Men United v Prostate Cancer
We can win this
prostatecanceruk.org
Miss Alice Hartley, Newcastle University
Welcome to our first Prostate Cancer UK Research Review. This has been quite a year for us, as I hope you’ll see from the following pages. We’ve set up our Grants Advisory Panel (GAP), awarded our first Career Development Fellowships, and launched the Movember Centres of Excellence programme for prostate cancer research – the first of its kind, and a shining example of how we’re stronger united. These collaborations bring together not only different areas of scientific expertise, but also colleagues from different departments, universities and even countries for the benefit of men with prostate cancer.

Our researchers are a vital part of Men United, our movement for change – they’re the men and women tackling prostate cancer head on, and thanks to The Movember Foundation and our other supporters we’ve awarded more grants this year than ever before.

All the grants we’ve awarded have been selected for their scientific excellence and relevance to men living with prostate cancer, as well as addressing an urgent area of unmet need in prostate cancer research, as laid out in our research strategy.

We have a responsibility to spend the generous donations of our partners, fundraisers and supporters well; to fund research that will make a difference to the lives of men with prostate cancer. I hope this review will demonstrate how seriously we take that responsibility. Whether you’re a man with prostate cancer, a researcher or clinician, a fundraiser or a donor, I’d like to take this opportunity to thank you for your contributions to our research portfolio and for helping us bring tangible changes to men with prostate cancer.

I look forward to continuing the fight with your support and reporting on our progress on a regular basis.

Dr Iain Frame
Director of Research
Prostate Cancer UK
I’ve got two related highlights from this year. The first was sitting in a room in Manchester on the morning of the first Movember Centre of Excellence site visit, listening to our International Expert Panel introduce themselves. They were from Australia, Canada, the US and Finland, and it really made me think about what a long way we’ve come in a year. We’re leading a global research effort, working towards a single goal for men with prostate cancer.

The second was attending the first meeting of the lead scientists from the Belfast-Manchester Movember Centre of Excellence and listening to the incredible enthusiasm and thirst for new knowledge that our support is fostering. I remember thinking that only good can come of this endeavour, feeling excited at being a part of it and wanting it to start as soon as possible.

We’ve also seen some exciting publications from projects we’ve funded this year, including from Hayley Whitaker and her team at the Cambridge Research Institute. They discovered that high levels of a protein called NAALADL2 are associated with aggressive forms of prostate cancer.

Iain, Director of Research
It’s been a busy year, and here’s what the Prostate Cancer UK research team thinks of as the highlights of 2013-14:

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My highlight was joining the team in November and immediately seeing that the research we’re funding has huge potential to improve the lives of men affected by prostate cancer. This year we’ve awarded our first ever Career Development Fellowships, a flagship joint clinical research award with the Chief Scientist Office in Scotland and a new joint fellowship scheme with the College of Radiographers – I’m not the only newbie this year!

Matt, Deputy Director of Research

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My highlight was establishing our very first Grants Advisory Panel, a group consisting entirely of people who have direct experience of prostate cancer. The enthusiasm of the group was clear to see and they made a real difference in deciding which research projects the charity should support. We’ve also been building up our team of researchers to such an extent that for the first time ever we had enough PhD students and fellows to organise an event to bring them all together at our Early Career Researchers Day to meet new friends and hopefully even future collaborators.

Simon, Head of Research Funding
SCIENCE
BY NUMBERS
Awards by type:

### Personal awards
- Daphne Jackson Trust Fellowship: £65,000
- Clinical Training Fellowships: £241,654
- Career Development Fellowships: £1,437,425
- PhD Studentships: £481,637

### Projects and Pilots
- Project Grants: £2,765,597
- Pilot Awards: £149,621

### Strategic awards
- Centres of Excellence: £6,461,584
Awards by research strategy:

1. Identifying men at risk of aggressive disease
2. Distinguishing between aggressive and non-aggressive disease
3. Treatments for advanced disease
4. Survivorship
5. Centres of Excellence – which span all areas of the strategy
NEW AWARDS
THIS YEAR
Project Grants and Pilot Awards

Project Grants are generally given to established experts, who have a solid track record, a good idea and promising early results that they want to develop and which will hopefully lead to major breakthroughs. Pilot Awards on the other hand are ‘high risk, high reward’ grants – they give an initial investment to allow exploration of a new, unexplored area of research. This year we awarded three Pilot Awards and eight Project Grants, proudly funded by the Movember Foundation, as well as two projects jointly funded by the Movember Foundation with the Northern Ireland Public Health Authority and the Chief Scientist Office respectively.

