UCD Impact Case Study

Developing New Treatments for Triple Negative Breast Cancer

Naoise Synnott, Bo Li, Dr Tríona Ní Chongaile, Dr Fiona Lanigan, Professor William Gallagher, Professor Joe Duffy, Professor John Crown, within the Irish Cancer Society Collaborative Cancer Research Centre BREAST-PREDICT

UCD School of Biomolecular and Biomedical Science and UCD School of Medicine

SUMMARY

Every year, hundreds of thousands of women are diagnosed with an aggressive form of cancer called Triple Negative Breast Cancer (TNBC). This type of breast cancer is not treatable using existing 'targeted' therapies, which tackle specific molecules present on tumour cells. In fact, chemotherapy is the only effective form of treatment for TBNC, and not all patients will respond to this successfully. Therefore, new and improved treatments are needed. Researchers at UCD, working within the BREAST-PREDICT team, have identified two novel therapies, APR-246 and THZ1, which successfully reduce the growth of TNBC cells in the laboratory. They now plan to progress this work towards clinical trials in TNBC patients.

By identifying and treating only those patients likely to respond to these new targeted therapies, we can reduce the cost of treatment while improving the outcome for breast cancer patients.

RESEARCH DESCRIPTION

Irish Cancer Society Research
Collaborative Cancer Research Centres
BREAST-PREDICT

Exciting new research carried out by the BREAST-PREDICT team at UCD[1] has identified two potential novel therapies for triple negative breast cancer (TNBC). TNBC lacks three important molecules on tumour cells, namely the estrogen receptor, progesterone receptor and HER2, and thus cannot be treated with targeted therapies. Chemotherapy is the only currently available treatment for these patients, but approximately 50% of TNBC patients do not respond well to chemotherapy, making it crucial to find new treatments. The BREAST-PREDICT team have recently developed two potential therapies that precisely target TNBC cells.

BREAST-PREDICT PhD student Naoise Synnott, Professor Joe Duffy, and Professor John Crown at St Vincent's University Hospital and UCD[2] focused on a new drug, known as APR-246. This drug specifically targets p53, a gene which is responsible for driving breast cancer growth and which is commonly altered in TNBC. APR-246 corrects or neutralises the altered form of p53 and the UCD team found that the drug can slow the growth of TNBC cells grown in the laboratory. This work is published in the *International Journal of Cancer*[3] and the team now hopes that APR-246 can be tested in clinical trials in TNBC patients in Ireland.

The BREAST-PREDICT team in UCD[4] have been working on targeting TNBC another way too, by blocking a gene called CDK7, which promotes the growth of TNBC cells. Research carried out by PhD student Bo Li, Research Fellow Dr Tríona Ní Chongaile, and Professor William Gallagher at the UCD Conway Institute, tested a new drug, known as THZ1, which targets CDK7 in TNBC. Their research shows that THZ1 can specifically kill TNBC cells in the laboratory, both alone and in combination with other therapies. This work was recently published in the journal *Cancer Research*[5].

RESEARCH IMPACT

Health Impact:
Breast cancer is the most common cancer in women worldwide. In 2012 alone, nearly 1.7 million new cases were diagnosed[6]. Approximately 15-20% of these cases are TNBC, equating to ~300,000 women worldwide each year, with 500 on the island of Ireland[7,8]. TNBC is aggressive and it contributes disproportionately to the 14% of all female cancer deaths caused by breast cancer[9]. It is also more likely to be diagnosed in younger women, and thus has a significant economic and societal impact on these women at a time in their lives when they are likely to be active contributors to the workforce or in raising children. **If better treatments such as those we have identified become available for TNBC, more patients with this diagnosis will survive and go on to live long and healthy lives.**

Scientific Impact:
We have published the research outlined here in two high-ranking international peer-reviewed journals, the *International Journal of Cancer and Cancer Research*. This type of publication **increases the international scientific profile of the researchers and associated institutes in the cancer arena,** which in turn will inspire additional spin-off research leading to further funding opportunities and publications

Economic Impact:
Cancer places a substantial economic impact on those diagnosed with cancer and on the world's economy, with an estimated global toll in 2008 of $895 billion[10]. A US-based study found that TNBC patients had 77% higher healthcare costs and double the risk of death compared to non-TNBC patients[11]. Thus, the development of more effective, tailored, and cost-effective therapies for TNBC is critically important in easing this economic burden. **By identifying and treating only those patients likely to respond to these new targeted therapies, we can reduce the cost of treatment while improving the outcome for breast cancer patients.**

Training Impact:
BREAST-PREDICT runs a structured training and education programme for researchers, which provides a framework for training visits between institutions, it funds conference and workshop attendance, it monitors training, and it holds regular skills workshops and educational events. To inspire the next generation of cancer researchers, BREAST-PREDICT facilitates outreach talks to schools, patient groups, and other public events. **The impact will be to improve the calibre of current trainees in cancer research, while promoting a career in cancer research as an admirable and attainable goal for the next generation.**

Social Impact:
The impact of a diagnosis of TNBC can be devastating for patients and their families, with a poor prognosis and relatively few treatment options, all of which come with significant side-effects. **By developing new therapies for TNBC, we can improve the lives of these patients and increase their chances of survival.**

