UCD Impact Case Study

epiCaPture: A Urine Test to Catch Prostate Cancer

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ACADEMIC ECONOMIC HEALTH SCIENTIFIC SOCIAL TECHNO-LOGICAL TRAINING

SUMMARY

A simple urine test could help save lives from prostate cancer. Research carried out on almost 500 men found that nearly 90% of those with aggressive prostate cancer had DNA changes in their urine, which were absent in healthy men.

The new test offers a 70% improvement in the specificity of the current standard blood test. This means that most men could be spared the trauma of an invasive trans-rectal needle biopsy to rule out prostate cancer. Further work is underway to validate these findings.

"Whilst still at an early stage, the epiCaPture platform has the potential to address many of the problems confounding the early detection of prostate cancer and has the unique selling point of selectively detecting high-risk disease. This sets it apart from other biomarker panels in the commercial pipeline"

RESEARCH

Ancient Romans used urine to whiten their teeth and as invisible ink to send secret messages. Over the years many myths have surrounded the potential virtues of urine, including its value as an antidote to jellyfish stings. Folklore aside, urine is "liquid gold" when it comes to the studying human disease because it provides a snapshot of what's going on inside the body - this research uses urine to pick up prostate cancer.

Prostate cancer is so common that most men will develop the disease at some point over their lifetime[1]. The good news, though, is that most of these prostate cancers are relatively harmless[2]. Yet it's still the fifth leading cause of cancer deaths worldwide[1], so early detection is vital to catch the disease before it spreads. Currently, tests to detect prostate cancer are not very accurate[3]. Dr Perry's research is addressing this problem by developing new ways to catch aggressive, potentially lethal prostate cancer from a simple urine test.

Over the last five years her team at UCD has worked with doctors, nurses, patients and other scientists from Ireland, UK, USA and Canada to study urine from almost 500 men. They showed that almost 90% of men with aggressive prostate cancer have changes in their DNA that could be found in their urine. These changes were absent in healthy men and men with low-grade disease. If these findings can be replicated, this research could contribute to a new, more accurate test to help catch aggressive prostate cancer and save many lives from the disease.

Dr Antoinette Perry, centre, with PhD students Eve O'Reilly and Alexandra Tuzova, right

epiCaPture

RESEARCH IMPACT

A trans-rectal needle biopsy is the current test recommended by GPs to rule out prostate cancer. Prostate cancer kills more than 300,000 men every year[1]. Early detection is vital to eradicate death from this disease.

Prostate biopsies are invasive, traumatic for the patient and expensive to carry out. Worst of all, most of them are unnecessary, due to the lack of an accurate method to identify which men actually need a prostate biopsy. An estimated five million prostate biopsies are performed every year worldwide, and two-thirds of these are negative[4-5]. With an aging Western male population, and improving life expectancies, this problem is only going to get worse.

Dr Perry's research group at UCD has developed epiCaPture to address this problem. epiCaPture is a first-in-field urine prognostic test for early detection of aggressive prostate cancer. The collaborative team of scientists, doctors and nurses works closely with patients, and has already made academic and scientific impact by increasing understanding of the biology of prostate cancer, by publishing research in leading international peer-reviewed journals[6-8] and presenting their findings at national and international scientific conferences.

epiCaPture has the potential to impact health by benefiting both patients and doctors. epiCaPture delivers a 70% improvement in specificity over the current blood test. As a urine test, it could save hundreds of thousands of men every year from having an unnecessary invasive trans-rectal biopsy. epiCaPture detects almost 90% of aggressive prostate cancers, and so has the potential to impact the number of men dying every year from this disease by helping to catch the disease early. epiCaPture could help doctors to make more informed decisions about which men need a prostate biopsy, whilst at the same time reducing over-detection of indolent low-risk tumours.

If commercialised and brought to market, epiCaPture could realise a major economic impact. Studies addressing the economic burden of cancer in the EU, have estimated costs for prostate cancer diagnosis and treatment over the next 20 years per 100,000 men at approximately €60million – €23million of which can be attributed to over-detected cancers[9-10].

This project has had a direct educational and training impact on the next generation of Irish scientists and clinician scientists. Sarah Kelly, Eve O'Reilly and Alexandra Tuzova all worked as graduate research assistants on epiCaPture since 2012 and are co-authors on a manuscript currently under review[11]. Igniting her passion for medical research, Sarah has since entered Graduate Entry Medical School at UCD.

Eve and Alexandra both successfully won PhD scholarships from the Irish Research Council and Irish Cancer Society, respectively, and continue to develop their careers in cancer research, under Dr Perry's mentorship at UCD.

Finally, the research has had a positive societal impact. By engaging in local outreach activities and talking openly about men's health, and more specifically prostate cancer, Dr Perry's team are increasing public awareness of the importance of early detection and getting checked, which is essential to save lives.

Endorsements

"epiCaPture has the potential to be revolutionary",
Paul Eros, Global VP of Marketing, DiaSorin, June 17th 2015

"I heard Dr Perry present early data from her urine DNA methylation project at a recent Prostate Cancer Symposium, "From the Bench to the Clinic" in Oslo, Norway. At this meeting, Dr Perry and I were able to share many insights and experiences and to discuss the commercial landscape of DNA methylation biomarkers (for prostate cancer) and their potential for risk stratification and personalized medicine. I have personal first-hand experience in this field holding several licensed patents. Whilst still at an early stage, the epiCaPture platform has the potential to address many of the problems confounding the early detection of prostate cancer and has the unique selling point of selectively detecting high-risk disease. This sets it apart from other biomarker panels in the commercial pipeline".
Excerpt from letter from Dr Bill Nelson. MD PhD, Director Sidney Kimmel Comprehensive Cancer Centre, Johns Hopkins University, USA, June 2014

RESEARCH REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr accessed on 02/05/2018.