Dr Christine Galustian, King’s College London
Pilot Award, £49,787
Project title: Does the absence of a protein, known as DARC, increase prostate cancer severity in African-Caribbean men?
African-Caribbean men are three times more likely to develop prostate cancer than white men of the same age and their cancers are often more aggressive, but we don’t know why. Dr Galustian’s team has identified a protein called DARC that’s missing in over 60% of African-Caribbean men. DARC normally helps prevent tumour growth, so the researchers want to test whether the lack of DARC in African-Caribbean men is associated with increased prostate cancer severity, to help identify men at high risk of developing aggressive disease so that they can be closely monitored.
**Professor Gwyn Williams, University of Keele**
Pilot Award, £49,839  
Project title: GAS5, a key regulator of advanced prostate cancer development and drug-resistance  
The researchers will investigate how GAS5, a type of newly discovered molecule called a long non-coding RNA, is associated with the development and drug resistance of prostate cancer. GAS5 can prevent harmful cell growth and is missing in prostate cancer cells that have become resistant to hormone therapy. Professor Williams and his colleagues will investigate the link between these two facts and find out how important the loss of GAS5 is in the progression to advanced prostate cancer.

**Dr Hector Keun, Imperial College London**
Pilot Award, £49,995  
Project title: Finding metabolic target genes in prostate cancer  
Like all cells, prostate cancer cells get their energy by breaking down nutrients in a process called metabolism. Because cancer cells grow so much quicker than normal cells, they alter their metabolism to keep up with the extra energy demand. Dr Keun’s team have identified a molecule called a microRNA that they think plays a significant role in controlling prostate cancer cell metabolism. The researchers will investigate exactly how the microRNA is controlling metabolism and whether blocking it would cut off the cancer cells’ energy supply and stop them growing.

**Professor Norman Maitland, University of York**
Project Grant, £192,658  
Project title: Can suppression of a stem cell control gene stop prostate cancer spreading?  
This research focuses on a protein called Latexin that normally controls the number of stem cells (cells that can replicate indefinitely) in bone marrow. Cancers are thought to contain stem-cell like cells, called tumour initiating cells or cancer stem cells. Professor Maitland and his team think that eliminating these cells may be the key to treating aggressive prostate cancers. They will investigate what happens when Latexin is lost from prostate cancer cells to find out if any of the affected genes can be used as targets to treat prostate cancer.

**Professor Johann de Bono, Institute of Cancer Research**
Project Grant, £393,414  
Project title: Precision medicine for a subtype of prostate cancer associated with loss of the gene CHD1.  
In the past few years a number of new treatments have become available for men with advanced prostate cancer including abiraterone, enzalutamide and cabazitaxel. Researchers in this lab have led on the development of these new drugs and although they are a big step forward there are still some prostate cancers that do not respond to any of these therapies. Now, Professor de Bono’s team want to find out whether the loss of a gene called CHD1, which is involved in DNA repair, can result in advanced prostate cancers that do not respond to any current therapies. They will then look for a new way to treat this particular type of aggressive disease.
Dr Amanda Swain, 
Institute of Cancer Research
Project Grant, £220,818
Project title: Identification of genetic changes that drive aggressive prostate cancer progression
Dr Swain and her team have already identified a list of genes that drive prostate cancer to a more aggressive stage in animal models of disease. In this project, they will compare that list to a list of genes known to be mutated in some men with prostate cancer. They’ll then carry out tests to confirm whether the genes and associated genetic changes that appear on both lists can in fact drive prostate cancer to a more aggressive stage. Next they’ll see which of the confirmed candidate genes or mutations within them are present in prostate cancer patients, and whether this correlates with survival outcome. The researchers then hope to be able to develop these genes or mutations into biomarkers to predict how aggressive an individual’s cancer will be.

Dr Anna Gavin, 
Queen’s University Belfast
Northern Ireland Public Health Authority
Project Grant, £109,148
Project title: Understanding how to improve the lives of men living with prostate cancer: Analysis of data on 3,504 prostate cancer survivors to investigate men’s experiences and physical and emotional wellbeing.
More and more men are living longer after prostate cancer treatment but we don’t really understand their needs. Dr Gavin’s team has already carried out questionnaires and interviews with 3,504 prostate cancer survivors diagnosed over the last 17 years. This grant will provide the funds to fully evaluate this valuable set of data. The work will help to identify the factors than mean a man has a good quality of life after prostate cancer treatment, which will help with the design of support services and policies aimed at helping men live better after prostate cancer.

