New anti-cancer compound shows promise for breast cancer

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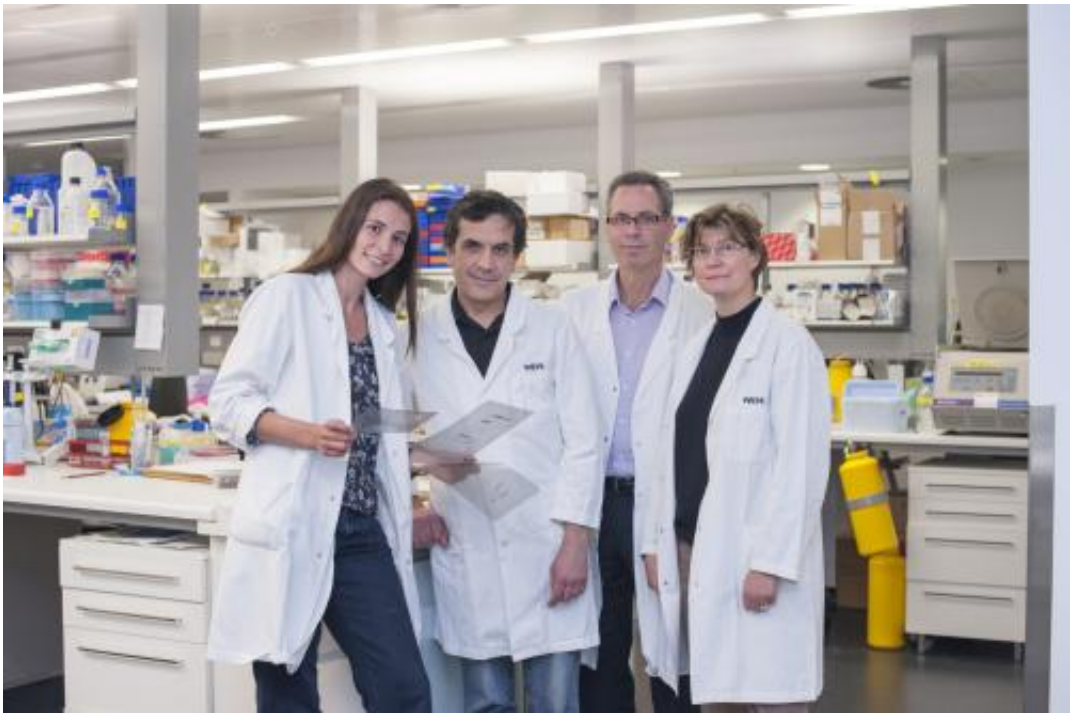

The research team was led by (from left to right) Dr Delphine Merino, Dr François Vaillant, Professor Geoff Lindeman and Professor Jane Visvader. Credit: Walter and Eliza Hall Institute of Medical Research

Melbourne researchers have discovered that anti-cancer compounds currently in clinical trials for some types of leukaemia could offer hope for treating the most common type of breast cancer.

The researchers, from the Walter and Eliza Hall Institute, found that the

compounds, called BH3-mimetics, were effective in treating aggressive oestrogen receptor-positive (ER-positive) breast cancers when combined with the breast cancer drug tamoxifen in preclinical models. Approximately 70 per cent of breast cancers are ER-positive.

The research team, led by Professor Geoff Lindeman, Professor Jane Visvader, Dr François Vaillant and Dr Delphine Merino from the institute's Breast Cancer Laboratory, said they hoped their results would lead to clinical trials of BH3-mimetics for treating ER-positive breast cancers in the next few years.

Professor Lindeman, who is also a medical oncologist at The Royal Melbourne Hospital, said that BH3-mimetics worked by neutralising a protein called BCL-2 in cancer cells, making them more susceptible to dying. Up to 85 per cent of ER-positive breast cancers have high levels of BCL-2, which is a so-called 'pro-survival' protein that helps cancer cells to become immortal, and can help them to survive chemotherapy and other treatments.

"Drs Vaillant and Merino looked at the effect of adding BH3-mimetics to the standard hormone treatment, tamoxifen, used for a subtype of ER-positive cancers called luminal B cancers, which had high levels of BCL-2," Professor Lindeman said. "They found that a BH3-mimetic called ABT-199/GDC-0199 improved the effectiveness of hormone therapy by stopping or delaying the growth of these aggressive tumours. In one of the tumour models, the combined treatment caused complete disappearance of the tumour, while standard treatment had only a partial and unsustained benefit."

Professor Visvader said there was a need to improve treatments for luminal B breast cancers, which are a more aggressive type of ER-positive breast cancer, associated with a poorer prognosis. In the study, the researchers used preclinical models of breast tumour samples

donated by Melbourne women undergoing cancer surgery to understand how real human cancers would respond to the treatment.

"We are excited by these results and what they could mean for women with breast cancer," Professor Visvader said. "ER-positive breast cancers are the most common type of breast cancer, so even a small improvement could have a substantial impact if more effective upfront treatment could prevent relapse," she said. "It is very early days, however, and the findings will need to be rigorously tested in clinical studies."

A landmark discovery in the late 1980s by Walter and Eliza Hall Institute scientists that BCL-2 promoted cell survival fuelled more than two decades of global research that has culminated in the design of BH3-mimetics. The investigational compound, ABT-199/GDC-0199, was discovered by scientists at Abbott (now AbbVie) and is currently being developed by Genentech, a member of the Roche group, and AbbVie.

Professor Lindeman said he hoped the recently established Centre for Translational Breast Cancer Research (TransBCR) could contribute to future clinical trials of the novel combination treatment. "Australian women who donated their tumour samples for research helped make this discovery possible," he said. "It would be great to see Australians among the first to benefit from clinical trials, should they proceed."

The research is published today in the journal *Cancer Cell*.

Provided by Walter and Eliza Hall Institute

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