2. Wilt TJ, Jones KM, Barry MJ, Andriole GL, Culkin D, Wheeler T, et al. Follow-up of Prostatectomy versus Observation for Early Prostate Cancer. N Engl J Med 2017;377(2):132-42 doi 10.1056/NEJMoa1615869.

3. https://www.cancer.gov/types/prostate/psa-fact-sheet

4. Heijnsdijk EA, Wever EM, Auvinen A, et al. Quality-of-life effects of prostate-specific antigen screening. *The New England journal of medicine* 2012; 367(7): 595-605.

5. Andriole GL. Pathology: the lottery of conventional prostate biopsy. Nature reviews Urology 2009; 6(4): 188-9.

6. Perry, Loftus, Moroose, Lynch, Hollywood, Watson, Woodson, Lawler. *In silico* mining identifies IGFBP3 as a novel target of promoter hypermethylation in prostate cancer. British Journal of Cancer (2007). DOI:10.1038/sj.bjc.6603767

7. Sullivan, Murphy, Barrett, Loftus, Thornhill, Hollywood, Lynch, Perry. IGFBP7 promoter methylation and gene expression analysis in prostate cancer. Journal of Urology (2012). DOI:10.1016/j.juro.2012.06.002

8. Perry, O'Hurley, Raheem, et al. Gene expression and epigenetic discovery screen reveal transient expression of SFRP2 during prostate cancer progression. International Journal of Cancer (2013). DOI: 10.1002/ijc.27798

9. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *The lancet oncology* 2013; 14(12): 1165-74.

10. Heijnsdijk EA, der Kinderen A, Wever EM, Draisma G, Roobol MJ, de Koning HJ. Overdetection, overtreatment and costs in prostate-specific antigen screening for prostate cancer. *British journal of cancer* 2009; 101(11): 1833-8.

11. O'Reilly, Tuzova, O'Meachair, Russell, O'Brien, Kelly, Dhomhnallain, DeBarra, Dale, Brugman, Clarke, Schmidt, Patil, Pellegrini, Finn, Manecksha, Cooper, Brewer, Bapat, Sanda, Clark, Perry. epiCaPture: a non- invasive urine DNA methylation test for early detection of high-risk prostate cancer. *Manuscript under Review*

Grant Information

Approximately €550,000 in competitive grant funding: 2016, Enterprise Ireland Feasibility Study €14,760 2015; Science Foundation Ireland TIDA €85,653 2013; Movember GAP1 Award €74,090 2011; US PCF Young Investigator Award €163,116 2009; Irish Cancer Society Post-doctoral Fellowship €212,627.

Awards

2015: Joint Winner, Get Started Technology Venture Programme, SFI/Ryan Academy http://ryanacademy.ie/portfolio/sfi-tida-innovation-entrepreneurship-skills-programme/

2015: Joint winner, EIT Health Innovation & Business Creation Summer School https://www.eithealth.eu/ https://www.youtube.com/watch?v=2rGpUYgxVRUU https://www.youtube.com/watch?v=mQFvYdCMfkg

2013: Movember launched their Global Action Plans, collaborative research projects. I am one of 12 funded principal investigators across 7 countries, involved in the Movember GAP1 Urine Biomarker Initiative, which aims to develop multidisciplinary urinary biomarkers for early detection of aggressive prostate cancer. https://ie.movember.com/about/prostate-cancer

2011: The US Prostate Cancer Foundation (PCF) created the Young Investigator Awards program in 2008 to identify a cohort of future research leaders who will keep the field of prostate cancer research vibrant with new ideas. In 2011, I was the first Irish person to receive this accolade and am one of only 11 researchers outside of the US to have received this prestigious award. https://www.pcf.org/bio/antoinette-perry/ https://www.pcf.org/news/pcf-young-investigators-ireland-researching-molecular-differences-aggressive-low- gleason-grade-cancers/

Outreach & Public Engagement

Dr Perry has spoken about epiCaPture at several public patient initiatives as well as on the radio and television. Radio: Sunshine FM (12/2011), and the Ray Darcy show, Today FM (02/2013) Television: TV3's Ireland AM (11/2013) Public talk: AOIFE (Association of Irish Floral Artists), Caher, Tipperary, June 2016 Committee member, UCD Patient Voice in Cancer Research

International scientific/medical conferences presentations

"A Urine DNA Methylation Test for Early Detection of Prostate Cancer". Early Detection Research Network (EDRN) teleconference, **USA** (2018).

"Translating Epigenomic Discoveries to the Clinic to Improve Patient Care". Medical Oncology Seminar Series, St Vincent's Hospital, **Ireland** (2017).

"Analysis of DNA methylation Biomarkers in Liquid Biopsies". Prostate Cancer Biomarker Symposium Oslo, **Norway** (2017).

"Translational Epigenetics for the Early detection of Prostate Cancer". Portuguese Oncology Institute, **Portugal** (2017).

Intellectual Property

Patent application "A DNA Methylation test for prostate cancer". Published as WO 2016 / 102674. In National Regional Phase in US & Europe. Inventor: Antoinette Perry

Education & Training

2018: Eve O'Reilly won a scholarship from the Irish Research Council to carry out a PhD (supervisor: Dr Antoinette Perry)

2015: Alexandra Tuzova won a scholarship from the Irish Cancer Society to carry out a PhD (supervisor: Dr Antoinette Perry)