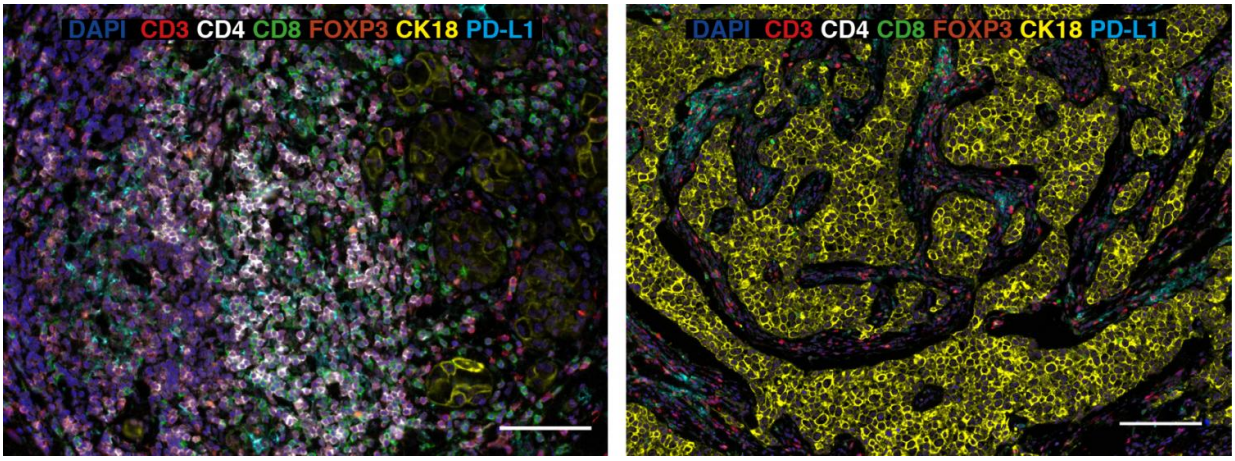
New treatment hope for women with BRCA1 breast cancers

June 7 2017



Microscopic image showing cells that could be targeted with anti-PD-L1 antibodies for immunotherapy (teal) in a biopsy sample from a triple negative breast cancer tumor. Credit: E. Nolan et al., Science Translational Medicine (2017)

Researchers have found a new way to use immunotherapy, a breakthrough mode of cancer treatment which harnesses the patient's immune system, to treat an aggressive form of breast cancer.

The researchers at Melbourne's Walter and Eliza Hall Institute and Peter MacCallum Cancer Centre have shown, for the first time, that combining two immunotherapy drugs could be effective in treating triple

negative breast cancers arising in women with BRCA1 mutations.

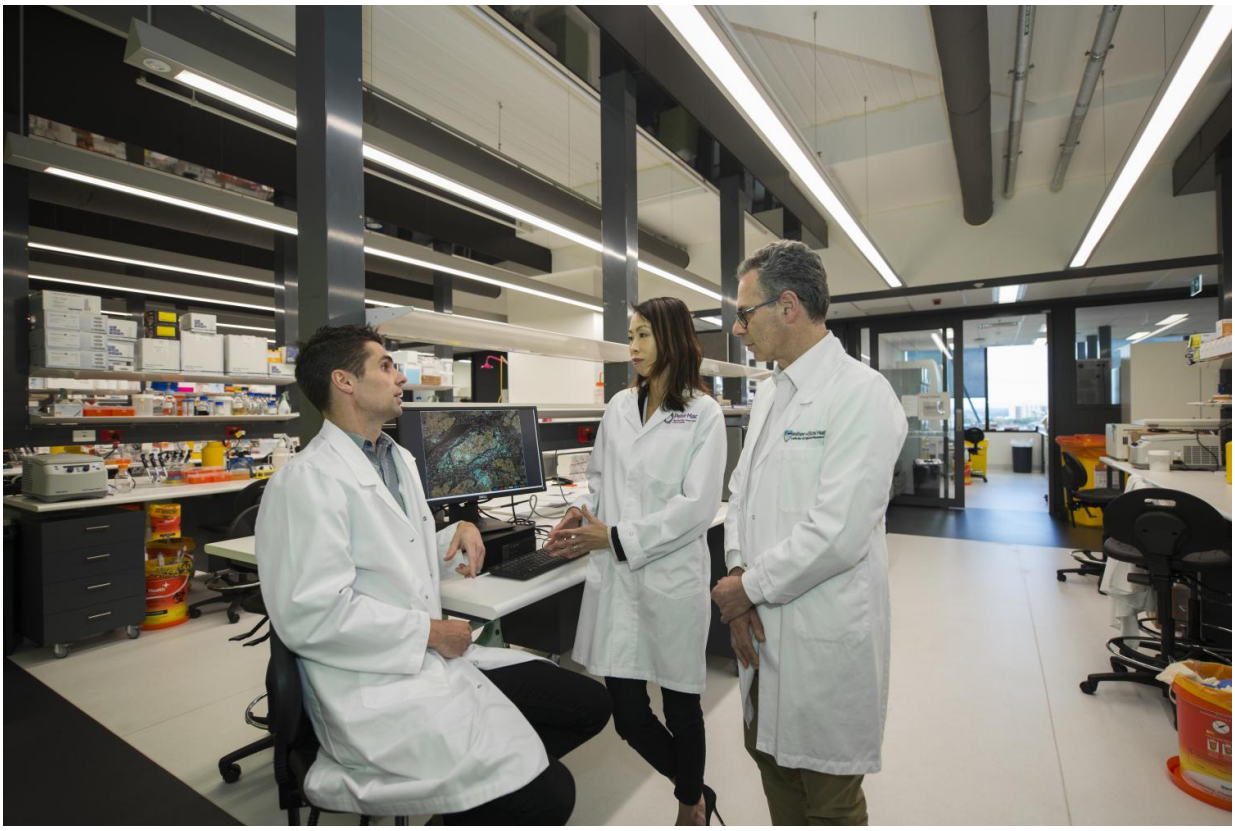
The findings suggest that clinical trials of combined immunotherapy should be considered in women with these breast cancers. Immunotherapy works by boosting the body's immune cells to attack tumours and has been a 'game-changer' for treating melanoma and lung cancers.

