

Issue 31 Spring 2015

search

For supporters of The Institute of Cancer Research



Meet our new Chief Executive
Training the next generation
A world-first cancer treatment

Our mission is to make the discoveries that defeat cancer.

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Editorial

With spring in the air I cannot help but feel excitement and anticipation for the year to come. Last year was such a thrilling year of scientific discovery, marked by some big initiatives which will take our research in pioneering and, we hope, very productive new directions.



We established our new Centre for Evolution and Cancer which will help us understand how cancers develop and design clever new ways to overcome or prevent drug resistance. Our new Centre for Cancer Imaging was completed and is being occupied as I write this.

We will now witness the fruits of these recent endeavours – our imaging capabilities going from strength to strength, a new generation of students starting on the path of scientific discovery, and we will embark on new plans to drive cancer drug discovery.

These initiatives are in no small part down to the commitment and generosity of you – our donors and supporters – and I thank you all. Last year you helped achieve an astonishing record in donations and we cannot make the discoveries that defeat cancer without you.

I hope you enjoy this issue of Search.

Lara Jukes

Director of Development
The Institute of Cancer Research, London

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ICR tops league table of university research excellence



The Institute of Cancer Research (ICR) has topped a national league table for the quality of its research.

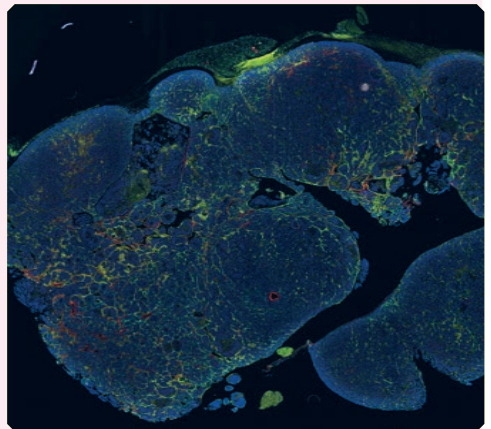
The Research Excellence Framework (REF) assesses all academic institutions in the UK and is the biggest and most detailed evaluation of research quality in the world. As well as coming top overall, the ICR ranked first in the UK for the impact its research has on society, in a powerful endorsement of its track record at translating its discoveries into real benefits for patients. The ICR was also assessed as having the highest concentration of high-quality research in the UK and came top of both biological sciences and clinical medicine.

Scientists map how childhood brain tumours relapse

A new study has traced the unique paths that the childhood brain cancer medulloblastoma follows when the disease returns after treatment.

Scientists at the ICR and Newcastle University looked at biopsies taken when children with medulloblastoma suffered relapse. They found a range of genetic changes that only took place when the disease returned and appeared to be responsible for the cancer becoming more aggressive. Researchers said the study showed biopsies should routinely be taken as soon as children relapsed, so they could identify subsets of patients who might be treatable with existing drugs that target the genetic faults.

Find out more at icr.ac.uk/tumourmap



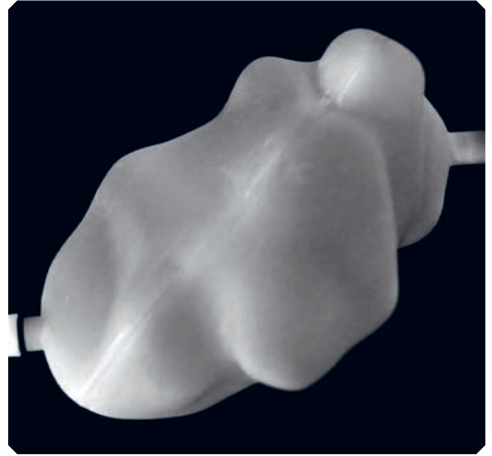
3D-printed models used to enhance radiotherapy

Our researchers have used 3D printing to produce replica models of tumours and organs of patients with cancer to help more accurately calculate the correct radiation dose to be given.

