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Issue 45 | Spring 2022



Dr Alex Radzisheuskaya

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Our mission is to make  
the discoveries that  
defeat cancer.

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## Editorial

Despite the challenges of the past two years, our research continues to bring hope to cancer patients. We started the year with the wonderful news that an innovative drug we discovered will be given to the first patients as part of a new clinical trial.

This is the 12th of our drug discoveries we've taken into clinical trials since 2005 – giving cancer patients hope that they will have additional treatment options and many more years with their loved ones. We hope to bring you further good news stories like these, now that our Centre for Cancer Drug Discovery is up and running.

On page 10, we introduce our new Team Leader in the Division of Cancer Biology, Dr Alex Radziskeuskaya, who joined us in November 2021. Dr Radziskeuskaya's research will focus on how proteins help to package up DNA in cells – and the role that this can play in cancer.

Vaccines have been a worldwide focus of the past year as a way out of the coronavirus pandemic.

But could we ever see a vaccine for cancer? We explore this and other exciting developments in the field of immunotherapy on pages 16-17.

In this edition, you will also meet two fundraisers who took on unusual challenges to support our research. I hope you will be inspired by their determination to raise money and awareness of our vital work.

With the support of people like you, we will continue to work together to give cancer patients a better future. Thank you.

#### Lara Jukes

Director of Development  
The Institute of  
Cancer Research

## Our research showcased in exhibition on cutting-edge cancer research

Members of the public can learn more about our pioneering research as part of a major new exhibition by the Science Museum Group titled *Cancer Revolution: Science, innovation and hope*.

The exhibition features examples across our research, from breakthroughs of the last few decades that have already transformed cancer treatment, to the cutting-edge science of today – seeking to understand and overcome cancer evolution.

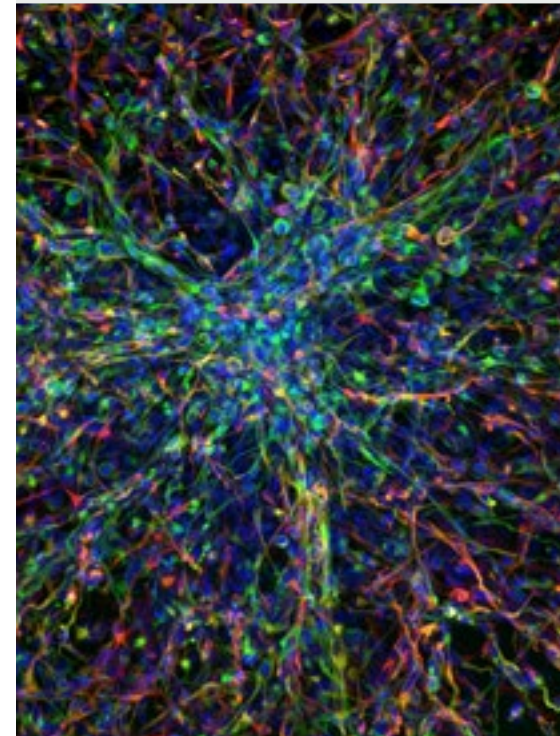
The exhibition is currently open at the Science and Industry Museum in Manchester and will open at the Science Museum in London in May 2022.

## Our latest drug discovery enters clinical trial

The first patients have received an innovative new drug which we discovered, thanks to a collaboration with the company Nuvectis.

The phase I trial of the drug, called NXP800, will focus particularly on women with advanced clear cell ovarian and endometrioid ovarian cancers. It is being led by Professor Udai Banerji, Deputy Director of the Drug Development Unit at the ICR and our partner hospital The Royal Marsden.

Our Chief Executive Professor Kristian Helin said: “NXP800 is the 12th of our drug discoveries we’ve taken into clinical trials for cancer patients since 2005, in collaboration with industrial partners. That track record is unrivalled in the academic world.”



## AI picks out new drug combination for childhood brain cancer

Our scientists have used artificial intelligence (AI) to come up with a new combination of drugs to treat the aggressive childhood brain cancer, DIPG.

The team, led by Professor Chris Jones, Professor of Paediatric Brain Tumour Biology, used AI to find a way of combining existing drugs that are already approved to treat other types of cancer, and found that one treatment extended survival when tested in mice with DIPG.

The next step will be for the drug combination to enter clinical trials. Professor Jones said: “Our study demonstrates just how much AI can bring to drug discovery for cancers like DIPG, in proposing new treatment combinations that would not have been obvious to people.”