Professor Rosalind Eeles and Dr Zsofia Kote-Jarai, 
Institute of Cancer Research
Project Grant, £205,703
Project title: Alterations in a man’s genetic make-up which lead to aggressive prostate cancer
In this study, the researchers will build on preliminary data that suggests that men with mutations in DNA repair genes are more likely to develop aggressive prostate cancer. This work will look at more men, and more DNA repair genes. They’ll identify the proportion of prostate cancer cases due to mutations in these genes, and confirm whether men with these mutations are more likely to develop aggressive disease. This information could be used to determine if men should be offered genetic testing so that those with relevant mutations can be offered targeted screening in the IMPACT study. This is investigating ways to detect prostate cancer early in men who have inherited an ‘increased risk’ gene.
Professor Charlotte Bevan, Imperial College London

Project Grant, £211,800

Project title: Predicting and reducing side-effects in prostate cancer therapy

Current prostate cancer therapies can sometimes result in severe side effects, partly because many therapies aim to stop prostate cancer cells responding to androgens. But as well as being required for prostate cancer growth, androgens – male sex hormones – also have other functions that will be affected by anti-androgen treatments, which is what causes side effects. This project aims to develop a model where an active androgen signal will “light up”, so can be observed by the scientists. This will let them study what happens when various drugs are used, so they can better predict the side effects that each drug might have. This will help in the discovery and development of more effective treatments with fewer side effects.
Dr Rich Williams, Queen’s University Belfast

Project Grant, £384,126
Project title: Development of Legumain based therapeutic for the treatment of advanced prostate cancer
Legumain is a protein found at high levels in the most aggressive prostate cancers and is associated with poor outcome for the patient. Dr William’s team has previously shown that when Legumain is blocked in cells grown in the lab, prostate cancer cells are killed while normal cells are not affected. They have also developed Legumain inhibitors and now want to optimise these so they can be used as drugs and tested in mouse models. This work could lead to a new therapeutic option for prostate cancers that currently have a poor prognosis.

Mr Ghulam Nabi, Dundee University

Chief Scientist Office Clinical Research Grant, £499,936
Project title: Advanced magnetic resonance imaging (MRI) for prostate cancer diagnosis
Over the past decade, there have been significant advances in the types of imaging used to detect prostate cancer. There is good data from small studies that suggests that using a special type of MRI before a biopsy, called multiparametric MRI, can help to reduce the number of biopsies needed to make a firm diagnosis, and possibly even help to distinguish between aggressive and non-aggressive prostate cancer. In this grant, Mr Nabi will expand these studies into a large trial and hopes that the evidence gained from this will help pass the benefits of advances in imaging techniques to large numbers of men.

Dr Shonit Punwani, University College London

Project Grant, £334,254
Project title: Developing imaging methods to better assess the spread of prostate cancer to other body sites
This project will investigate whether an advanced MRI imaging technique called multi-parametric MRI is more sensitive than current imaging techniques for diagnosing advanced disease. Dr Punwani’s team will directly compare their multi-parametric MRI technique with the computed tomograph (CT) and bone scan that are currently used to detect metastatic prostate cancer in the hope that a more sensitive imaging technique will make it possible to detect smaller volumes of metastatic cancer, and so aid in early diagnosis of advanced disease.

Dr Tania Maffucci, Queen Mary University London

Project Grant, £213,740
Project title: Search for a new way to identify and treat advanced prostate cancer
Dr Maffucci’s team have discovered that human prostate cancer cells contain increased amounts of a protein called PI3K that helps the cells to move, possibly allowing them to spread out from the prostate. No-one has ever looked at this particular protein in prostate cancer before, so the researchers aim firstly to establish if there’s any relationship between levels of this protein and either disease severity or patient outcome, which may indicate that the protein could be used as a new diagnostic tool. Secondly, they want to find out whether blocking this protein can stop tumours growing and spreading, and what the best way to block it might be to see if it has any potential as a new therapeutic option.
Career Development Fellowships

Making the leap from postdoctoral researcher (or postdoc, a scientist with a PhD who works in a lab) to group leader (the person in charge of the lab) is tough. Worldwide, only about 20% of postdocs get the funding necessary to start out on their own. Our Career Development Fellowships not only help brilliant young scientists make the jump to independence, but also safeguard the future of prostate cancer research, making sure that we have the scientific leaders we need for years to come.

This year, we awarded two Career Development Fellowships, proudly funded by The Movember Foundation.

Dr Wafa Al-Jamal,
University of East Anglia
Career Development Fellowship, £749, 218
Project title: Nanomedicine for prostate cancer

Dr Al-Jamal works in a relatively new field called nanomedicine, which uses really small particles (called nano-carriers) to deliver a drug to where it is needed. In this case, it will be used to target chemotherapy drugs to prostate cancer cells, while avoiding healthy cells. By specifically killing the cancerous cells, Dr Al-Jamal hopes to reduce side effects from chemotherapy. The nano-carriers can recognise prostate cancer cells wherever they may be in the body, so this technique could also provide an effective treatment for cancer that has spread to other parts of the body (metastasised).

“I moved to the University of East Anglia in August to set up my lab space. Setting up your own lab is always the dream for a scientist, but it was a bit crazy in the beginning to start completely from scratch – it felt like waking up into hard reality! But now everything’s coming together, it’s really worth it. I’m really excited about starting new collaborations, interacting with new people, hiring new lab members and especially working on my own ideas! Fellowships like this are important, because they give you both time and money to become established, and once you’ve invested five years in prostate cancer research, you’ll carry on! It’s like a studentship – it’s important to create links, draw people in, and train them to stay in the field.”

