ICR The Institute of Cancer Research

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search

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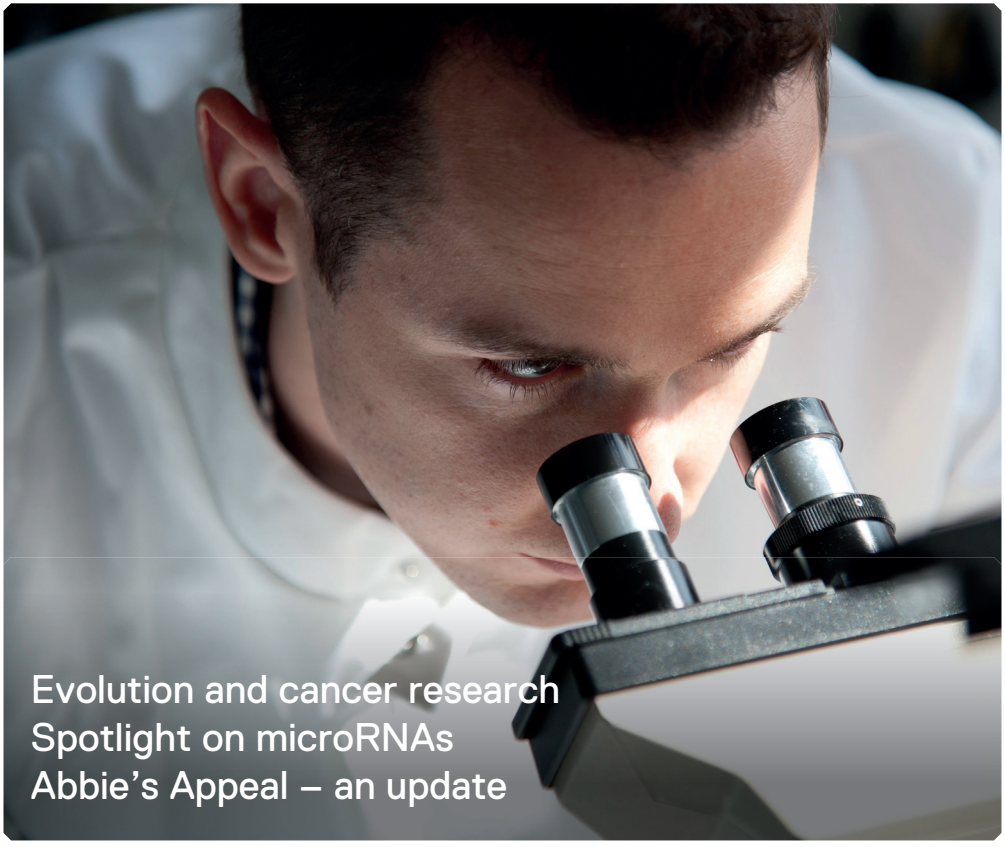

Evolution and cancer research
Spotlight on microRNAs
Abbie's Appeal – an update

Our mission is to make the discoveries that defeat cancer.

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Editorial

The start of the academic year is an exciting time at the ICR: PhD students begin their scientific careers, new projects are launched, and long-standing research continues apace.

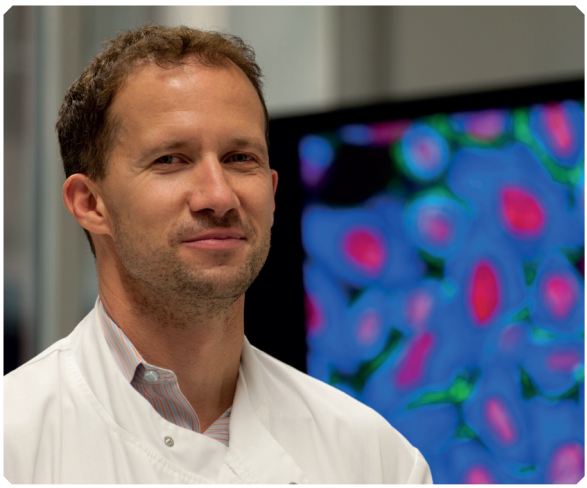
The Centre for Evolution and Cancer is one of our newest initiatives and by studying Darwinian principles our scientists are hoping to answer some of the biggest questions in cancer research such as why do so many people get the disease and why do some patients become resistant to treatment. This information could potentially revolutionise our understanding of cancer and ultimately help us stop it in its tracks. It truly is an exciting prospect.