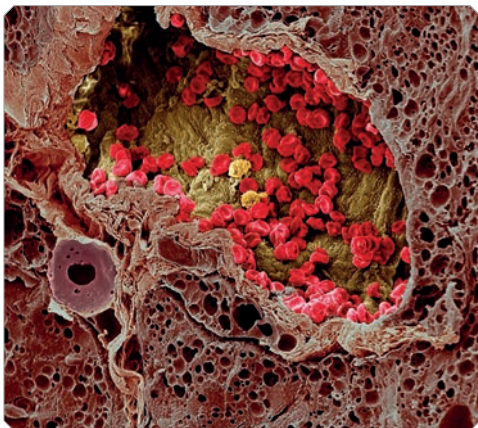
Initial tests show that the models, known as 'phantoms', accurately replicate the shape of a tumour and surrounding organs. They can help researchers to measure the dose of radiation that has been delivered – so it can be adjusted for future treatments.

The phantoms, printed by researchers from the Joint Department of Physics at the ICR and The Royal Marsden, are based on scans of real patients during treatment.

Find out more at icr.ac.uk/3dprinting



New targeted drugs could treat drug-resistant skin cancer



A new family of cancer drugs designed to block several key cancer-causing proteins at once could potentially treat incurable skin cancers, research jointly led by the ICR and the Cancer Research UK Manchester Institute has found.

Existing drugs target faulty versions of a protein called BRAF which drives about half of all melanomas, but while initially effective, cancers almost always become resistant. The new drugs – called panRAF inhibitors – could be effective in melanoma patients who have developed resistance, as well as in some patients for whom current drugs don't work at all.

Find out more at icr.ac.uk/BRAF

Record-breaking income raised in 2014

Donors and supporters of the ICR contributed a record-breaking £12m in charitable donations in 2014.

This record-breaking income smashes the previous year's achievement by more than



£3m and marks an extraordinary level of generosity and commitment on the part of all those who have made a donation, raised funds for us, or remembered the ICR in their Will.

Lara Jukes, the ICR's Director of Development, said: "I would like to thank everyone who supported the ICR in 2014. I know that many of you have very personal reasons for supporting us. Others of you are simply fascinated by the discoveries that our scientists make. However, the fact that we are able to make such discoveries is in no small part thanks to all of you. Together, we are making the discoveries that defeat cancer."

The ICR's Annual Report and Financial Statement 2014 is available at icr.ac.uk/about-us

Climb of Life raises more than £100,000

The annual Climb of Life event took place in November and raised a fantastic £100,157, bringing the grand total raised by the team over the last eight years to more than £600,000.

Organised by Graeme Chapman MBE and comprising 11 challenging mountain treks, the event took place in the glorious setting of the Lake District National Park.

Some 120 people took part including the ICR's own Dr Udai Banerji. Dr Banerji, a keen mountain walker, said: "I was touched by the enthusiasm and selfless energy of everyone involved in raising funds for the ICR. Congratulations and thank you to everyone involved."



The 2014 Climb of Life was dedicated to the memory of keen climber Cyril Rothwell who sadly died of cancer just a few weeks before the event.

The Rothwell family are strong supporters of the event with Cyril, his son and daughter having often led some of the more challenging climbs.

Carols from Chelsea fundraiser raises £95,000

Actor Laurence Fox, comedian John Sessions and actress Dame Penelope Keith were among the readers at the ICR's annual Carols from Chelsea event in December.

More than 400 guests attended the sold-out event, which raised £95,000 for the ICR's leading-edge research, and was hosted in the beautiful Wren Chapel of the Royal Hospital, Chelsea.

The evening began with a candlelit procession by the Chapel Choir to 'Silent



CAROLS FROM CHELSEA CHAIR LIZ VYVYAN
WITH GUEST READERS LAURENCE FOX,
DAME PENELOPE KEITH AND JOHN SESSIONS.

Night', followed by musical performances by soprano Valda Wilson, French horn player Anna Douglass and BBC Radio 2's Young Choristers of the Year Tom King and Helena Paish. The broadcaster Sarah Montague and Chelsea In-Pensioner Norman Mitchell also gave readings.

