Personalising the use of chemotherapy in breast cancer treatment

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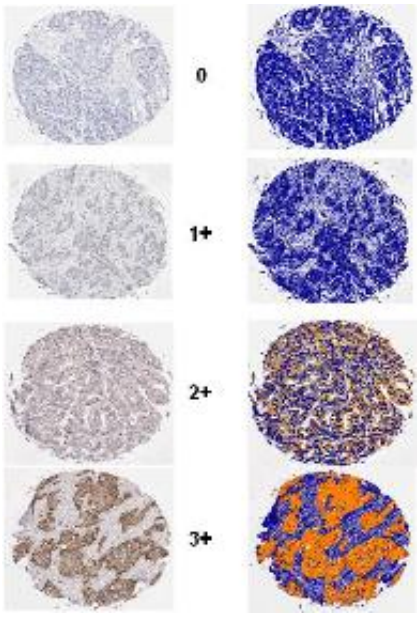

Manual and automated immunohistochemical analysis of CART expression. Immunohistochemical analysis of primary breast cancer with corresponding markup images of automated algorithm used to quantify CART expression. Stromal tissue is mapped in blue on the markup image, and CART expression is mapped on an increasing scale from yellow (low levels of expression) to red (high levels of expression). For manual analysis, CART expression is in brown, with stromal tissue counterstained in purple.

(Medical Xpress) -- UCD researchers have identified a novel biomarker that can identify those women with breast cancer who will have a poor response to tamoxifen, one of the principle anti-hormone drugs used to

treat the disease. This may allow clinicians to tailor the treatment of early stage breast cancer patients appropriately.

Conway Fellow, Professor William Gallagher and his team who form part of the Science Foundation Ireland-funded strategic research cluster, *Molecular Therapeutics for Cancer Ireland (MTCI)*, examined the breast cancers of over 1,000 patients. They found that those with high levels of a protein named CART (cocaine-and-amphetamine-regulated transcript) had a significantly poorer outcome when treated with tamoxifen compared to those patients with zero or low levels of the protein.

Tamoxifen works by blocking the growth-promoting action of oestrogen in breast cancer cells. The results of this research published in a leading scientific journal, Oncogene, describes how CART can intervene and prevent tamoxifen from killing the cancer cells. Commenting on the findings, Dr Darran O'Connor, senior scientist and joint lead author of the research said, "Identifying early stage breast cancer patients who need additional chemotherapy is a matter of intense clinical interest. We believe that CART profiling will facilitate the stratification of lymph node-negative breast cancer patients into high- and low-risk categories and allow for the personalisation of therapy."

Dr Donal Brennan, UCD School of Medicine, National Maternity Hospital and joint lead author of the work added, "We clearly demonstrate that both pre- and post-menopausal, early stage breast cancer patients with high CART expressing tumours have a poor outcome and do not respond well to treatment with tamoxifen. Due to this, we believe that they should receive aggressive adjuvant chemotherapy."

At present, women diagnosed with early stage, hormone receptor-positive, lymph node-negative breast cancer undergo surgery coupled

with anti-hormone therapy and chemotherapy. However, current research suggests that many patients would do equally well with surgery and anti-hormone therapy without the addition of debilitating chemotherapeutic regimens.

The findings of the UCD team, in collaboration with colleagues at Lund University in Sweden, could help clinicians to accurately identify those patients who do not require chemotherapy and for whom surgery and anti-hormone therapy alone is sufficient to treat their cancer. In addition to improving the patients' quality of life, this can also reduce the economic burden associated with unnecessary supplementary treatment.

While CART has been widely studied in other areas as a key regulator of body weight and the body's response to drugs such as cocaine, the researchers are the first to demonstrate a link with breast cancer.

Looking to the future for this research, Professor William Gallagher, associate professor of cancer biology, founder and chief scientific officer of Oncomark, a UCD molecular diagnostics spin-out company said, "As translational researchers, our goal is to bring our findings from the laboratory into the clinic. Our intention now is to develop a clinically approved test so that we can identify those patients who will benefit most from tailoring their therapy based upon the CART status of their cancer".

Provided by University College Dublin

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