But research like this is only made possible because of people like you. As you read this edition of Search I hope you feel proud of, and excited by, the work that your support allows us to undertake. You are helping us make the discoveries that defeat cancer.

Thank you.

Lara Jukes
Director of Development
The Institute of Cancer Research, London

Cancer's cellular factories could be treatment targets



Researchers at the ICR have identified how cells churn out the building blocks they need to keep growing.

Understanding how cellular factories go into overdrive will provide important clues to cancer and its treatment.

Study leader Dr Chris Bakal, from the ICR, said: "The endoplasmic reticulum is the factory of our cells, creating the building blocks for new cells. We've discovered how this is sent into overdrive, providing potential new targets for future treatments."

Read more at **icr.ac.uk/factories**

Genetic flaw links childhood cancer with rare syndrome

ICR scientists led a team that discovered genetic similarities between two distressing childhood diseases.

A quarter of patients with diffuse intrinsic pontine glioma (DIPG) had a rare genetic flaw within their tumours that is also found in patients with Stone Man Syndrome, where muscles turn into bone.

The ICR's Dr Chris Jones said: "We believe the genetic defect linking these diseases is a potential target for cancer therapies because drugs already exist against similar targets in other cancers."

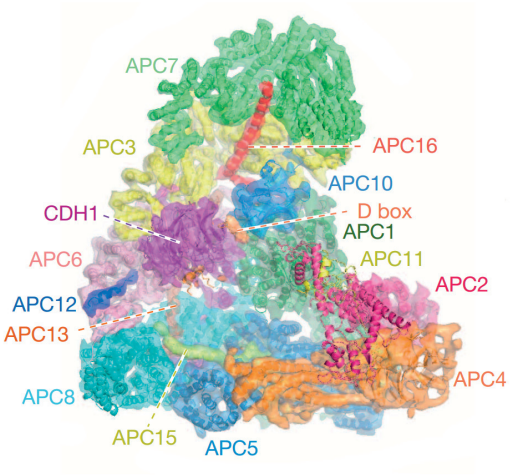
Read more at **icr.ac.uk/dipg**

Scientists map one of most important proteins in life – and cancer

Scientists have revealed the structure of an important protein in cell division – a fundamental process in life and the development of cancer.

The protein – known as anaphase-promoting complex (APC/C) – could ultimately be a target for cancer treatments.

Professor David Barford, who led the study at the ICR, said: "We hope our discovery will open up new avenues of research that increase our understanding of mitosis – the process by which a cell duplicates into two genetically identical cells – and lead to the discovery of new cancer drugs."



Read more at **icr.ac.uk/mitosis**

New clues to skin cancer development show sunscreen is not enough

Research carried out at the ICR and Cancer Research UK's Manchester Institute has explained how UV light leads to melanoma.

UV light directly damages the DNA in the skin's pigment cells, causing faults in the *p53* gene, which normally helps protect from the effects of DNA damage caused by sunlight.

The study also showed that while sunscreen can greatly reduce the amount of DNA damage caused by UV it does not offer complete protection.

Read more at **icr.ac.uk/sunscreen**

If you would like to keep up to date with our latest research news, you can follow us on Twitter @ICR_London or like us on Facebook.

Researchers in the ICR's new Centre for Evolution and Cancer are using the principles of evolution and ecology to seek answers to the biggest questions in cancer research – why is cancer so common and why is it so difficult to treat?

Understanding cancer evolution

Charles Darwin famously saw the secret of life through natural selection – in which some individuals inherit advantageous traits that make them more likely to survive and pass on those traits to their offspring. His theory of evolution by natural selection helps explain the gradual emergence of all species of animal and plant on earth – and we now know that it is the driving force for the development of cancer too.

Scientists at the ICR have begun to think about tumours as diverse populations of individual cells, gradually accumulating mutations that in some cases provide a selective advantage, by helping them become better adapted to their tissue microenvironment. The ICR's new Centre for Evolution and Cancer has been established to study the evolution of cancers in action, as they constantly evolve and often become resistant to treatments.

