UPDATE

Prostate Cancer Research

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SPRING 2022

Decoding the genetics of cancer

Putting the brakes on advanced cancer

Hundreds of DNA changes or 'mutations' are associated with cancer, but it can be tricky to identify which mutations drive the cancer and which are not important. By unravelling the genetics underlying prostate cancer, Dr Jorge de la Rosa will move us closer to new and better treatments.

'We aim to identify and understand the faulty genes that cause human prostate tumours to spread. I am very grateful to PCR and I feel very excited about this work, which I hope will bring new therapeutic opportunities for people with prostate cancer.'

Dr Jorge de la Rosa
Lead researcher
UNIVERSITY OF CAMBRIDGE

Start date: November 2019

Duration: 54 months, with quarterly evaluations

The research at a glance

1 Cells have on and off signals that tell them whether to grow or to stop growing. Tumour suppressor genes are special 'off signals' that tell cells to stop growing, and prevent normal cells becoming cancerous.

2 PTEN is a tumour suppressor gene that doesn't work properly in almost half of primary and almost all advanced cancers.

3 As cancer is such a complicated disease, scientists know that PTEN is probably not acting alone when it triggers cancers to grow and spread.

4 Lots of other genetic changes happen when PTEN stops working, but we don't fully understand what these changes do.

5 Jorge's unique project will develop and use a new genetic tool to find out what extra genetic changes need to happen for loss of PTEN to promote cancer.

6 By revealing the genetic changes that cause prostate cancer to advance, we hope to support the design of better treatments.

Brakes and accelerators

Two types of gene are particularly important in cancer:

1. Oncogenes act like the accelerator in a car, telling cells to grow and reproduce.
2. Tumour suppressor genes act like the brakes, telling cells to stop growing and reproducing.

Cancers develop when certain mutations change how these genes work. PTEN is an important brake that fails to work properly in many prostate cancers, making these tumours more likely to become aggressive, spread outside the prostate and be difficult to treat. Almost all prostate cancers that spread and about half of primary prostate tumours have lost PTEN: if we knew more about what else happens in a cell after PTEN has failed, we could find new ways to trigger stop signals for cancer, to replace the role that PTEN should have.

Unravelling the many changes triggered by PTEN failing makes us more likely to design better treatments and identify patients at higher risk of advanced disease. However, this would have taken years, had PCR not funded Jorge to develop a new genetic tool based on the Nobel prize-winning CRISPR gene-editing technology, which can massively speed up this process.

Success so far, and the next level

The first stage of Jorge's project is complete: he has successfully developed and validated his new gene technology, which will shave years off the time it would normally take to make the discoveries involving multiple genes that make new treatments possible.

A new team member, Alex Hart, has just joined, to help take the project to the next level. Alex's expertise lies in her specialist knowledge of how genetics affect how cells send signals to each other, and also how immune cells move within cancers. Together, Jorge and Alex are starting to find the genetic causes of cancer spreading and the possible vulnerabilities in cancer cells that could change prostate cancer treatment.

Did you know?

DNA stands for deoxyribonucleic acid. But what is it? All of our cells contain DNA. Each piece of DNA contains multiple genes that tell the cell what to do – how to behave, grow, reproduce and die. Genes are good at picking up changes (mutations) that happen naturally or in response to external factors. Cells can often repair gene mutations but may self-destruct if the damage is severe. Our immune systems can also recognise abnormal mutations and kill offending cells altogether (this can help protect us from cancer). But mutations in important genes can stop cells understanding their instructions, causing them to multiply, not repair or die when they should do. These mutations can lead to cancer, and are a particular focus of cancer researchers.

TACKLING RESISTANCE TO HORMONE THERAPY

Hormone therapy is one of the main treatments for prostate cancer. It starves prostate cancer by cutting off its food supply: hormones such as testosterone. Unfortunately, for many patients, hormone therapy eventually stops working. Our researchers are leading the way to develop new treatments that keep hormone therapy working for longer, to build a future free from the uncertainty of current treatments.

- Professor Iain J. McEwan and his team at the University of Aberdeen are developing and refining new drug combinations to outsmart cancer's tricks to avoid the effects of hormone therapy.
- Dr Luke Gaughan and his team at the Newcastle University Centre for Cancer are investigating how prostate cancers initially become resistant to hormone therapy, and eventually stop resistance in its tracks.

MCL-1: A NEW THERAPY FOR PROSTATE CANCER?

MCL-1 is a protein that plays a crucial role in the development of many cancers, including breast cancer. It has also been linked to resistance to hormone therapy. New research shows that men with advanced prostate cancer also have high levels of MCL-1, but we don't yet know enough about its importance in the disease. Dr Kirsteen Campbell and her team at the Beatson Institute in Glasgow will uncover the protein's role in helping prostate cancers grow, so that they can push forward new treatments.

OUR MISSION
Together, we will develop and deliver breakthrough medicines and treatments.

OUR VISION
A world where people are free from the impact of prostate cancer.