery, so I had my ovaries and fallopian tubes removed at the end of last year.

I have two young children. They know all about my cancer and my treatment, but I haven’t told them about the BRCA mutation yet. When they’re old enough, I’ll tell them about it and explain what it might mean for them.

In the meantime, it’s very reassuring to know about the success olaparib has been having on the OlympiA trial. I’m so thankful this treatment might be available by the time my children are grown up, and hopefully will be there to help anyone who is diagnosed in the future.”
In focus

Scientists’ lab coats transformed into wearable works of art

Three lab coats belonging to our scientists have been turned into powerful works of art emblazoned with intricately hand-stitched quotes and illustrations inspired by cancer patients.

Leading British textile artist Rosalind Wyatt worked with personal letters, poems, drawings and recollections given by cancer patients and their families, with rare and hard-to-treat cancers.

The artist then meticulously recreated these alongside original decorative features using hand stitching over a period of several weeks – threading the contributions onto the blank canvas of each lab coat.

The artworks were created to symbolise our unwavering determination to urgently find new treatments and to improve outcomes for patients with the rarest and hardest-to-treat cancers, including childhood cancers, brain, lung and pancreatic cancers, and sarcomas.

Ahead of them going on permanent display in our buildings, we were delighted that Professor Chris Jones, Dr Paul Huang and Valeriya Pankova wore the unique lab coats to promote our vital research.

To find out more and support this area of our research go to ICR.ac.uk/labcoat

Patient focus

“He inspires everything we do”

Luke Bell was just eight years old when he died from neuroblastoma. Inspired by Luke, his family set up the TeamLuke Foundation to improve the diagnosis and treatment of childhood cancer.

Luke loved gaming, rugby, school, playing with his friends and most of all spending time with his family. He was incredibly active and full of energy, so it came as a surprise when he started to become tired very easily in early 2017. Following various tests, Luke was diagnosed with high-risk neuroblastoma – a cancer of the developing nervous system.

Luke began a gruelling course of treatments, including high-dose chemotherapy, extensive surgery to remove the tumour, radiotherapy and immunotherapy – but by spring 2018 he had relapsed. Further treatment commenced over the following six months. However, routine scans and tests in November revealed that the cancer had spread aggressively throughout Luke’s body, and the family were informed that the cancer was now terminal.

Determined not to give in, Luke was accepted onto a clinical trial in Barcelona, but he didn’t make it. Luke died just before Christmas in December 2018.

Luke’s dad Mark says: “The TeamLuke Foundation was set up to create a legacy for Luke, in the spirit of his personality. Luke was very inquisitive and took a great interest in the treatment he was going through. He was also a very helpful boy, who did not like to see any sadness or suffering. He inspires everything we do.”

A key priority for TeamLuke is funding research that will improve the diagnosis and treatment of childhood cancer – and ultimately prevent it. To fulfil this aim, TeamLuke is supporting the research of Professor Louis Chesler, Head of the ICR’s Centre for Paediatric Oncology Experimental Medicine.

The foundation has generously pledged £15,000 per year towards a Senior Staff Scientist post in Professor Chesler’s team, and Dr Chiara Gorrini has been recruited to the role. She says: “I’ll be focused on driving forward the team’s exciting project portfolio which will lead to smarter and kinder treatments for children. Thank you to TeamLuke Foundation for helping to make this possible through its tireless work.”

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