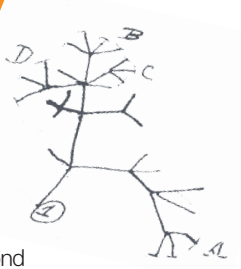
Evolution already has some important applications in the world of medicine, in our understanding of how bacteria become resistant to antibiotics, for instance. By investigating the patterns of evolution in cancer, ICR researchers are attempting to understand whether it is possible to predict how cancers will develop and whether they will become drug resistant.

Describing the evolutionary trees of different cancers is also important because it can help to identify the founder mutations that arose right at the start of the disease's development and have helped to drive its progression in every cell in a tumour. Finding these mutations is crucial, because they are likely to be excellent targets for cancer treatment.

In the articles that follow, we profile Professor Mel Greaves, the world-leading ICR scientist leading the centre, and highlight some of the vital projects it is hosting.

A pioneer convinced that studying evolution can uncover cancer's secrets

Drawing cancer's family trees



Professor Mel Greaves is fond of showing an 1837 drawing by Charles Darwin in his lectures. It is a sketch of a complex, branching family tree – showing how Darwin saw the evolutionary relationship between different species.

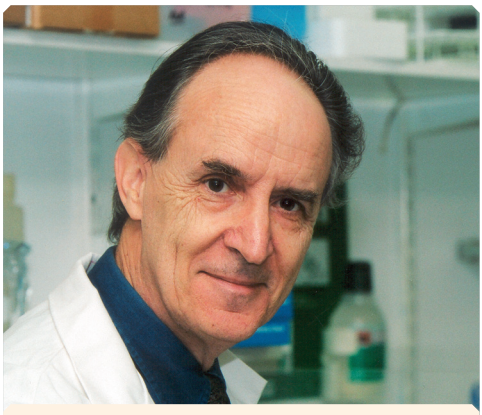
As the Director of the ICR's new Centre for Evolution and Cancer, Professor Greaves has used the study of evolution to revolutionise our understanding of leukaemia. By drawing family trees much like Darwin's, Professor Greaves' team can depict the precise genetic alterations occuring at different stages in the disease's development. Professor Greaves believes that understanding how cancers evolve genetically will offer vital clues in how to treat them more effectively.

In his early career, Professor Greaves pioneered new tests for different types of leukaemia and identified key mutations which drive the disease.

He is investigating what triggers leukaemia in children between the ages of two and five years old, and has accumulated evidence of an evolutionary explanation – a delay nowadays in exposure to common infections in infancy which the immune system has evolved to anticipate.

Professor Greaves believes that applying Darwinian principles to cancer biology could forge a paradigm shift in the way we understand the disease. "The implications are profound," he says.

"Treatments could be targeted at the earliest cancer-causing mutations, present in every cancer cell. Drugs could be combined to avoid or slow down resistance. Or the most effective cancer treatments might target the tumour environment, changing the selective pressures in evolution, rather than cancer cells themselves."



CV

Name: Professor Mel Greaves

Joined the ICR: 1984

Specialist subjects: Pre-clinical natural history, clonal evolution and causes of childhood acute lymphoblastic leukaemia (ALL).

In his own words: "By treating cancer early with drugs that target either the earliest mutations present in cancer cells or the microenvironment of the tumour, we are removing positive selective pressure on the cancer cells to evolve drug resistance. Our major challenge is to work out how best to thwart the evolutionary resilience of cancer."

From Darwin's finches to drug resistance

Researchers in the ICR's Centre for Evolution and Cancer will examine how evolution has helped shape our risk of cancer and how tumours themselves evolve in response to their surrounding environment. Here are a few of the areas our researchers will be studying.

Why humans get so much cancer

Our modern lifestyles are very different from the ancestral environments for which we were adapted – and that stresses our tissues, causing mutations within our cells. Our longer lifespans also provide more time for these biological accidents to happen. The centre will attempt to understand how features of today's lifestyles appear to be driving up our risk of cancer – so we can develop new strategies to prevent the disease.

Professor Mel Greaves says: "Our research has shown that cancer can be an evolutionary force. In the context we've looked at, particularly in equatorial Africa, in Black Africans who are albinos, we see that lethal skin cancer occurs in their twenties where it has a huge impact on reproductive outcome. The idea is that the early humans, who were pale and naked, would have been similarly susceptible to skin cancer and so would have evolved dark, pigmented skin for protection."

