



'Hedgehog' signalling pathways in cells could lead to new treatment for skin cancers

A signalling pathway in certain cancer cells that encourages cell growth, named 'Hedgehog', may hold the key to shutting off cancer growth in skin cells, according to research presented at the Australasian College of Dermatologists' Annual Scientific Meeting.

Dr Ivor Caro, a dermatologist based in California, described to delegates how trials are currently underway that are using GDC-0449 (co-developed by Curis and Genentech/Roche) – a molecule in the form of a once-a-day pill – to stop the signalling pathway that is encouraging the growth of basal cell carcinomas (BCCs) in patients with an advanced version of the disease.

"The 'hedgehog' signalling pathway was first noticed in the fruit fly embryo which, under the microscope, looked like a tiny hedgehog, hence the 'hedgehog' nickname," says Dr Caro.

"These signalling pathways are active in utero and are crucial in the growth and development of a foetus, for example by defining how fingers and toes develop and grow.

"However, in adults, the signalling pathways are normally turned off – that is, except when a person carries a particular gene mutation, which can be caused by damage from sun exposure, or inherited.

"This gene mutation activates the 'hedgehog' signalling, leading to the growth of BCCs."

Armed with this knowledge, scientists have been able to identify a molecule that would act as a 'hedgehog' pathway inhibitor, in effect 'switching off' the signalling pathway and giving hope to advanced BCC sufferers, especially those for whom there is no alternative therapy.

"GDC-0449 is a fairly well tolerated, once-a-day pill, which can easily be absorbed when taken orally," says Dr Caro.

An initial study, reported late last year in a medical journal, showed promise. A larger follow-up study in Europe, the US and Australia is ongoing but no longer open to new patients and the results will be available next year. If the overall response rate proves to be positive, this may be the first therapy available specifically for advanced BCCs.

More than 370,000 new cases of non-melanoma skin cancers, including BCCs, are diagnosed in Australia each year.

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