The study, led by the Walter and Eliza Hall Institute's Dr Emma Nolan, Professor Geoff Lindeman, Dr Daniel Gray and Professor Jane Visvader, and Peter Mac's Associate Professor Sherene Loi and Associate Professor Phillip Darcy, was published today in *Science Translational Medicine*.

Breast cancer affects one in eight women in Australia. Triple negative breast cancers typically account for around 15 per cent of breast cancers, affecting around 2400 women each year, but are much more common in women with BRCA1 mutations.

Professor Lindeman, also a medical oncologist at the Royal Melbourne Hospital and Peter Mac, said triple negative breast cancers were more aggressive and more likely to recur than other breast cancers.

"Triple negative breast cancers have not seen the same improvement in targeted therapies, or survival, as some other types of breast cancer," Professor Lindeman said. "Our study showed that combining anti-PD1 and anti-CTLA4 immunotherapies with chemotherapy halted the growth of BRCA1-related tumours and significantly improved survival in laboratory models."



Researchers have shown for the first time that combining two immunotherapy drugs could be effective in treating triple negative breast cancers arising in women with BRCA1 mutations. Dr. Daniel Gray, Associate Professor Sherene Loi and Professor Geoff Lindeman (L-R) from the Walter and Eliza Hall Institute and Peter MacCallum Cancer Centre led the research. Credit: Walter and Eliza Hall Institute

Some cancer cells survive by hijacking and 'switching off' immune cells that would otherwise destroy the tumours. Anti-PD1 and anti-CTLA4 immunotherapies are so-called 'immune checkpoint inhibitors' that release the brakes on critical immune cells, enabling them to attack the tumour.

Dr Gray said previous research had shown that immunotherapy was

particularly effective at treating tumours that had accumulated many mutations. "BRCA1-related triple negative breast cancers have some of the most 'chaotic' genomes, and we see many immune cells accumulate in and around the tumour," Dr Gray said.

"This suggests that the immune cells can readily detect that something is awry, but they aren't able to respond properly, because they have been disabled by tumour cells. We showed that a combination of anti-PD1 and anti-CTLA4 therapies restored their ability to attack and kill triple negative breast tumour cells, and very effectively control tumour growth."

Associate Professor Loi, head of breast cancer clinical trials research at Peter Mac and for the Parkville precinct, said work was already underway to translate these important findings from laboratory models of breast cancer into a clinical trial for women with the disease.

"Our lab-based findings provide compelling evidence to progress to a clinical trial of this combination of immunotherapy drugs, and chemotherapy, in women with BRCA1-related breast cancer," Associate Professor Loi said. "There is also a rationale to consider the same for BRCA2-related cancers and triple negative breast cancer more broadly.

"Importantly, there are already a number of immunotherapy-based clinical trials underway in breast cancer and these two drugs - anti-PD1 and anti-CTLA4 - are in use for other cancers, so we would hope to begin a trial of this specific combination of immunotherapies in suitable breast cancer patients in the near future."

Professor Lindeman said the study was a great example of what the Victorian Comprehensive Cancer Centre (VCCC) partners could achieve. "Our study brought together researchers with diverse expertise across several institutions, including PhD students from the University of

Melbourne. We also benefited from our close collaboration with kConFab, a national consortium focused on familial breast cancer," he said.

More information: E. Nolan el al., "Combined immune checkpoint blockade as a therapeutic strategy for BRCA1-mutated breast cancer," *Science Translational Medicine* (2017). stm.sciencemag.org/lookup/doi/ … scitranslmed.aal4922

Provided by Walter and Eliza Hall Institute