## Prostate cancer drug could halve risk of death

Our researchers have shown that adding abiraterone to the standard treatment for some prostate cancers, where the cancer has a high chance of spreading, could halve the risk of death from the disease.

Abiraterone – one of our major discoveries – could now be made available for more NHS patients in England and Wales as a result of the latest findings. Chief trial investigator Professor Nick James, who leads our Prostate and Bladder Cancer Research Team, explained:

“Abiraterone is licensed to treat prostate cancer that has spread to other parts of the body or has stopped responding to standard hormone therapy. But our new findings suggest the drug can also benefit men whose cancer is at an earlier stage.”



Professor Nick James



## The Princess Royal officially opens new drug discovery centre

Her Royal Highness The Princess Royal has officially opened our Centre for Cancer Drug Discovery and toured the centre to learn more about our work to overcome cancer's deadly ability to evolve and become resistant to treatment.

Her Royal Highness met scientists from a range of disciplines. They showed Her Royal Highness some of the building's cutting-edge equipment and demonstrated how this helps them make important discoveries.

Dr Olivia Rossanese, Head of Cancer Therapeutics at the new centre, said: "I was immensely proud to meet Her Royal Highness with my team. Our collaborative approach will accelerate our work to find urgently needed smarter and kinder therapies and help us stay one step ahead of the disease."

“ ”

Our work has never been more urgent, as delays in diagnosis and treatment as a result of the pandemic have left many cancer patients more vulnerable than ever.

**Dr Olivia Rossanese**



## Christmas appeal raises £140,000

We are hugely grateful to all our readers who kindly supported our Christmas appeal. So far, £143,500 has been donated to help our cutting-edge prostate cancer research, which will make a real difference to men and their families.

Our wide-ranging programme of prostate cancer research has had huge benefits for patients, delivering new targeted cancer drugs and more accurate radiotherapy. Yet survival rates when the disease is diagnosed at a later stage remain low – so we are also pioneering brand new genetic approaches, with the aim of developing a test to pick out men at high risk of prostate cancer.

Thank you for helping us improve treatments for men today, as we look towards a brighter future for tomorrow's patients.

There is still time to donate to our prostate cancer appeal. Visit [www.icr.ac.uk/brighterfuture](http://www.icr.ac.uk/brighterfuture)

## Carols returns to Chelsea

Following a virtual celebration in 2020 due to the pandemic, we were delighted to welcome back guests to our flagship event, Carols from Chelsea, on 7 December.

The service, held in the stunning Wren Chapel of the Royal Hospital Chelsea, marks the start of the festive season for many of our supporters. This year actors Toby Jones, Patricia Hodge and Céline Buckens gave readings at the service, alongside former MP Sir Nicholas Soames. The event raised £90,000 to support our research.

We are already looking forward to our Carols from Chelsea 20th anniversary event on 6 December 2022.



David Webb

## 24 marathons in 24 days

While most of us were opening a new door on our advent calendar each day of December, David Webb was warming up his lungs and limbs to run a new marathon. This is the fourth year opera singer David has fundraised for us, and #Carols4Cancer2021 saw him complete an incredible 24 marathons in 24 days. His festive feat raised a total of £13,426.

David kicked off his challenge by singing a Christmas carol, and nominating three people to do the same – to help spread cheer, and to spread the word about our cancer research. David chose to fundraise for us in honour of his close friend Polly, who died from cervical cancer aged 32.

David said: "Having someone to fundraise for spurs you on. Polly was a big part of my life, and the reason for every step I took. I'm truly grateful to everyone who got involved with #Carols4Cancer and helped it grow. It's been amazing, and I'm so pleased we were able to raise such a great total".

## New PhD studentship fund made possible by major donation

We have received a substantial donation to provide long-term support towards training the future leaders of cancer research. The major donation will support the cost of a student's PhD each year.

The Rhonda and Sean Ryan Postgraduate Studentship Fund will support a succession of PhD students. We will select a student every four years to receive an award to cover the duration of their PhD.

Rhonda, who has a background in pension fund management, and Sean, a scientist, have been personally affected by cancer. They are passionate about helping us invest in training the cancer research leaders of tomorrow.

As a member institution of the University of London, we are dedicated to educating and training the next generation of scientists and clinicians who will go on to be leaders in cancer research. Our PhD studentships last four years and support independent research, aiming to encourage the student's intellectual curiosity, creativity, talent and diligence, under the guidance of an experienced member of our Faculty.