Fellowships like this are important, because they give you both time and money to become established, and once you’ve invested five years in prostate cancer research, you’ll carry on!

Photo by Wafa Al-Jamal: Balls of close-packed prostate cancer cells that have been treated with the anticancer drug doxyrubicin - shown in blue. The drug is often deep inside the balls of cells, as a result of being delivered inside tiny nanoparticles which can travel deep into the tumour.
Dr Kelly Coffey, Newcastle University

Career Development Fellowship, £688,207

Project title: Characterisation of KMT5A, a potential therapeutic target to treat advanced prostate cancer.

In this project, Dr Coffey will be studying what happens to certain proteins, including one called KMT5A, that help control androgen receptor activity when prostate cancer cells stop responding to hormone therapy. She hopes that this approach will help to identify new targets for treatments that could be used in addition to, or instead of, hormone therapy to help prevent the cancer progressing to an advanced stage.

“I couldn’t believe it when I won the fellowship – I was jumping around – I think I was smiling for a fortnight! I’m really excited about pulling away to do my own research. I’ve had a small team working with me for a while, but this is completely different – the buck stops here now! I like a good puzzle, which is partly why I became a scientist, but like many cancer biologists I have a family history of a number of cancers – the thought that one day I might be able to make a difference drives me. Also, science really grabs you as soon as you first dip your toe in. Finally getting an answer you’ve been looking for is the best feeling in the world. The fellowship was really important to let me set up my own research group, and Prostate Cancer UK fits into a ‘niche’ for men’s cancers that gets swept under the carpet a bit by other charities. A lot of good scientists can get lost because it’s so difficult to get a fellowship, but it’s also good that it’s so competitive; it drives you to work hard - first to get funding and then to deserve it!”

“I like a good puzzle, which is partly why I became a scientist, but like many cancer biologists I have a family history of a number of cancers – the thought that one day I might be able to make a difference drives me.
Clinical Training Fellowships and Daphne Jackson Trust Fellowship

We’ve joined forces with the Medical Research Council (MRC), Royal College of Surgeons, and the College of Radiographers to award grants that allow medical professionals, such as radiographers and urologists, to undertake research training. Working together with these other professional organisations helps us reach the professionals we want to apply for our grants.

This year, we’ve awarded three Clinical Training Fellowships, jointly funded by The Movember Foundation. We’ve also awarded one Daphne Jackson Trust Fellowship at the University of York to allow a researcher to return to the lab after a career break.

Miss Alice Hartley, Newcastle University

Royal College of Surgeons Clinical Training Fellowship, £53,040

Project title: Characterising prostate cancer cells in blood

This project will study cells, called circulating tumour cells (CTCs), that escape from the main bulk of a prostate tumour and circulate around the body in the blood. Miss Hartley will see whether the amounts of certain proteins, called Transcription Factors, in the CTCs can predict how the patient will respond to hormone treatment.
Dr Deborah Enting, King’s College London
MRC Clinical Training Fellowship, £237,281
Project title: Using the body’s immune system to fight prostate cancer
Dr Enting is studying how the body’s own immune system can be used to fight advanced prostate cancer by investigating how a receptor called NKG2D works. This receptor, found on the surface of immune cells, seems to be involved in the detection and killing of prostate cancer cells, while ignoring healthy cells. The ultimate aim is to increase levels of this receptor to help the body find and kill prostate cancer cells by itself.

James Stirling, Mount Vernon Hospital
College of Radiographers Clinical Training Fellowship, £188,614
Project title: A new method to identify men suitable for treatment of recurrent prostate cancer
Currently, around 2,000 men in the UK are diagnosed with recurrent prostate cancer after radiotherapy each year. This study aims to find a way to precisely identify the area and extent of cancer recurrence within the prostate, thus allowing the development of targeted treatments. This could potentially reduce the severity of any side effects, and make elimination of remaining prostate cancer a viable treatment option.

Dr Amanda Noble, University of York
Daphne Jackson Trust Fellowship, £60,127
Project title: Investigating a new way to stop prostate cancer cells from growing and spreading
Dr Noble is looking at the enzyme Phospholipase D, which is a key component of major signalling pathways that control how cancer cells grow and spread. She’s looking at when and where this protein is active in patient-derived prostate cancer cells and will investigate what happens to cancer cell growth and spread when this enzyme’s activity is blocked.
PhD Studentships

We award a number of PhD Studentships each year to established researchers who have a strong track record in their field, and experience of supervising students. By funding PhD students, we hope that not only will they advance our understanding of prostate cancer during the three years of their studentship, but also remain in the field in the future. This year, we awarded five PhD studentships, proudly funded by The Movember Foundation. In October, these students will join seven other Movember-funded PhD students, who started in their labs last year.