How tumours adapt to their environment

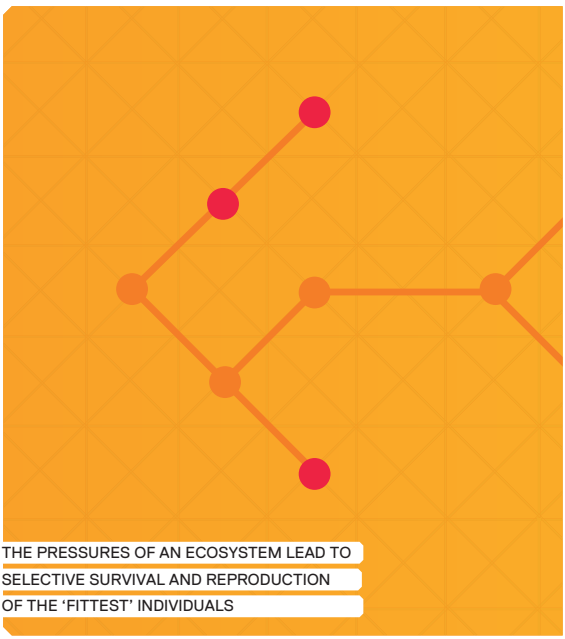
Just like Darwin's finches, which had adapted to a range of different habitats and lifestyles, cancers also adapt to the microenvironment within the patient's body. Understanding this is key to appreciating how they grow and spread.

Dr Yinyin Yuan is using image recognition software to do exactly this. She develops techniques to measure the interactions between tumours and their microenvironments.

One truly forward-thinking idea is that drugs which change a tumour's microenvironment could promote the survival of less harmful cancer cells, giving them an edge in the evolutionary battle against their more dangerous neighbours.

Tracing cancer evolution within tumours

It is becoming clear that patients' cancers don't evolve as one homogenous mass, but instead that there is huge genetic variation within an individual cancer. This genetic variation is part of what allows tumours to continually evolve over time – and to become resistant to treatment.



THE PRESSURES OF AN ECOSYSTEM LEAD TO SELECTIVE SURVIVAL AND REPRODUCTION OF THE 'FITTEST' INDIVIDUALS

"We are looking at single cells in a tumour to construct a detailed historical map of the mutations in a patient's cancer"

DR NICOLA POTTER

Dr Marco Gerlinger is working to understand how genetic variation within individual tumours can lead to the development of metastasis and drug resistance.

He has shown that variation in kidney cancers is due to a series of genetic mutations which happen at different times and in different places within a patient's tumour. Rather like a branching tree, evolution gives rise to different subtypes of cancer cell, and it is this variation which makes cancers difficult to treat.

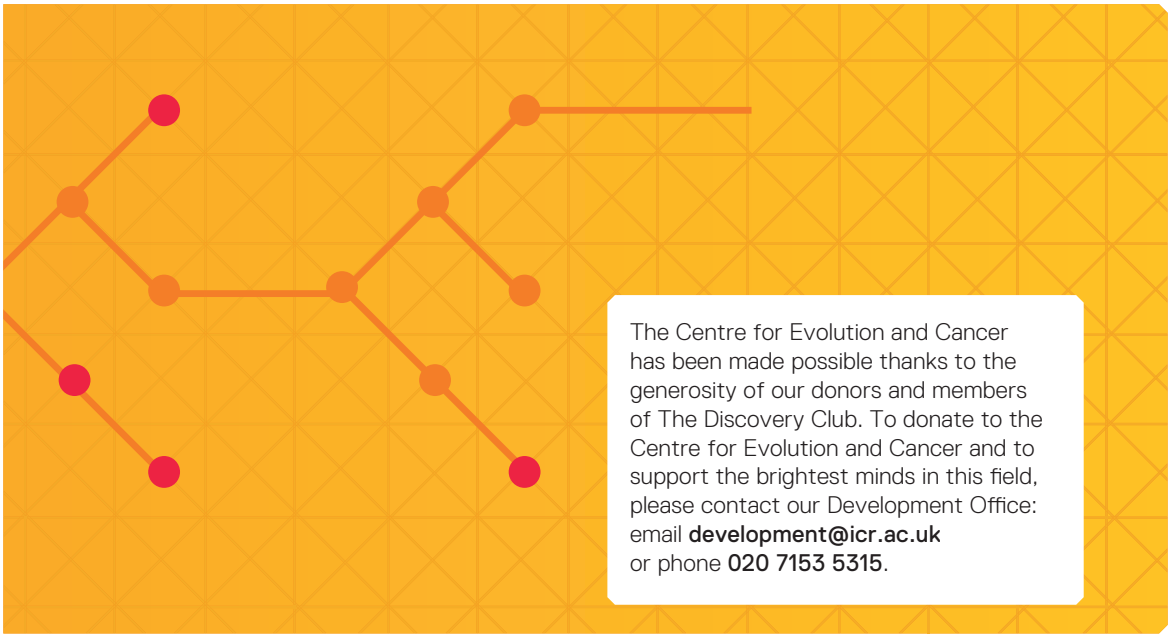
Dr Gerlinger says: "The ideal drug targets are found on the common trunk of the evolutionary tree in an individual cancer. Early genetic changes are present in every cancer cell within the tumour, and may prove effective therapeutic targets."