Rhonda described her and Sean's motivation for establishing the endowment: "We were both incredibly impressed with the work that the ICR is doing. It is just so important and makes such a huge difference to the lives of cancer patients and their families. The scientists are our



Rhonda Ryan

heroes. The endowment will help the ICR's researchers understand and treat cancers while training the specialists of the future."

Major donations to the ICR are vital for ensuring the long-term sustainability of our pioneering research. We are so grateful to Rhonda and Sean for their incredible support.

**To find out more about making a philanthropic gift, please contact Hannah Joyce, Deputy Director of Philanthropy, at [hannah.joyce@icr.ac.uk](mailto:hannah.joyce@icr.ac.uk)**



### 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 later this year. For more information visit [icr.ac.uk/sports](http://icr.ac.uk/sports) or email [sports@icr.ac.uk](mailto:sports@icr.ac.uk)

### Upcoming events

- Great North Run  
Sunday 11 September 2022
- Terry Fox Run UK  
Sunday 18 September 2022  
(subject to confirmation)
- Virtual London Marathon  
Sunday 2 October 2022
- Royal Parks Half Marathon  
Sunday 9 October 2022

## Moped marathon goes viral

Paul Taylor made headlines last year when he embarked on an epic journey of 1,800 miles through some of the UK's silliest and rudest named places – all on his 49cc moped with a top speed of 28mph.

His journey took him via Pity Me in Durham, Booze in the Yorkshire Dales, Brawl in the Highlands, Happy Bottom Nature Reserve in Dorset and Cockpole Green in Berkshire to name just a few. Sadly his moped broke down on a remote mountain pass 1,200 miles into the expedition, but he was undeterred and completed the challenge in a hire car.



His adventure truly captured the public imagination, with Paul being interviewed live on BBC Breakfast TV and other media outlets around the world. He ended up raising £25,000 for our research, far surpassing his original £1,800 target.

Paul decided to undertake the challenge after his close

friend Alexis died of cancer. Paul said: "My friend Alexis was the bravest person I've ever met. He first had surgery for lymphoma when he was 18 and had several further operations over the years. Even after his cancer returned and it was clear he would not survive, Alexis remained positive, saying he had nearly died at 18 so he was thankful for those extra years. He was 55 when he died in 2020.

"I was sick of cancer taking the lives of so many wonderful people and felt I had to do something to help beat this disease. I thought this trip was a suitably ridiculous place to start!"

**See photos from Paul's adventure at [www.instagram.com/moronicmopedmarathon](http://www.instagram.com/moronicmopedmarathon)**



Alexis and Paul



## Dr Alex Radzischeuskaya

Dr Alex Radzischeuskaya joined us in November 2021 as Team Leader in Chromatin Biology. Her research seeks to understand how changes to proteins in chromatin called histones can help to turn genes on and off and to repair DNA damage – and the role that this can play in cancer.

### Joined the ICR

November 2021

### Specialist subjects

Chromatin biology and cell biology

### Interests

Outside of the lab, Dr Radzischeuskaya likes to play board games and explore nature with her two young children.

“ ”

I wanted my next step to be at the ICR because it values the importance of integrating the fundamental science with the clinical to design better therapies.

Earlier in her career, Dr Radzischeuskaya secured two postdoctoral fellowships working in our Chief Executive Professor Kristian Helin's lab at the Biotech Research and Innovation Centre in Copenhagen and in Memorial Sloan Kettering Cancer Center in New York. She moved with Professor Helin to the ICR, where their labs investigate different questions in cancer epigenetics – showing how regulation of the way the DNA code is read can play an important role in the development of cancer.

Chromatin is a complex of DNA and protein that packages up DNA, squeezing whole genomes into the cell nucleus. Histone proteins play a key role in this process, acting as spools that wrap strands of DNA tightly around them. Dr Radzischeuskaya's research focuses on the chemical modifications of histones to shed light on how they affect cell biology

and identity. By looking at cell and animal models that possess or lack specific histone modifications, her team can see how these changes regulate genes that control how cells specialise into particular types, or how they become cancerous. Ultimately, this could help to understand their role in cancer and help create more personalised treatments.

She says: "This is an exciting field of research with the potential to open up new avenues for treatment. But we need a much better biological understanding of the role of histones in cells, which I hope can help to show how changes to these proteins could contribute to cancer. If we understand more about this crucial area of cancer biology, it can point us to new precision medicines targeted at changes within the cells of an individual patient's cancer."