Carols from Chelsea, now in its 12th year, is the flagship event of our fundraising calendar and has raised more than £1m in total.

Reception celebrates ICR discoveries

At the Victoria and Albert Museum in London, the third annual reception for members of The Discovery Club took place in November celebrating the ICR's scientific creativity and thanking the donors who have helped make our discoveries possible.



PHD STUDENT PARISA
RAZAZ ADDRESSES
THE DISCOVERY CLUB

During the evening Professor Paul Workman, Chief Executive of the ICR, showcased the depth and breadth of the research carried out at the ICR – achievements which have been made possible thanks to philanthropic investment. He was joined by Parisa Razaz who gave a first-hand account of the invaluable learning experience she has gained as a PhD student at the ICR.

Fundraising priorities for The Discovery Club in 2015 include further investment in the Centre for Evolution and Cancer, the ICR's training of young researchers, and a major capital initiative to raise funds for a new Centre for Cancer Drug Discovery.

To find out more, please contact the Development Office on 020 7153 5315 or email development@icr.ac.uk

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

Professor Paul Workman was unanimous choice after global search

ICR appoints world-leading cancer researcher as new chief executive

Professor Paul Workman, a world-renowned expert in cancer drug discovery, has been appointed as Chief Executive of the ICR.

Professor Workman had previously served as Deputy and then Interim Chief Executive of the ICR, and was the unanimous choice of our Trustees after a global search.

Professor Workman says: "It is an incredible honour for me to take the helm at one of the world's most influential cancer research organisations and I am determined to repay the faith that has been shown in me by driving further advances for cancer patients.

"I am taking over as Chief Executive in exciting times for the ICR, with world-class programmes in basic cancer research, genetics and innovative drug discovery, a pioneering Centre for Evolution and Cancer, and ambitions to lead the world in precision radiotherapy. I am extremely grateful to all of our donors and supporters for their generosity and fantastic dedication to the ICR."

Professor Workman is a passionate advocate of personalised cancer treatment and has successfully built major drug discovery and development groups in academia and industry.

He first moved to the ICR in 1997 to build up the Cancer Research UK Cancer Therapeutics Unit. A keen promoter of collaborative and entrepreneurial approaches to science, the unit has conducted many of its drug discovery



projects in partnership with industry.

In his work in the lab, Professor Workman is carrying out pioneering research on drugs that block molecules that are essential for the growth and survival of cancer cells, in particular molecular chaperones to which tumour cells become 'addicted'.

He says: "By working through collaborative team science within the ICR, and increasingly in partnership with other leading organisations, we can deliver transformative change for the benefit of cancer patients. Through our world-class research and education we will make innovative and creative discoveries to defeat cancer."

Dr Vivanco's career was inspired by a fascination with how cancer cells avoid the ageing process

Calling time on cancer

Dr Igor Vivanco says his interest in cancer research stems back to a fascination with how cancer cells avoid the usual ageing process and keep dividing forever.

"My father is a geriatrician and he is fascinated by the concept of immortalisation – which is one of the characteristics of cancer cells," he says. "I inherited that fascination with molecular biology – it's an interest that goes back to high school."

A new team leader in molecular addictions at the ICR, Dr Vivanco's research focuses on how cancer cells become reliant on – addicted to even – a signalling pathway called PI3 kinase, which is altered in the majority of human cancers.

"For reasons that are not well understood, when a cell becomes a cancer cell it often mutates and becomes dependent on the fuel of a single protein. This is known as oncogene addiction and is the basis of all the targeted therapies we are trying to develop."

Dr Vivanco is focused on finding treatments for patients that don't just stop tumours from growing, but kill cancer cells by knocking out the proteins they have become addicted to.

