Scientists unravel resistance to breast cancer treatment

October 31 2012

Scientists have identified a molecular 'flag' in women with breast cancer who do not respond or have become resistant to the hormone drug tamoxifen.

Tamoxifen – used alongside traditional chemotherapy and radiotherapy – blocks the female hormone oestrogen that, in certain breast cancers, is required by the tumour to grow; it has been shown to improve cancer survival rates by up to one third.

However, about one third of patients with the appropriate type of breast cancer – known as oestrogen receptor positive breast cancer – do not respond to tamoxifen or develop resistance to the drug. Oestrogen receptor positive breast cancer is the most common form of the disease accounting for 70% of cases.

Now, a team from the University of Manchester's Paterson Institute for Cancer Research has identified a molecular flag or biomarker that will help doctors predict which patients will respond best to complementary (adjuvant) hormone therapy with tamoxifen.

"The identification of molecular flags to classify subgroups of breast cancer and so determine the best treatment for each patient is of increasing importance in cancer therapy," said study lead Professor Göran Landberg.

"Tamoxifen has been shown to be highly effective in some breast cancer

patients when used alongside traditional cancer therapies but, in a third of cases, the result has not been what we would hope. If we can predict which patients will respond to tamoxifen, and those who won't, then this is clearly advantageous as it means the correct treatment is provided instantly which will improve disease outcomes."

The research, funded by the charity Breakthrough Breast Cancer and published in the journal PLoS One, looked at the connective tissue surrounding the tumour, which is known to send signals that help the cancer to grow. The team, part of the Manchester Cancer Research Centre, found that fibroblast cells – the cells that make up connective tissue in our bodies –differ in their characteristics from patient to patient and can give clues about tamoxifen treatment response

Co-author Dr Susann Busch said: "We analysed tissue samples from 564 women with invasive breast cancer, some of whom were given tamoxifen and some who weren't; this allowed us to make a comparison between treatment responses.

"We discovered that women who had low levels of a protein known as pERK in their cancer-associated fibroblasts did not respond to tamoxifen. Testing patients for the pERK flag could help doctors determine whether tamoxifen is an appropriate treatment for their patient or whether alternative therapies should be explored, so saving time and money."

The researchers now plan to further study molecular flags that are characteristic for cancer-associated fibroblasts. Understanding how fibroblasts help the tumour to grow will allow the development of new strategies to block their harmful signals and overcome drug resistance.

More information: 'Low ERK Phosphorylation in Cancer-Associated Fibroblasts Is Associated with Tamoxifen Resistance in Pre-Menopausal

Breast Cancer' by Susann Busch et al, *PLoS One*.