James Grey, University of Newcastle
Supervised by Professor Craig Robson
PhD Studentship, £100,330
Project title: Understanding key regulator molecules important to the progression of advanced prostate cancer

This research focuses on developing new ways to target the androgen receptor for prostate cancer treatment. James will study a group of proteins called phosphatases, which regulate the activity of the androgen receptor, to see if they are potential drug targets. We hope that by increasing our understanding of how the androgen receptor works, we will improve our ability to target it for prostate cancer therapy.


**Mario de Piano, King’s College London**
Supervised by Dr Claire Wells and Dr Mieke van Hemelrijk
PhD Studentship, £99,710
**Project title: Insight into the mechanisms linking the metabolism of fat to prostate cancer progression**
This study will expand on some existing research, which suggests that there is a link between fat metabolism (the process by which dietary fat is absorbed and broken down) and the growth and spread of prostate cancer (how aggressive it is). The ultimate goal of this work is to find a new way to diagnose aggressive vs. indolent prostate tumours, and possibly also identify future drug targets to treat prostate cancer.

**Carmen Aguirre Hernandez, Queen Mary University London**
Supervised by Dr Gunnel Hallden
PhD Studentship: £99,996
**Project title: A novel strategy to improve prostate cancer treatment by using a killing virus and drugs**
Dr Hallden’s lab has artificially altered a virus so that it cannot cause disease but instead enters dividing cancer cells and kills them – so taking advantage of the fact that cancer cells grow and divide much faster than normal cells. Carmen will test whether using this virus at the same time as conventional chemotherapy will make treatment for advanced prostate cancer more effective.

**Katrina Reilly, University of York**
Supervised by Dr Mark Coles
PhD Studentship, £99,136
**Project title: A novel approach to stop tumour growth**
This project will study a group of proteins called adhesion molecules in the non-cancerous supporting cells around a tumour. Scientists think that changes in these molecules allow cancer cells to escape from the primary tumour and spread. In this project, Katrina will test how drugs against these molecules in mixed prostate cancer/supporting cell cultures affect cancer cell spread. She hopes this might be the first step in developing a new treatment to prevent prostate cancer metastasis.

**Maria Sadiq, University of Bradford**
Supervised by Dr Klaus Pors
PhD Studentship, £99,325
**Project title: Aldehyde dehydrogenases in prostate cancer**
This project will look at the expression of enzymes called aldehyde dehydrogenases (ALDH) to find out how they are involved in the development of aggressive prostate cancer. The short term aim of this research is to increase our understanding of prostate cancer biology and our ability to predict how likely a tumour is to grow and spread. In the long term, scientists hope to build on Maria’s research to find an ALDH enzyme that can be used to identify aggressive prostate cancer.

**Grace Cole, Queen’s University Belfast**
Supervised by Dr Helen McCarthy
PhD Studentship, £97,070
**Project title: A new DNA vaccine for prostate cancer**
This project proposes a new DNA vaccine, a specific sequence of DNA that makes the same protein that is expressed on the surface of cancer cells. This triggers the body’s immune response against the ‘foreign’ vaccine-produced protein, and also the cancer cells where the same protein is expressed. This proposed project offers advantages over other DNA vaccine therapies, because it uses short protein sequences called peptides to protect the DNA and improve delivery into the cell. Additionally, the vaccine will be given using micro-needles applied as a patch onto the skin so delivery of the vaccine will be rapid and painless for the patient. During her PhD, Grace will refine and test this system in a laboratory setting.
Flavia Fioretti, Imperial College London

Supervised by Professor Charlotte Bevan
PhD Studentship, £99,155

Project title: Development of a transcriptional repressor based approach for the treatment of prostate cancer

This project will be an in depth study of a new molecule that inhibits the androgen receptor. This molecule is made up of two subunits; the first binds tightly to the androgen receptor and the second stops it from working. Flavia will try to change the two inhibitor subunits to improve the molecule’s effectiveness by making androgen receptor binding more specific and inhibition stronger. She will test the inhibitor to see how well it works in various prostate cancer cell lines, and then investigate different delivery methods to find a way to deliver the therapy specifically into the cancer cells while not affecting normal tissue.
What the scientists say

“As a relatively recently established group studying novel therapies and putting forward new ways to stratify prostate cancer risk, the support of Prostate Cancer UK has been critical in driving our work forward to the point where we can publish our findings and are able to progress with the development of our new agents.

Dr Christine Galustian

“Prostate cancer research has long been underfunded and Prostate Cancer UK is aiming to redress the balance. They have made an enormous difference in the UK and every grant awarded really moves the field on. This grant will enable us to study some quite fundamental, important unanswered questions in prostate cancer as well allowing us to bridge gaps between our laboratory work and potential new therapies.

Professor Charlotte Bevan

“Prostate Cancer UK do so much work promoting men’s health and publicising prostate cancer that it’s great to be involved with them. I think it helps the patients relate to the research when they meet doctors and scientists that are involved.