"Cancer cells are smart. They can develop resistance to drugs by activating a different



CV

Name: Dr Igor Vivanco

Joined the ICR: 2014

Specialist subject: Molecular addictions

Greatest achievements: "I hope the greatest achievement in my career hasn't happened yet but the proudest moment of my life was when my baby son was born six months ago. Being a father has been better than I ever thought it would be."

In his own words: "I am fascinated by the biology of disease in general but there are so many unanswered questions about cancer. It is a disease that likes to play twist."

signalling pathway that bypasses the drug-induced blockade. If we can target the two signalling pathways simultaneously, we could effectively inhibit tumour growth.

"I joined the ICR because I wanted to work on creating new treatments for patients while also having the freedom to carry out research. There are very few places in the world where you can do both. The ICR is one where you can – and one of the best."

Training tomorrow's scientists and clinicians is essential to continue the ICR's work – and it couldn't happen without your support

How your support helps train the next generation of scientists

Research students and clinical research fellows play a vital role in the life of the ICR. Training the next generation of scientists is a central part of our mission – crucial to ensuring that we continue to make the discoveries that defeat cancer in the coming years and decades.

But our educational role isn't just important for the future – we couldn't do our research today without the contribution of a small army of PhD students and clinical fellows who work in our labs while learning from our world-class scientists.

Around 500 people a year apply to do a PhD at the ICR. Candidates undergo a rigorous interview process, and only the very best are selected to work and study here. Training a new cancer scientist is a long-term investment. Studying for a PhD at the ICR lasts for four years, and funding must cover a stipend for the student plus laboratory expenses.



The ICR itself funds some of our student places, some are supported by organisations such as Cancer Research UK and the Wellcome Trust, and others are funded through the generous support of ICR donors and charities such as Abbie's Army (see below).

"Philanthropic investment is essential to the ICR as we have very little government PhD funding available to us," says Dr Barbara Pittam, the ICR's Director of Academic Services.

Students are expected to spend long working days in the lab – at least five days per week – so self-financing through part-time employment is not possible.

"The ICR is passionate about offering fully funded studentships. We need to ensure we attract the highest calibre graduate students, but we are also dedicated to safeguarding the breadth and quality of students in cancer research – after all these are leaders of the

Katy Taylor – inspired by Abbie's memory

Katy Taylor is a fourth-year PhD student studying brain cancers in children.

After graduating in Biomedical Sciences at Portsmouth University, Katy worked for three years as a scientific officer at the ICR before beginning a PhD.

"My degree trained me for diagnostics but I wanted to test out pursuing a career in research and I loved the work," she says.

Katy decided she wanted to work on a rare, incurable childhood brain cancer called diffuse intrinsic pontine glioma (DIPG). She first approached the glioma team leader Dr Chris Jones before submitting her formal application to research what drives these tumours and identify therapeutic targets.

Katy's studentship is directly funded by Abbie's Army, a charity set up in memory of Abbie Mifsud, a little girl who died of DIPG. This leads to a close working relationship – Katy writes an annual report for the charity on how her work is progressing. She also attends charity events in Abbie's memory, gives talks and offers tours of her lab.

"We know a lot about the families and it does make you feel emotionally responsible. It makes the work we do feel all the more important, that it really means something," she says. "This work has been more rewarding than I ever thought it would be."



Katy says one of the most humbling things she has done is go into an operating theatre where a DIPG biopsy was being taken, before collecting the sample and taking it straight back to the ICR lab.

Her work on the discovery of a link between DIPG and a very rare congenital disorder called stone man syndrome, in which soft connective tissues turn into bone, led to her being awarded a Paediatric Brain Science award in the US.

Now due to finish her PhD this September, Katy is hoping to next carry out postdoctoral research into brain development overseas.

future who will deliver benefits to patients.”

The ICR is also dedicated to training academic clinicians. Having already qualified as medical doctors, our clinical research fellows bring the worlds of cancer research and clinical practice together by forming a vital link between our science and the patients it is designed to help – they exemplify our ‘bench to bedside’ ethos.

Clinical research fellowships provide clinicians with the opportunity to do scientific research and gain a postgraduate degree.

