



First step towards switching off breast cancer and leukaemia

8 August, 2008

Australian scientists have identified a way to 'switch off' a molecule, a key player in the molecular processes that trigger breast cancer and certain forms of leukaemia.

The molecule, known as Gab2, operates downstream of a major breast cancer oncogene, HER2, the target of the drug Herceptin.

A research team from the Garvan Institute of Medical Research, led by Professor Roger Daly, has found a novel way of blocking signals to and from Gab2, preventing it from fulfilling its role in cell proliferation. The finding is published online today in the *EMBO Journal*.

In 2002, Professor Daly identified the important role of Gab2 in breast cancer. His task since then has been to work out exactly how Gab2 functions, and how to stop it.

"Gab2 is a signalling protein, which means that it's involved in transmitting signals from the cell surface to the interior of the cell, instructing it to do specific things, such as divide or migrate" he said.

"Gab2 performs a number of signalling roles in normal cells throughout the body, and is usually switched off when it's not needed. Our task has been to work out how the body switches off Gab2, so that we can mimic that process in abnormal cells."

"We've identified a completely novel mechanism for switching off Gab2. This uses another molecule that attaches to Gab2 and acts as a kind of shield, preventing it from transmitting further proliferative signals."

"This binding partner, or 'off switch', is called 14-3-3, and is used to disable Gab2 in a number of cellular settings, when it is no longer needed."

"As Gab2 plays key roles in signalling systems that underpin both normal physiological responses and oncogenesis, it's very important to understand its control mechanisms."

"Our next step will be to obtain more structural information about how 14-3-3 shields Gab2. Once we know that, it should be possible to design drugs to combat Gab2-activated diseases in novel ways."

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 approximately 400 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation, Bone, 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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