Miss Alice Hartley

“Prostate Cancer UK support is essential for my research as it not only provides a financial component, without which research of this nature simply couldn’t take place, but also provides a developmental infrastructure, exposing young researchers to various aspects of a career in science.

James Grey
SUCCESS STORIES
Dr Hayley Whitaker: biomarkers of aggressive disease

Results from a project funded by Prostate Cancer UK and Masonic Samaritan Fund in Dr Hayley Whitaker’s lab were covered in various national newspapers including the Daily Mail and The Times.

Dr Whitaker and her colleagues carried out an elegant study identifying a protein that may prove to be a clinically useful biomarker for aggressive prostate cancer. They found that expression of the protein, called NAALADL2, was associated with both the presence and aggressiveness of the disease, and that high levels of this protein could predict poor survival in patients who have had their prostate surgically removed.

At the end of their experiments, Dr Whitaker’s lab concluded that changes in NAALADL2 expression can impact cell signaling pathways that promote cancer growth and that this protein might one day be useful in a test to diagnose prostate cancer, and to tell the difference between aggressive and non-aggressive disease.

Photo by Hayley Whitaker: Human prostate tissue stained for NAALADL2. NAALADL2 is shown in brown in the tumour glands. The normal glands nearby have no NAALADL2 and so no brown staining. To help identify individual cells, the nuclei – the cells’ control centre – is stained blue.
Professor Ros Eeles: understanding risk

One of the major challenges for men diagnosed with prostate cancer, and the doctors treating them, is to decide not only which treatment option to choose, but whether treatment is necessary in the first place. This is because while some prostate cancers will be aggressive - that is they will grow quickly and spread outside the prostate - which can be life-threatening, other prostate cancers will neither grow nor cause any symptoms, meaning that a man could continue to live with it, with no health problems at all.

Professor Eeles at the Institute of Cancer Research has been a driving force in understanding the genetic basis of prostate cancer risk. Overall, there are now around 100 genetic changes known to convey an increased risk of prostate cancer, and Professor Eeles’ lab has discovered 76 of these – including the ‘breast cancer genes’ BRCA1 and BRCA2.

Work from her lab suggested that a man with a BRCA1 mutation is 3.4 times more likely to develop prostate cancer by age 65 than a man without this mutation. And that this is 8.6 times more likely for a man with a BRCA2 mutation.

Genetic testing for high-risk men

Earlier this year, Professor Eeles and her colleagues published some research that was funded by Prostate Cancer UK and suggested that genetic testing might be a useful way to predict whether men at high-risk of prostate cancer are likely to develop the aggressive form of the disease. This story was picked up by lots of national newspapers, including The Guardian, The Times, The Independent, The Daily Telegraph and The Daily Mail.

The scientists took blood samples from 191 prostate cancer patients with a family history of prostate cancer and looked at the DNA sequence of 22 known cancer-risk genes. They found that 14 men had a mutation in one of
eight genes, which included some genes that have been linked to prostate cancer before, like BRCA1 and BRCA2. Importantly, these men were more likely to have aggressive prostate cancer that had spread outside the prostate and into the lymph nodes.

This suggests that genetic testing for cancer gene mutations in men with a family history of prostate cancer might be able to identify which men are likely to develop aggressive disease. These men could then be closely monitored and treated very quickly upon diagnosis – so helping to eliminate some of the dilemma about whether or not treatment is necessary.

**Scaling up**

This would be a major step forward, but before we’ll be able to say for certain that genetic testing can help identify who is at risk of aggressive prostate cancer, it needs to be tested in a bigger trial, and there are currently two clinical trials relevant to this question.

The first is the IMPACT study, which is investigating whether screening men with BRCA1 and/or BRCA2 mutations, which are known to increase prostate cancer risk can help detect cancer earlier and save lives. In this case, screening means that the men involved in the study will have a PSA test every year. The second relevant clinical trial is the PROFILE study, which follows on from research in this paper directly. This trial hasn’t started yet, but will be offering genetic testing for men with a family history of prostate cancer alongside regular screening to compare prostate cancer diagnoses and outcomes in men in different risk categories, as defined by the results of their gene test.

**What does this mean for the future?**

We hope that research like this, and the bigger trials it’s feeding into, mean that we’re getting closer to being able to identify which men are at risk of aggressive prostate cancer, and being able to suggest with confidence that these men should be monitored and recommended for treatment immediately upon diagnosis. Hopefully, this will not only save lives, but will also give men some reassurance that they’re making the best decision with respect to treatment versus active surveillance.

What this kind of research can’t yet tell us is whether genetic testing can help define which treatment is the most appropriate for a man. However, we hope that through research programmes like the Movember Centres of Excellence, in which Professor Eeles will play a big part, we might be able to start answering the question of which treatment will work best for which men soon.