Tracking evolution of single cancer cells

Every cancer cell has a unique genetic code and it is this variation at the individual cell level which often leads to the emergence of drug-resistant cancers. Dr Nicola Potter is delving deeper into cancer evolution by developing a method to analyse genetic mutations within single cancer cells.

Dr Potter says: "We are looking at samples of single cells in a tumour and constructing a detailed historical map of the mutations in a patient's cancer."

Dr Potter's research has shown it is possible to assess single cells for different subtypes of acute lymphoblastic leukaemia. This research offers the chance to spot the driver mutations that cause the disease and could be targets for future treatments.



The Centre for Evolution and Cancer has been made possible thanks to the generosity of our donors and members of The Discovery Club. To donate to the Centre for Evolution and Cancer and to support the brightest minds in this field, please contact our Development Office: email **development@icr.ac.uk** or phone **020 7153 5315**.

A new team at the ICR is investigating a tiny and mysterious kind of RNA – like DNA, a carrier of vital code in our cells – and its potential as a target for cancer treatment

Targeting cancer's messengers

Scientists have spent years studying the genes within our cells and the careful control these exercise over our cellular processes and metabolism. We now know that if these control mechanisms are lost or altered in some way, due to a mutation in a particular gene, the result can be cancer.

But genes are not the only parts of our genetic make-up responsible for controlling our cells. MicroRNAs are a mysterious product of the human genome which have a role in regulating normal cell processes, by turning the level of gene activity up and down. Acting as vital 'workers', microRNAs are responsible for putting into action the instructions the genes give them, even where these messages are corrupted in some way by a cancer-causing gene mutation.

Did you know?

MicroRNAs were first discovered in 1993 by researchers at Harvard University

They contain about 22 nucleotides – the building blocks of DNA

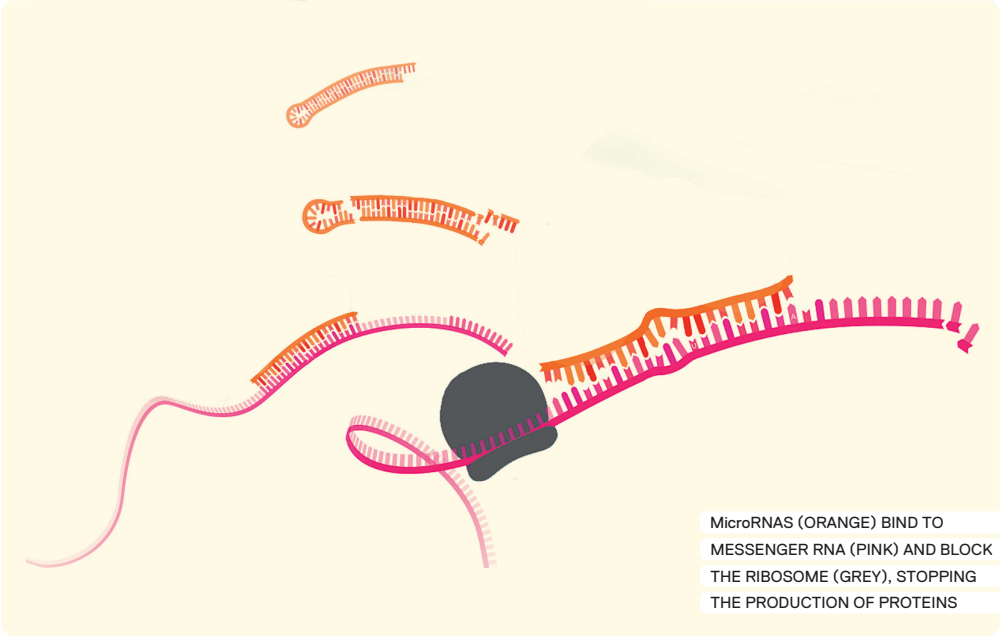
MicroRNAs control activity of 50% of all protein-coding genes