They lead translational research projects, taking scientific research and working out how to apply it to real people, and clinical trials, in which we test out the latest cancer treatments.

“Clinical fellows, and our close partnership with The Royal Marsden, help drive a constant two-way interaction between scientists and clinicians,” explains Dr Pittam. “This is essential for ensuring our research delivers real benefit to patients.”

Sir Mike Stratton – kick-starting a prestigious career

For an example of how a studentship at the ICR can launch a prestigious career in science look no further than Professor Sir Mike Stratton, who obtained his PhD in the molecular biology of cancer at the ICR.

With a keen interest in the genetics of cancer, Professor Stratton then continued to work at the ICR for many years. He led the team that discovered the BRCA2 gene mutations, which are strongly linked with the development of breast, ovarian and some other cancers. He also initiated the hugely ambitious Cancer Genome Project to hunt for genes that cause different types of cancer. He continued this work when joining the Wellcome Trust Sanger Institute, of which he is now Director. He continues to make hugely important contributions to understanding how changes in our DNA can lead to cancer.

A Fellow of the Royal Society, Sir Mike was knighted in the Queen’s Birthday Honours in 2013.



If you would like to learn more about how you could help us invest in the next generation of cancer researchers, please contact Thomas Bland, Deputy Director of Development: phone 020 8722 4200 or email thomas.bland@icr.ac.uk

At the end of 2014, olaparib was approved in Europe for use in some ovarian cancer patients – making it the first drug targeted at an inherited gene mutation. The ICR played a key role at every stage in taking this treatment to patients.

How the ICR pioneered a world-first cancer treatment

The ICR got an early Christmas present late last year, when we learned that the first of a class of drugs called PARP inhibitors was approved as a new treatment for some women with ovarian cancer.

The new drug, olaparib, is the very first approved treatment to be targeted at an inherited genetic fault and its development was underpinned by ICR science – so we're very excited to see it on the way to reaching more patients.

ICR researchers played a vital role at every stage in the research that lies behind PARP inhibitors – from discovering one of the genes they target, to devising the idea for the new treatment, to running the clinical trials that proved they work. Here is how we did it.



Back in 1995, an ICR team including Professor Alan Ashworth, our former Chief Executive, won the race to identify the breast cancer gene BRCA2.

For many years, scientists had suspected that breast cancer ran in families and research groups around the world were searching for a genetic basis. In 1994 other researchers found that the BRCA1 gene was faulty in a number of such families but they soon realised that it was not responsible for every case of inherited breast and ovarian cancer.

A few months later, an ICR team led by Professor Sir Mike Stratton discovered the location of the second breast cancer susceptibility gene, BRCA2, and then in collaboration with another ICR team led by Professor Ashworth, they identified the gene itself.

Mutations in the BRCA2 gene greatly increase the carrier's risk of developing not only breast cancer but a number of other cancers, including ovarian and prostate cancer.

The discovery of the BRCA2 gene has enabled families with a history of these cancers to be assessed for future risk, and where necessary offered preventative measures or close monitoring.

It was also a critical step in the development, 10 years later, of PARP inhibitors, as a novel form of therapy targeted at BRCA-associated cancers.



Professor Ashworth at the ICR was studying how mutations in the BRCA genes led to cancer, when he spotted an exciting opportunity for treatment.

The ICR team had helped uncover the functions of the BRCA genes, and shown that they were normally used by our cells as one way of repairing faults in our DNA.

Professor Ashworth hypothesised that cancer cells that lacked either BRCA1 or BRCA2 function would be highly sensitive to drugs that inhibit PARP – another molecule used to repair faulty DNA.

In 2005, further research by Professor Ashworth showed that anti-PARP drugs were indeed highly effective at killing cancer cells with BRCA mutations. Normal cells were left relatively unharmed because they could still use the BRCA genes to repair their DNA even where PARP function was blocked.



Now olaparib – the first approved PARP inhibitor – is taking advantage of the genetic weakness spotted at the ICR to treat patients with BRCA-mutant cancers.