## Dr Chiara Gorrini

Dr Chiara Gorrini joined Professor Louis Chesler's lab after 10 years in Canada studying the biology of breast cancer. Her research now focuses on two types of childhood cancer: neuroblastoma, a type of cancer that develops in nerve tissues, and medulloblastoma, a type of brain tumour.

### Joined the ICR

January 2020

### Specialist subjects

Tumour microenvironment and tumour immunology

### Interests

Interior design, environmental sustainability, reading

Dr Gorrini joins us with years of experience developing the latest techniques to improve the way we study cancer – including highly specialised mouse models and state-of-the-art imaging technologies, which can track cancer in unprecedented detail.

Dr Gorrini says: "I started approaching these technologies in my breast cancer lab in Canada which worked closely with the engineering faculty. It's so exciting to join a lab that's using these techniques for childhood cancer.

"There's a huge knowledge gap when it comes to childhood cancers and this really struck me after moving from a breast cancer lab. Childhood cancers are so diverse, and we really need to unravel their underlying biology, so that we can create better treatments."

In the UK, around 100 children are diagnosed with neuroblastoma and 55 children

with medulloblastoma each year. Compared with more common cancers, the relatively small number of cases presents major challenges in studying the diseases.

Dr Gorrini will work to improve the models available for studying these childhood cancers, to accelerate the discovery and development of new treatments. She is also using models of patients' tumours to better understand cancer evolution – that is, the ability of cancer to change over time and evolve resistance to treatment.

Dr Gorrini's post is being supported by the TeamLuke Foundation, which has pledged £15,000 per year.

The Foundation was set up as a legacy for Luke Bell, who died from neuroblastoma at just eight years' old.



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New technologies are allowing us to study childhood cancers in more detail than ever before and it's a really exciting time to be at the ICR.



# Damaged DNA – wielding a double-edged sword against cancer



Microscopy analysis of cancer cells dying in an experiment mimicking chemotherapy in cell culture. Cells indicated with arrowhead are in the process of dying. DNA is stained in magenta.

Our scientists are seeking to understand how cells respond to damage to DNA – and the tricks cancer uses to stay alive despite suffering genetic damage. Understanding this intricate network of sensors and signals could lead to new ways of attacking cancer by reactivating cells' natural defences.

Everything from sunlight to 'copy and paste' errors in cell growth and division leaves a mark on our DNA. This everyday damage is manageable because of our cells' built-in repair system known as the DNA damage response. However, if something goes wrong in this complex signalling system, or too much damage builds up, it can lead to cancer.

## Unravelling the DNA damage response

In the 1960s, our scientists uncovered the first conclusive evidence that DNA damage was the fundamental cause of cancer. Over the decades, we have created treatments targeting cancer cells with faulty repair systems, such as those with mutations in the BRCA breast cancer genes.

However, the cell's DNA damage response is hugely complex and has many moving and interconnected parts – making it difficult to target. Our scientists are exploring the underlying biology of the DNA damage response system and its interconnected pathways to open up new ways of attacking cancer.

## Exploiting cancer's vulnerability

Dr Christian Zierhut leads our Genome Stability and Innate Immunity Team. His team studies how defects in the systems for detecting and repairing DNA damage can have major consequences for cells.

He says: "In cancer, the DNA of cells becomes unstable and prone to damage. This instability can allow cancer cells to adapt, evolve and become more aggressive. But it also leaves cancer more vulnerable in ways we can exploit."

## Igniting our innate immunity

Dr Zierhut's team is currently focusing on a pathway connected to the response to DNA damage which can trigger a type of immune mechanism called innate immunity. Unlike acquired immunity, in which the body produces antibodies in response to infection, innate immunity keeps cells on constant alert so they can recognise and combat viruses.

Dr Zierhut says: "This pathway is like a double-edged sword. In principle, it should help the immune system eliminate cancer – but cancer cells can undergo changes to either silence it or use it to their own ends. We need to find ways of wielding this double-edged sword against cancer."

## Recreating a pathway in a test tube

The key to harnessing this pathway is by studying its biology. We need to understand how it works on a mechanistic level and why each part can contribute to cancer cell growth or death in different situations.

To study this pathway, Dr Zierhut's team recreates its biochemistry in the lab. The team studies the role of individual components of the system by either purifying them in a test tube or by using extract from cells. The researchers have also designed cells that light up with fluorescence to show what is happening when the system is activated.