Our goal is also to raise awareness of cancer research activities in Ireland among patients and the general public and to generate interest in the new treatments being developed and in the new clinical trials being opened to patients. When PhD student Naoise Synnott and Professor Joe Duffy published findings on APR-246 as a potential new treatment for TNBC, it was heavily featured in the Irish media, including major articles in the *Irish Examiner*, *The Irish Times* and *The Irish Independent*, RTÉ News and national radio. **By raising awareness of cancer research activities in Ireland, we can contribute to public understanding of research, and science in general.**

Quote from Director of BREAST-PREDICT, Professor William Gallagher:

"Over the last two decades, drugs such as Herceptin have been discovered to target or block proteins that are responsible for the growth of some breast cancers. However, finding a similar drug therapy for triple-negative breast cancer has so far eluded scientists, making these findings all the more important. If successful in clinical trials, APR-246 will be shown to have been effective in targeting a gene known as p53, a gene which is altered in almost all cases of triple-negative breast cancer.

"BREAST-PREDICT is proud to have supported Naoise in her work in this area. Since our establishment in 2013, we have grown to a team of more than 50 researchers around the country, all committed to improving our understanding of breast cancer and finding new and better ways to treat the disease."

RESEARCH

1. www.breastpredict.com
2. Research co-funded by Cancer Clinical Research Trust – www.ccrt.ie
3. Research co-funded by EU FP7 RATHER project – www.ratherproject.com
4. Synnott, N.C. et al., Int J Cancer. 2017; 140(1):234-246. doi: 10.1002/ijc.30425.
5. Li, B. et al. Cancer Res. 2017; Apr 28. doi: 10.1158/0008-5472.CAN-16-2546. [Epub ahead of print]
6. www.globocan.iarc.fr;
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11. Baser, O. et al. Curr Med Res Opin. 2012; 28(3):419-28. doi: 10.1185/03007995.2011.628649
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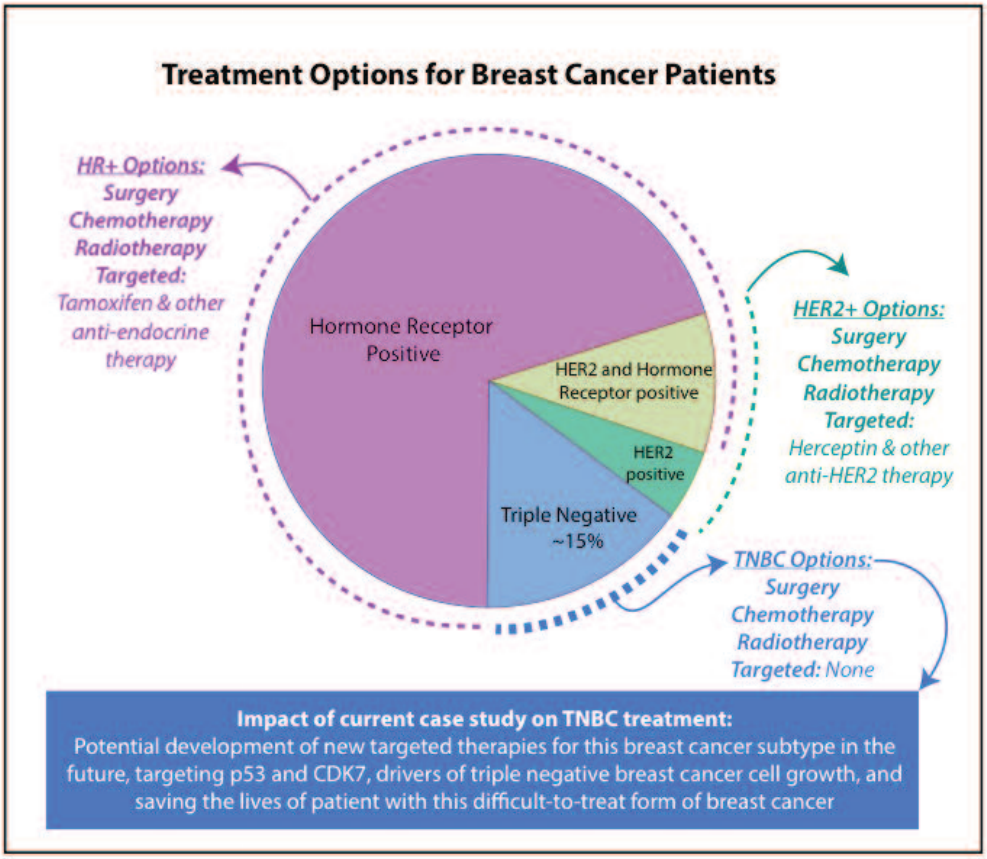

Quote from BREAST-PREDICT PhD student Naoise Synnott:

"At the moment the only form of drug treatment available to patients with triple-negative breast cancer is chemotherapy. While this will work well for some patients, others may find that their cancer cells don't respond as well as might be hoped to chemotherapy, leading to patients suffering the side effects of this treatment without any of the desired outcomes.

"I decided to focus my BREAST-PREDICT research on triple-negative breast cancer because it was clear that work needed to be done to provide better and more targeted treatment for these patients. I hope that the work of me and my colleagues in St Vincent's and UCD will be a big step in providing better treatment and hope to future triple-negative breast cancer patients."