MicroRNAs regulate almost all cellular process

There are 800 known microRNAs in humans

"Our findings may have an important impact on the way we treat patients with bowel cancer"

DR NICOLA VALERI



MicroRNAS (ORANGE) BIND TO MESSENGER RNA (PINK) AND BLOCK THE RIBOSOME (GREY), STOPPING THE PRODUCTION OF PROTEINS

Dr Nicola Valeri has established a new team at the ICR to study how microRNAs might be exploited to help patients with gastrointestinal cancers, such as bowel cancer. MicroRNAs play a key role in cancer development and progression, and their levels in cancer tissues and blood are often higher than normal in people with cancer.

Dr Valeri's work aims to establish whether microRNAs can be used as markers to predict how a patient with a gastrointestinal cancer responds to their treatment. The goal is to identify microRNA signatures that could be used to better match drugs to patients.

His team is also investigating whether microRNAs can be used as potential targets for new cancer drugs in their own right. Dr Valeri recently published an important paper suggesting that a particular microRNA (called microRNA 135b) is employed by several important cancer genes to drive the growth of bowel cancers.

Dr Valeri said: "We have shown that a specific microRNA can drive the development of bowel cancers and is a key 'worker' responsible for putting into action the instructions from many cancer-causing mutations. Patients with the highest levels of this molecule have the most difficult-to-treat cancers, and inhibiting the molecule prevents tumours from growing. Although the research is at an early stage, our findings may have an important impact in the way we treat patients with bowel cancer in the future."

Although treatments targeting bowel cancer mutations have been developed, patients often develop resistance. Inhibiting microRNA 135b could be an exciting way to attack cancers without resistance occurring by blocking the effects of multiple cancer-causing mutations simultaneously.

The findings also suggest that testing levels of microRNA 135b could help identify patients likely to develop aggressive bowel cancer, and who might need the most intensive treatment.

Dr Nicola Valeri – a new team leader changing our understanding of gastrointestinal cancer

Using microRNAs to treat bowel cancer

Dr Nicola Valeri is a clinician scientist who is using his research expertise to bridge the gap between the discoveries made in the laboratory and the treatment of patients in the clinic.

He is discovering novel biomarkers for gastrointestinal cancers and he hopes this work will lead eventually to new treatments for bowel cancer.

Dr Valeri received his medical training in Italy where he completed his fellowship in medical oncology. He spent five years training in the US and became captivated by the promises and challenges of microRNAs.

He moved to Glasgow University as a senior clinical lecturer in medical oncology, and was next appointed as one of the ICR's new team leaders in our Division of Molecular Pathology.

Dr Valeri is an accomplished clinician and has a string of prestigious awards to his name – including the American-Italian Cancer Foundation International Fellowship, the Kimmel Foundation Translational Award and the Medical Research Society Prize at the Academy of Medical Sciences Clinician Scientist Spring Meeting.

"I am fascinated by the study of microRNAs. They are very important because they could give us a completely different route to new cancer therapies," said Dr Valeri.

"The role of microRNA is part of an incredibly complex picture of gene regulation in bowel cancer which we are now only beginning to understand."

CV

Name: Dr Nicola Valeri

Joined the ICR: 2013

Areas of work: Discovering new tests and therapeutic targets for gastrointestinal cancers, particularly bowel cancer, and stomach and throat cancers.

Recent achievement: Winning the AstraZeneca Student Prize Award in recognition of his exceptional work demonstrating the importance of microRNA in bowel cancer.

