New hope for hormone resistant breast cancer

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A new finding provides fresh hope for the millions of women worldwide with oestrogen receptor positive breast cancer. Australian scientists have shown that a specific change, which occurs when tumours become resistant to anti-oestrogen therapy, might make the cancers susceptible to treatment with chemotherapy drugs.

Seventy percent of breast cancer patients have oestrogen receptor positive cancer, and most patients respond well to anti-oestrogen therapies, for a few years at least. Within 15 years, however, 50% will relapse and eventually die from the disease.

Dr Andrew Stone, Professor Susan Clark and Professor Liz Musgrove, from Sydney's Garvan Institute of Medical Research, in collaboration with scientists from Cardiff University, have demonstrated that the BCL-2 gene becomes epigenetically 'silenced' in resistant tumours. This process is potentially detectable in the blood, providing a diagnostic marker. Their findings are now online in the international journal *Molecular Cancer Therapetics*.

Epigenetics involves biochemical changes in our cells that directly impact our DNA, making some genes active, while silencing others. Epigenetic events include DNA methylation, when a methyl group - one carbon atom and three hydrogen atoms - attaches to a gene, determining the extent to which it is 'switched on' or 'switched off'.

Dr Stone and colleagues have shown in human disease, as well as in

several different cell models, that BCL-2 is silenced in oestrogen-resistant tumours by DNA methylation.

"The main purpose of the BCL-2 gene is to keep cells alive, so when the gene is silenced, cells become more vulnerable to chemotherapy," said Dr Stone.

"The next step will be to test our findings in clinical studies. We propose that if the BCL-2 gene is silenced, patients with oestrogen receptor positive breast cancer would benefit from combination therapy. In other words, tamoxifen could be used in combination with a chemotherapy drug, to kill off vulnerable tumour cells."

"Excitingly, this is something that could be implemented into clinical practice very quickly, since the technology now exists to profile methylation of BCL-2 in all patients – both oestrogen responsive and oestrogen resistant patients. In addition, the proposed chemotherapy drugs are already in use."

"If such a test were to be implemented, we believe it could help patients much earlier – hopefully shutting down tumours at an early stage."

Provided by Garvan Institute of Medical Research