Soon after Professor Ashworth first proposed that PARP inhibitors could treat patients with BRCA-mutant cancers, a series of drug trials opened designed to test the theory. These trials were led by researchers at the ICR, The Royal Marsden and Guy's Hospital.

The early trials focused on patients with breast, ovarian and prostate cancers carrying BRCA mutations. Despite the fact that these patients had undergone several previous rounds of chemotherapy that had failed to keep their cancers in check, a significant number showed strong and sustained



Research suggests olaparib might benefit patients with other cancer types.

anti-tumour responses when treated with olaparib. The side-effects in patients treated with olaparib were relatively mild compared with conventional chemotherapy.

Further trials provided more evidence that PARP inhibitors are effective in BRCA-mutant patients. Then at the end of last year, both the European Medicines Agency and the US Food and Drug Administration approved the use of olaparib in ovarian cancer patients with mutations in their BRCA1 or BRCA2 genes.

We hope that olaparib really will make a difference to ovarian cancer patients worldwide. But there is no sense of complacency. Wider groups of patients including those with breast and prostate cancer could benefit from PARP inhibitors – and our researchers are working to ensure that they do.

Dr Chris Lord is a team leader at the ICR who worked with Professor Ashworth on much of the PARP inhibitor work. He sums up the ICR's sense of achievement over development of the drugs: "As a scientist it is very satisfactory to see such results. It makes up for all the times research does not turn out the way you thought it would."

On their own, PARP inhibitors will probably only benefit a relatively small group of patients, so the key will be to find out how to use them in combination with other treatments.

"Sometimes patients choose not to go through with therapies that have a lot of side-effects as they prefer to keep a certain quality of life instead. If we can come up with alternatives to chemotherapy, then everyone here at the ICR will have done their job."



Olaparib recently featured in the BBC Panorama programme 'Can You Cure My Cancer?' in an episode focused entirely on the pioneering work of the ICR and The Royal Marsden.

The programme told the stories of cancer patients taking part in clinical trials of new drugs at the ICR and The Royal Marsden. One such story followed Tami Morris (pictured) as she took part in a trial of a drug from a family called MEK inhibitors. When this treatment stopped working, Tami started treatment with olaparib, on a different trial.

Tami has participated in a number of clinical trials and was selected for them based on in-depth genomic analyses of her cancer, which helped select the best course of treatment.

'Can You Cure My Cancer?' featured the research programmes of several team leaders at the ICR, many of whom are also treating patients through our unique partnership with The Royal Marsden.

It also explored how huge advances in genetics are transforming our understanding of the disease and how to combat it – and how some patients previously given just months to live are keeping the disease at bay for years. These individuals are pioneering the development of new cancer treatments.

'Can You Cure My Cancer?' is still available to watch on the BBC Panorama website bbc.co.uk/programmes/b052sjsg

The ICR's success at making the discoveries that defeat cancer owes a huge debt to the generosity of the organisations that support us.

How charitable trusts and foundations underpin our work

Charitable trusts and foundations have contributed to some incredible research discoveries, from vital insights into how cancers grow and spread, to new drugs and combination therapies for a variety of cancers, to novel ways to image tumours.

Pump priming from these philanthropic organisations enables the ICR to embark on truly innovative research – often providing the investment in the early stages of research where proof of principle is required, and projects are too high risk for commercial organisations to take on.

The trusts and foundations that support the ICR vary greatly in size – from small trusts led by parents or other family members in memory of a close relative, to large established philanthropic organisations that support a variety of causes.

Thomas Bland is the Deputy Director of Development at the ICR and has managed our

trusts team for nearly six years. He says: "I love the variety of working with charitable trusts. I am humbled and inspired in equal measures by their benevolence. It is incredibly moving to work with people that are dedicated to raising money in remembrance of a loved one so other families don't have to go through the same pain."

Big or small, they all provide crucial funding for a wide range of projects and initiatives including essential laboratory equipment, launching the career of a young scientist through PhD studentships or the construction of new buildings.