**Dr Sophie Papa: from pilot study to clinical trial**

Last year, Prostate Cancer UK offered a Movember funded Pilot Award worth £50,000, to Dr Sophie Papa at King’s College London. Dr Papa is trying to find an effective way of directing the body’s own immune cells to kill prostate cancer.

Researchers have started to make huge leaps forward with this type of treatment, known as immunotherapy, for blood cancers where the cancer cells move freely through the blood vessels, but it is harder to apply to solid tumours like prostate cancer. This is because solid tumours are very good at making the area around them hostile to immune cells, so that they don’t work properly near the tumour, and can’t kill it.

Dr Papa is trying to overcome these problems and has already made great progress in developing a mouse model – the first step in designing a new therapy. On the strength of the work carried out during her Prostate Cancer UK Pilot Award, Dr Papa has recently been awarded an MRC Clinician Scientist Fellowship. This is a larger grant, with more money, which will allow her to build up her research group and progress her prostate cancer research into a clinical trial within the next four years.

Dr Papa said: “Without the Pilot Award from Prostate Cancer UK, I definitely wouldn’t have been in a position to get the MRC Clinician Scientist Fellowship yet. There’s still a long way to go, but we’re hopeful that we’ll be able to overcome any obstacles, and establish immunotherapy as a viable treatment option for men with prostate cancer.”
Spotlight on... the Movember Centres of Excellence

Throughout the world, centres of excellence bring leading researchers across different scientific disciplines together with a single goal: to tackle important unanswered questions and move research towards patient benefit as quickly as possible. Earlier this year, the UK’s first Movember Centres of Excellence for prostate cancer research opened their doors for business, thanks to the partnership between Prostate Cancer UK and the Movember Foundation.

One of the two Movember Centres of Excellence is based in London, across the Institute of Cancer Research, the Royal Marsden Hospital, University College London and Imperial College London. The other is in Belfast-Manchester, at the Centre for Cancer Research and Cell Biology at Queen’s University Belfast, the Christie NHS Foundation Trust, the University of Manchester and the Cancer Research UK Manchester Institute respectively.

Each Centre has its own research strategy, informed by the expertise of the researchers who are working together as part of this programme. The London Centre of Excellence, led by Professor Johann de Bono, will concentrate on understanding the genetic basis of prostate cancer, particularly on the search for gene signatures that can be used to identify men at high risk of aggressive disease and optimising treatment choices based on a man’s genetic information. The Belfast-Manchester Centre of Excellence, led by Professors Richard Marais, David Waugh, Noel Clarke and Joe O’Sullivan, aims to optimise the use of DNA-damaging therapies as treatment for localised high-risk and metastatic prostate cancer.

Professor David Waugh told us how the Belfast-Manchester collaboration came about: “The initial collaboration stemmed from a discussion with Noel Clarke during a visit to Belfast. Within days, Joe O’Sullivan and I were on an afternoon flight to Manchester. Two hours in an airport hotel bar and the Belfast-Manchester Centre of Excellence was born! Partners from both institutions joined enthusiastically in support of our focused research programme, adding real depth and expertise in all the relevant disciplines. This programme will concentrate on developing knowledge that will lead to the optimal use of radiotherapy, DNA-damage, and radionuclide therapy for men with prostate cancer. Specifically, we’ll seek to develop clinically-useful tests to identify which patients will respond well to these therapies.”

Professor Joe O’Sullivan added: “Radiotherapy has always been, and will continue to be, an important method of treating prostate cancer. This grant will help us make it work better; to find out who will respond and at what dose, and if a man won’t respond, why not? This grant will really help us move towards tailored treatments – being able to understand an individual’s cancer and what it tells us about how to treat him.”

Professor Johann de Bono described what the London Centre of Excellence is setting out to achieve: “Our aims are to optimise the treatment of advanced prostate cancer, decrease the overtreatment of non-aggressive disease and identify aggressive cancers early. Overall this would have a major impact on men suffering from this common disease. Our group has previously developed abiraterone and led on the development of cabazitaxel, enzalutamide and radium 223. We hope that we can continue to improve the treatment of the most aggressive prostate cancers, improve patient survival and critically, improve patient quality of life.”

The Movember Centres of Excellence represent exciting developments for prostate cancer researchers and patients alike. Professor Joe O’Sullivan said: “The Centre of Excellence title isn’t just words – it really means something. It gives patients confidence and hope, and lets them know that research is at the core of our business. It will be hugely beneficial to us in terms of managing our patients and their care experience.”
This is an international team of experts in radiation, biomarker discovery, genetic modeling and tumour biology who will use their individual talents in a collective and focused manner, which I believe will make significant discoveries to benefit and extend the lives of men diagnosed with prostate cancer.

Professor David Waugh
We have a responsibility to make sure that we’re funding research that will really make a difference to the lives of men with prostate cancer. Last year, we set up a Grants Advisory Panel (GAP) to help us make sure that we’re not only funding the best science by the best people in the best places, but also the science that’s most valued by those affected by prostate cancer.