Dr Christian Zierhut

## From the lab to the clinic

Ultimately, building our understanding of the basic mechanics of a cell is crucial in helping patients. Dr Zierhut's team is currently collaborating with scientists and clinicians specialising in genetics, epidemiology, radiotherapy and immunotherapy. When his team has a promising lab result, they can see whether it aligns with patterns in patient data. Or they can learn from the experience in the clinic in planning new lines of inquiry for experiments. This overlap is especially promising in areas such as radiotherapy, which can cause DNA damage, and immunotherapy, which relies on activating cells' immune system.

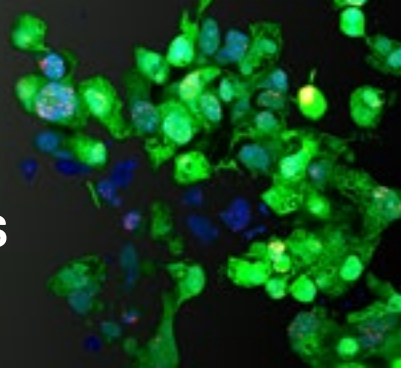
Dr Zierhut says: "We are trying to understand all the layers of complexity from biochemistry to cell biology and all the way up to patients. If we can understand how this pathway works, we could create tools to manipulate the system and to start using cells' natural defences against cancer."

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# A field rich for discovery: realising immunotherapy's potential



**Immunotherapy is an exciting type of cancer treatment that harnesses our immune system to recognise and attack cancer cells, which often conceal themselves from the body's natural defences. It is now being used to treat several cancers, including melanoma and lung cancer – but there is still much untapped potential.**

Immunotherapy has been extremely successful for some patients. But the current generation of immunotherapy drugs only work in some cancers, and we still don't have good ways of judging who is most likely to respond. The overall response rate to immunotherapy is low at around 15 per cent across all cancers.

## **The next generation of immunotherapies**

Now, our researchers are learning much more about the biology of the immune system – and how to turn it against cancer. We are studying the different components of the immune system, including molecules which act as accelerators or brakes on the immune response. The next challenge is to convert this knowledge into a new generation of immunotherapies, or ways of making the current drugs work more effectively.

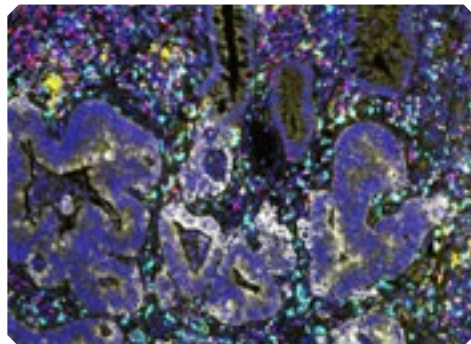
Our researchers are seeking to uncover strategies which lead to more effective, targeted use of immunotherapy.

One key strategy which has emerged through research is to combine immunotherapies with other types of treatment, such as chemotherapy and radiotherapy, to improve their effectiveness.

## **Combination attack**

Cancers can be resistant to radiotherapy just as they can be to drugs. However, combining radiotherapy with immunotherapy could make it harder for cancer cells to remain resistant, and lead to more effective treatment.

A study led by Dr Anguraj Sadanandam, who heads our Systems and Precision Cancer Medicine Team, suggested that bowel cancers that have become resistant to radiotherapy might be made susceptible again with targeted immunotherapy. Researchers believe these findings could also be relevant for other cancer types.



Stained bowel tumour section

## **Cancer vaccines**

We are starting to understand that immunotherapy drugs work best on tumours that have already had some immune response triggered against them. These are known as immunologically 'hot' tumours, while 'cold' tumours have stimulated little to no pre-existing immunity and generally respond poorly to immunotherapy drugs. One way to turn cold tumours hot lies in a form of treatment that uses viruses to infect and kill cancer cells.

These are known as oncolytic viruses, and they support another avenue of immune exploration – cancer vaccines. In this approach, oncolytic viruses are used to kill cancer cells and release specific molecules called antigens – boosting an anti-cancer immune response at the same time as turning the tumours 'hot'. Because of the specificity of this approach, oncolytic virus-induced cancer vaccination is effectively personalised to target a patient's individual cancer.

## **Using viruses to kill cancer**

Professor Kevin Harrington, Professor of Biological Cancer Therapies, and Professor Alan Melcher, who leads our Translational Immunotherapy Team, are exploring how to use these modified oncolytic viruses to kill cancer cells and spark the immune system into action.

