



Calculating how breast cancers will respond to tamoxifen

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A discovery by Australian scientists could help clinicians decide which women with breast cancer will make good candidates for anti-oestrogen therapies, such as tamoxifen, and which will not.

Over 12,000 Australian women are diagnosed with breast cancer each year, roughly 70% of which will have cancers treatable with tamoxifen. Unfortunately, 30% or more of these women may not respond well to such anti-hormone therapy long-term.

Work done by a research team headed by Associate Professor Liz Musgrove and Professor Rob Sutherland of Sydney's Garvan Institute of Medical Research has correlated expression of certain functionally-related oestrogen-regulated genes with predictable clinical outcomes. This expanded knowledge about oestrogen action and endocrine resistance should allow clinicians to make better, more informed, choices in the future.

The novel findings were published in the August issue of the *Public Library of Science* journal *PLoS ONE*.

"What we call 'breast cancer' is actually many different kinds of cancer, some of which appear to be driven by the female hormone oestrogen," said Professor Musgrove. "We found roughly 800 genes that are regulated by oestrogen, each with a different function in the cell, so you can imagine how complicated the picture can become when you are trying to correlate the effects of all these genes with multiple cancers."

In fact, the scale of such calculations, and complex biochemistry behind them, requires the help of large relational databases, powerful software and the agile minds of bioinformatics specialists to crunch and analyse data.

Out of the undifferentiated pool of oestrogen-regulated genes, the team has identified four groupings of genes, with each group relating to one aspect of breast cancer cell behaviour: cell cycle (proliferation), cell growth (actual size of the cell), cell death and gene transcription.

Professor Musgrove stresses the clinical relevance of the findings. "In collaboration with colleagues at the Peter MacCallum Cancer Centre in Melbourne, we took these 4 groups of genes and asked whether they were related to outcome in a sample of 246 women who'd been treated with tamoxifen. We were able to directly relate 3 out of the 4 groups, all but gene transcription, to whether a woman had done better or worse when treated with tamoxifen."

"We then went on to ask whether we were looking at three different ways of identifying the same women, or whether the three groups of genes identified distinct groups of women, with different breast cancers. It appears as if they identify distinct groups of women with different cancers."

“Developing pure lists of genes that are involved in single processes gives us a good conceptual and experimental framework. In time we hope to understand how these groups of genes interact, and exactly how they affect disease or health.”

ABOUT GARVAN

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with approximately 400 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation, Bone, and Neuroscience. The Garvan's mission is to make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan's discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

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