



Silencing a deadly conversation in breast cancer

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While it is already known that breast cancer cells create the conditions for their own survival by communicating their needs to the healthy cells that surround them, Australian researchers have identified a new way of turning off that cellular cross talk.

They have shown that a molecule known as 'hedgehog' sits at the centre of the switchboard in breast cancer, transmitting biochemical signals between the cancer cells and healthy cells.

When this conversation is blocked – or hedgehog is 'silenced' – tumours shrink and stop their spread.

While the finding applies to all breast cancers, it is particularly relevant for women with basal breast cancer, for which there is no current targeted therapy.

The good news is that drugs for silencing hedgehog are already undergoing Phase 2 clinical trials in other cancer types.

Clinical Associate Professor Sandra O'Toole and Dr Alex Swarbrick, from Sydney's Garvan Institute of Medical Research, analysed breast tumour samples from a cohort of 279 women with advanced breast cancer, revealing that the higher the level of hedgehog, the more aggressive the cancer.

Having discovered high levels of hedgehog in some breast cancer patients, they went on to over-produce the protein in mouse models of basal breast cancer. Mice developed tumours that grew and spread through the body rapidly. When hedgehog was blocked, the tumour growth and spread were significantly slowed.

These findings are published in the prestigious international journal *Cancer Research*, now online.

"We are hopeful that our findings will drive the progress of clinical trials for anti-hedgehog drugs in breast cancer," said Dr Alex Swarbrick.

"Finding an effective drug target for basal breast cancer is a very high priority. It is often referred to as 'triple negative disease', because it doesn't produce any of the oestrogen, progesterone or HER2 receptors, targets of the drugs tamoxifen and Herceptin, which are very effective in other breast cancers."

A/Prof O'Toole, also a pathologist at Sydney's Royal Prince Alfred Hospital, undertook the study as part of her PhD. "These findings may provide some hope to the many women who succumb to breast cancer each year, especially the basal sub-type, although obviously it is early days," she said.

“More work in animal models is needed to understand exactly how best to block this pathway.”

“Our study demonstrates that starving breast cancer cells of hedgehog significantly slows their growth and spread.”

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 over 500 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation and Neuroscience. 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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