Professor Harrington says: "Early evidence shows that oncolytic viruses could act as effective cancer vaccines against different cancer types, but we still don't fully know how they work best in patients. We are working to understand the science behind these viruses that will allow us to design and run clinical trials ultimately to make these cancer vaccines a reality."



Professor Alan Melcher

## **A new vision for immunotherapy**

We are leading efforts to propel progress in immunotherapy research. Our Centre for Translational Immunotherapy, led by Professor Melcher and The Royal Marsden's Dr Andrew Furness, and supported by a major donation from CRIS Cancer Foundation, is connecting different research teams working in cancer immunology to share their expertise, inspire ideas and foster collaboration. New research is under way across cancer types, disciplines and exploring a range of treatment combinations.

Professor Melcher says: "Immunotherapy is extending well beyond where it first started in the treatment of melanoma, as we're recognising it can help in an increasing number of fields of cancer research. Valuable conversations and collaborations are building around the Centre, and I'm very excited about the attention it is generating both within the ICR and further afield."

Making immunotherapy work better, and for more people with cancer, is a vital challenge – and one our researchers are determined to meet. With their efforts, we can expect a brighter future for immunotherapy, and for cancer patients.

## “Immunotherapy is giving hope to cancer patients like me”

In October 2018, I found a tiny lump in my neck and my GP referred me to the ear, nose and throat department at my local hospital. CT and MRI scans were inconclusive, so I had a biopsy and ultrasound, then went for a PET scan that highlighted little spots on my chest membrane.

I was told the cancer had actually started in my lungs and that I had non-small cell lung cancer. The day before I had run 15 miles – I just couldn't believe it. And then I was told that I had a year left to live. It was devastating – the biggest blow of my life.

Thankfully I was referred to my amazing thoracic consultant. He said 'we'll fight this' and referred me for immunotherapy, alongside chemotherapy. For the first three months I was on pemetrexed and carboplatin as well as pembrolizumab – an immunotherapy drug.

I then went on to just pembrolizumab and pemetrexed, and it was called an immuno maintenance programme – the chemo on its own wouldn't have worked for me. And I stayed on that up until November 2021. Three years after my diagnosis I have no cancer in my body. It may come back, it may not. I'm just living day by day.

I'm 61 now and I have two children in their 20s – I've been given more time with them. I work part-time as a waitress. The treatment has taken a toll on my body, but I was able to run a marathon last year and while that was gruelling it's given me so much joy.

Immunotherapy has made many of us realise that we can live with cancer, and we are hearing of new targeted treatments and new trials on a weekly basis. It's giving hope to cancer patients.



Alison, patient with non-small cell lung cancer

“ ”

The treatment has taken a toll on my body, but I was able to run a marathon last year and while that was gruelling it's given me so much joy.

## “Knowing we helped – that will be Ollie's legacy”

Ollie Young died of glioblastoma, the day before he turned six. To help improve the future for other children with cancer, his family and friends set up the Ollie Young Foundation.

Ollie was a typically mischievous five-year-old. He loved joking, so when he first complained of dizziness, his parents thought he was messing around. But it quickly became clear that something was wrong.

After several GP visits, and while waiting on a referral to hospital, Ollie started dragging his right leg, so his parents insisted he be seen immediately.

A CT scan and biopsy confirmed that Ollie had a grade 4 glioblastoma – a form of brain cancer in children for which no targeted drug treatments are available. The location of the tumour meant surgery was not possible, and his parents were told that Ollie would be lucky to survive two weeks.

Ollie moved straight into a local hospice, where he and his family spent the next 12 weeks together. He died one day before his sixth birthday.

The Ollie Young Foundation has partnered with us to support the work of bioinformatics researcher, Dr Yura Grabovska, who is studying the biology of gliomas to understand why they are so resistant to treatment. His research will help identify weaknesses that can be targeted with new treatments.

Sarah, Ollie's mum, said: “Ollie was so lovable and happy, and I think his love of life kept him going as long as possible. As I hugged Ollie that final morning, I thought how incredibly proud I was of him, and I resolved that his name would never be forgotten. The enthusiasm of Yura and his team is inspiring. We can see their research developing, and we've got a lot of faith in our project going forward. Knowing that we helped – that will be Ollie's legacy.”



“ ”

Ollie was clearly a caring and popular boy, and I feel honoured to be working in his name. I am truly grateful to the Ollie Young Foundation for their generous support, and I will work hard to make sure that every penny they raise helps to create a brighter future for other families.

**Dr Yura Grabovska**





## 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](http://icr.muchloved.org) to find out more.