"Charitable trusts and foundations provide the touch paper that has ignited some of our most cutting-edge research projects. They help the ICR remain fast-moving and entrepreneurial. This is very important to us – we sometimes have to take risks to succeed," explains Thomas.

"The trusts team is driven by a desire to help people through the ICR's research, and we're



THOMAS BLAND

passionate about building close relationships with trusts and foundations to enable them to meet their charitable objectives.”

The ICR has been lucky to receive very positive feedback from our trust donors, who have appreciated the chance to visit our sites in Sutton and Chelsea, meet our scientists and see the difference their money makes.

For successful, long-term relationships it is vital that the ICR and the trusts and foundations that support us are all working to a common goal – to make the discoveries that defeat cancer.

If you are a trustee and would like to find out more about working with the ICR, please contact Thomas Bland: phone 020 8722 4200 or email thomas.bland@icr.ac.uk



Abbie's Army, a charity set up in memory of Abbie Mifsud by her family, has raised funds for the ICR's research into DIPG – a rare and fatal form of childhood brain cancer. So far they have donated £166,500. Part of this went to Katy Taylor as a studentship to cover the costs of the last two years of her PhD (see feature on training the next generation, pgs 10–12).

Take a trek to raise money

Each year we work with our trek partners to bring together a programme of exciting challenges that provide life-changing experiences for those taking part and raise vital funds for our world-class research.

From the mesmerising landscapes of the Sahara Desert to the ancient wonders of Machu Picchu the ICR has a trek for all abilities and interests.

As a keen supporter of the ICR, Rosemary Dunstan from Sonning Common, Oxfordshire, has taken part in four challenging treks, including Annapurna in Nepal, the Great Wall of China and Ancient Petra in Jordan. In November 2014 she took part in her most recent trek to Angkor Wat, Cambodia, and has now raised an impressive £11,000 for the ICR's research.

Rosemary says, "I enjoy travelling and visiting exotic locations and I like to use this as a great opportunity to raise funds for the ICR. If I can travel and support the ICR's work at the same time then I really feel as though

I have accomplished something worthwhile. Cancer is a disease which statistically is likely to affect me or someone in my family eventually, so raising money to find a cure (or a way of preventing the disease) is extremely important. I know that 83% of the ICR's expenditure directly supports research activities and I am very proud to play a part in making a difference."

Our 2015/16 treks programme is now open for bookings so please visit the ICR website for further details of these exciting challenges:

Peru Inca Trail

05 Sep 2015

Kilimanjaro Machame Trail

24 Sep 2015

Great Wall of China

03 Oct 2015

Ancient Petra

17 Oct 2015

Sahara Desert

19 Nov 2015



ROSEMARY DUNSTAN
IN ANGKOR WAT

To find out more, please visit icr.ac.uk/challenge or contact the team on 020 7153 5307 or email sports@icr.ac.uk

Events calendar

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

Run

Virgin Money London Marathon
26 Apr 2015

Edinburgh Marathon Festival
30/31 May 2015

BMW Berlin Marathon
27 Sep 2015

Royal Parks Foundation Half Marathon
11 Oct 2015



ICR SUPPORTER IAN SPARKS RUNS
THE ROYAL PARKS FOUNDATION
HALF MARATHON 2014

Cycle

Euro Cities
27 May 2015

London to Paris
10 Jun 2015

Prudential RideLondon – Surrey 100
02 Aug 2015

Unite and Bike Against Cancer – Cuba
15 Oct 2015

Vietnam to Cambodia
14 Nov 2015



NICHOLAS WARD COMPLETES
THE LONDON TO PARIS CYCLE
RIDE IN AID OF THE ICR

Other event dates are available in 2015 and 2016. For more information on any of our events call us on 020 7153 5307 or email sports@icr.ac.uk

Please go to icr.ac.uk/events for full listings or to download our fundraising pack. Registration fees and minimum sponsorship levels may apply.

www.icr.ac.uk