Targeting aggressive breast cancers by putting them to sleep

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It is well established that Id1, a gene normally produced only in embryonic development, is reactivated in many 'solid' cancers, or carcinomas.

In the case of breast cancer, the Id1 gene is active only in the more aggressive and metastatic varieties of cancer. Typically those cancers do not possess the oestrogen receptor, and for that reason cannot be treated with Tamoxifen (a drug that interferes with the action of oestrogen), the most effective breast cancer treatment available.

The outcomes for women with breast cancers producing Id1 are therefore much worse than for women with other forms of breast cancer.

Findings by Dr Alex Swarbrick, a scientist at Sydney's Garvan Institute of Medical Research, in collaboration with Professor J. Michael Bishop, Nobel Prize winner and Chancellor of the University of California San Francisco (UCSF), may provide hope for such women in the future. Their article, published online this week in the international journal Proceedings of the National Academy of Sciences, USA (PNAS), shows that Id1 drives some breast cancers.

Dr Swarbrick initiated the Id1 project three years ago while working as a post doctoral researcher in the laboratory of Professor Bishop He conducted much of the experimental work for the project at UCSF, then analysed the data and tissue samples at Garvan. "We happened to ask the right questions about the right gene," he said. "Up to that point, no-one

else had asked whether or not Id1 actually contributed to the origin and behaviour of breast cancer".

"By artificially activating the Id1 protein in mouse mammary glands, we demonstrated that Id1 indeed contributes to cancer - and that mammary cancers with high levels of Id1 become very aggressive and highly metastatic."

"We also showed that if we genetically switch off the Id1 gene in an established tumour, those mice live much longer than mice with continual Id1 expression in their tumour. In fact about 40% of them were cured and the tumours just shrank away."

"One of our most surprising findings was that although the tumours went away, the cells making up the tumour didn't die, as you'd expect."

Instead, the vanishing tumours underwent 'senescence' a tumour suppressive mechanism that scientists are only just beginning to understand. The word is derived from the Latin 'senescere', to grow old. For cells, it means they permanently lose the ability to divide.

Swarbrick believes that as well as trying to kill aggressive breast cancers, it may also be effective to drive them into senescence, to put them to sleep. "You induce a terminal sleep, and then the immune system just gobbles them up."

"Many cancers mutate the genes involved in cell death, so it's hard to kill them. Our results suggest that in the future if we can therapeutically target the genes controlling senescence, such as Id1, we can force these tumours to senesce."

Source: Research Australia