In his own words: "I was captivated by the promises and challenges of microRNA research when completing my clinical training and decided to pursue a PhD in this area of research. I now have my own team working to make a difference to the lives of patients with gastrointestinal cancers."

Remembering Rudy

At 26 years old, Rudy Menon had his whole life to look forward to. But tragically he developed gliomatosis cerebri (GC), a form of brain cancer that would take his life just four months after his initial symptoms developed.

Rudy's parents Vidhu and Somnath are raising funds to support the ICR's work into GC and to help ensure that no other family experiences a loss like theirs.

Vidhu explained: "We were so proud of the man Rudy had become – such a kind, caring and respectful human being.

"He hadn't long returned home to Nottingham after visiting us in Dubai when he experienced his first symptoms. There was nothing too specific to start with and although concerned about him, we weren't worried. I never for one moment thought that less than five months later we would watch as our baby slipped away.

"GC is extremely rare and because it doesn't manifest itself as a lump it's very hard to detect. Even once it is discovered, it's resistant to both surgery and radiotherapy. When we received Rudy's diagnosis we were in denial; there was just no question that there wouldn't be any treatments – there just had to be. But there weren't.

"In the past, practically no research has been carried out into GC and so very little is known about it. This has to change and that is why we're raising money to support the ICR's Dr Chris Jones. He and his team are the only scientists in the UK currently working on the cancer, so it's essential that they have the resources they need to continue their work collecting and analysing samples.

"Research is the only way we will be able to develop treatments and stop other young people dying from GC."

To support our research into gliomatosis cerebri, please donate now at **icr.ac.uk/rudy**.

Team ICR heads to the Royal Parks this October

ANGELA AND ALAN CARTER

On 12 October dedicated ICR supporters will be taking part in the Royal Parks Foundation Half Marathon in London. As one of the most popular half marathons in the UK, it's a must for any running enthusiast, and over the years those who have taken on the challenge have helped raise thousands of pounds towards our research.

Angela and Alan Carter will be part of Team ICR again this year, having already run the half marathon three times in the past. Angela said, "We love the atmosphere on race day and knowing that with every step we're helping the ICR's wonderful work."

Why not join us on 12 October and help cheer on all our runners? You'll find us at mile nine of the course.

The Discovery Club meets our drug discoverers

A key, a double-decker bus and a pile of building blocks – not items normally associated with the development of new, targeted cancer drugs, but used to great effect in explanations by our scientists at the ICR's latest Discovery Club event.

At the Royal Society of Chemistry, in London's Piccadilly, members and guests heard from our award-winning cancer therapeutics team about the discovery and development of new personalised cancer treatments. Our track record in this area remains unparalleled in academia; since 2005, we have discovered 17 drug candidates, progressed seven into clinical trials and one, abiraterone, has been accepted for use in the NHS.

PROFESSOR PAUL WORKMAN ADDRESSES DISCOVERY CLUB MEMBERS

We are extremely grateful to all our Discovery Club members for their ongoing philanthropic investment in our research. To find out more please contact the Development Office on 020 7153 5304 or email **development@icr.ac.uk**.

Our research into prostate cancer gets a £500,000 boost

We are thrilled that the Bob Champion Cancer Trust has awarded £500,000 to the ICR in support of a new project led by Professor Ros Eeles. The research will identify genetic changes in prostate cancer of young onset patients – men diagnosed at 60 years or less – who are at an increased risk of disease progression in their lifetime.

This gift continues our partnership with the Bob Champion Cancer Trust who have generously supported our pioneering male cancer research for more than 15 years.

Bob Champion MBE commented, "We are delighted and very excited to be able to support Professor Eeles in this project and hope to be able to do more in this area to improve care for prostate cancer patients."

Funding the future of cancer research

Long-standing ICR supporters Justin and Lucy Bull have generously pledged to fund a PhD studentship over four years. Under the supervision of Dr Chris Bakal, the new researcher will be investigating the complex communication pathways that regulate the shape of melanoma cancer cells and allow them to spread around the body.

"PhD students form the bedrock of the ICR's research capacity, and we learnt that funding for studentships can be hard to secure. By supporting a doctoral student, we are investing in the next generation of cancer researchers," confirmed Lucy.

To find out more about supporting the next generation of cancer researchers, please visit **icr.ac.uk/support-us**.