You may ask what Derek, Barry, Trevor, Stephen, Chris, Roger, Neville, Stuart, Keith, Iain, Kuljeet, Kenneth, Robert and Robin know about what makes a good research proposal? And the answer may be not much. But they do all know what it’s like to live with, or be affected by, prostate cancer. We don’t expect panel members to have specific scientific knowledge or understanding of the research process. We just want to know whether they think the ideas proposed are important ones for us to invest in.

Robin Porter

The biggest challenge is representing the views of all men with prostate cancer.

Robin answered an advert for volunteers with prostate cancer to be lay members of the Research Advisory Committee (RAC) in 2008, and was invited to join the committee soon after that. His experience of being diagnosed with prostate cancer, and having to choose what he felt was the best treatment for him as well as a keen interest in medical science, made joining the RAC a good way for Robin to contribute to Prostate Cancer UK’s work.

‘I consider being part of the Research Advisory Committee, and also now the GAP, a great privilege. I’ve learnt a lot over the last few years, and find the whole area fascinating. It’s hard work being on the RAC and GAP, but really interesting to learn about cutting edge advances.’

In terms of the challenges involved in representing the lay view on the RAC, and the benefits that setting up the GAP has brought, Robin says, ‘The biggest challenge is representing the views of all men with prostate cancer. The GAP has made this a lot easier, because it’s given us a broader platform of prostate cancer experience to speak from. And it’s apparent that the experts assessing the grants value what the GAP has to say.’

Kenneth Jeffers

For me, the ‘holy grail’ of prostate cancer research would be a cure for advanced prostate cancer, but that’s probably a long way off. So instead, I’ll say a better diagnostic test – one that will do the job it’s supposed to do.

Kenneth has been working with the campaigns and information teams at Prostate Cancer UK for six and half years now. He joined the GAP this year, because he was interested in learning more about what Prostate Cancer UK was doing to fight prostate cancer through research.

He says, ‘reading the applications was challenging and time consuming, but it was very interesting and I really enjoyed seeing how scientists are trying to tackle the important questions in prostate cancer research. Some applications were really well written and easy to understand, but others were very difficult. I had to read them six or seven times with a tea-break in the middle to try to figure out what was going on! Mind you, I felt better about that after speaking to one of the scientists, who told me that if the GAP thought an application was badly written and hard to understand, they probably did too!’

Kenneth then said, ‘I was surprised by how often the scientists agreed with the lay panel about which proposals covered important priorities in prostate cancer research. I think the only exceptions were when the science didn’t add up!’

Thank you to the GAP members for their hard work and support over the past year.
THANK YOU

Thank you to all the funders, trusts and individuals who worked with us to support our research programme including:

- The Barbour Trust
- The Chief Scientist Office
- The David and Jutta Morris Charitable Trust
- The EBM Charitable Trust
- The Holbeck Charitable Trust
- The Hoover Foundation
- The Howard Foundation
- The HW Abbott Will Trust
- The Mackintosh Foundation
- The Masonic Samaritan Fund
- The Mike Gooley Trailfinders Charity
- The Northern Ireland Public Health Agency
- The Philip King Charitable Trust
- The Robert Luff Foundation
- The Steel Charitable Trust
- The Tom and Sheila Springer Charity.

We’d also like to say a special thank you to the Pioneers; a vital part of Prostate Cancer UK and an exceptional group of highly motivated individuals. Like us, they envisage a dramatically different future for men with prostate cancer. By pledging regular support they will be investing in world class research for effective diagnosis and treatment of prostate cancer.

For more information about joining the Pioneers please contact pioneers@prostatecanceruk.org

Becoming a Pioneer is much more than a commitment to donate. It’s a commitment to be part of a powerful network of leaders driving a movement for change.

Mark Emberton, Founder Pioneer, Professor of Interventional Oncology, Director Division of Surgery and Interventional Science UCL, Honorary Consultant Urologist UCLH NHS Foundation Trust

With special thanks to The Movember Foundation.

The Movember Foundation is the leading global organisation committed to changing the face of men’s health. They achieve this by challenging men to grow moustaches in Movember (the month formerly known as November) to spark conversation and raise funds for prostate cancer, testicular cancer and mental health problems. Since its humble beginnings in 2003 in Melbourne, Australia when 30 men grew moustaches, Movember has become a truly global movement, inspiring more than four million men and women to participate across 21 countries. The Movember community has raised over £346 million, and has funded more than 800 programmes to date. Their goal is to make a significant impact on men’s health through increased understanding of the health risks men face, encouraging men to take action to remain well, and ensuring that when men are sick they know what to do and take action.

Prostate Cancer UK is the main beneficiary of the Movember campaign. The amazing efforts of the Mo Bros and Mo Sistas from across the UK have significantly contributed to our research initiatives and have supported men by investing in our services.
We’ve signed for #MenUnited