Earlier this year we wrote to some of our supporters about a little girl called Abbie Shaw and the work that Dr Louis Chesler is doing in order to identify and develop new treatments for the childhood cancer neuroblastoma

Thank you to everyone who supported Abbie's Appeal

Abbie was 21 months old when she was diagnosed with neuroblastoma – a cancer that starts in the nervous system. Despite multiple rounds of intensive treatment – including chemotherapy, radiotherapy and a stem cell transplant – and short periods of being cancer-free, she lost her fight against the cancer aged just five years.

Despite some recent advances, there are currently no targeted treatments for childhood cancers such as neuroblastoma, which is why the work that Dr Chesler and colleagues are undertaking is so important.

"I'm thrilled that so many people decided to support our appeal"

DR LOUIS CHESLER

They are studying the biological alterations that drive the development of neuroblastoma so that they can ultimately discover new treatments, or identify existing ones, that would be more effective against this type of cancer.

Our scientists also want to change the EU rules that govern drug testing, as currently an opportunity is being missed because pharmaceutical companies are allowed to opt out of testing their cancer drugs in children. Treatments that are proven to work in adults could also hold the key to treating childhood cancer but until the rules are changed, children with cancer will have to rely on traditional, non-specific treatments like those Abbie had.

The response we received to the appeal was phenomenal, with over a thousand supporters taking the time to send in donations. Thanks to your generosity we raised over £20,000 to help fund our vital research.

We also received some wonderful messages of support for our campaign, with many of you summing up your point by simply saying, "because I want to stop children suffering".

Dr Louis Chesler said: "I'm thrilled that so many people decided to support our appeal. Abbie's story is truly heart-breaking, but I'm convinced that by continuing to invest in research like mine we'll one day be able to stop children, and adults alike, dying from cancer."

You can donate to Abbie's Appeal online at **icr.ac.uk/abbie** or by phone on **020 7153 5387.**

Your legacy could uncover our next discovery

Legacies are an exceptionally important source of funding for the ICR and an excellent way for you to make a difference to the lives of cancer patients in generations to come

This year the ICR has received more than £4 million in legacy income, with one exceptionally generous supporter leaving us more than £700,000 in their Will.

But it's not just big gifts that are important to us as Russel Caulfield, Head of Legacies, explains: "It's always wonderful to receive notification of a large gift but really, every legacy can make a difference to our work.

"Cancer research takes time and a huge amount of financial investment, but knowing that we will be receiving legacies in future years allows us to plan for the long term."

There are a number of different types of legacies you could consider leaving us. A residuary gift is a percentage of your estate once all other costs and bequests have been settled. A pecuniary gift is a set amount of money. And a specific gift is an item of value such as an antique or piece of jewellery.

If you would like more information and to request your copy of our legacy booklet, contact Russel and his team today. They would be pleased to help you.

Contact Russel Caulfield, Head of Legacies, on 020 7153 5387 or **legacy@icr.ac.uk**.

Events calendar

Take part in the challenge of a lifetime and help us to make the discoveries that defeat cancer

Run

Royal Parks Foundation Half Marathon*

Sunday 12 October 2014

Join us for Britain's most beautiful city run. This stunning 13.1-mile route starts and ends in Hyde Park with a fun family festival afterwards to celebrate your achievement.

Cycle

London to Paris*

Wednesday 8 April 2015

Sign up today for this classic cycle ride. Five days and 300 miles of tough road racing until you reach the Eiffel Tower. Unbeatable!

Trek

Peru Inca Trail*

Saturday 5 September 2015

This time next year, you could be in Peru! Discover the fascinating Inca Trail for yourself and explore the historic site of Machu Picchu while raising vital funds to further our work.

ROYAL PARKS FOUNDATION HALF MARATHON 2013


CAROLS FROM CHELSEA 2013

Social

Carols from Chelsea

Wednesday 2 December 2014

Our annual Carols from Chelsea service will once again be held in Christopher Wren's beautiful chapel at the Royal Hospital Chelsea. It's the perfect start to the festive season.

*Registration fee and minimum sponsorship levels apply.

Contact us

For more information on any of our events call us on 020 7153 5307 or email **sports@icr.ac.uk**.

For other challenge destinations and dates available, see **www.icr.ac.uk/sports** for full listings, or to download our fundraising pack.

www.icr.ac.uk