'Molecular assassin' targets disease gene

July 3 2006

University of New South Wales researchers have announced they are developing a new class of experimental drug that has the potential to treat a diverse range of health problems, from inflammation and cancer through to eye and heart disease. The research is published in the July issue of *Nature Biotechnology*.

Certain types of skin cancers and blindness due to age-related macular degeneration (AMD) and diabetic retinopathy are likely to be among the first uses for the drug. AMD is the most common cause of blindness in Australia (Macular Degeneration Foundation).

The experimental drug has already been shown to be effective on skin cancers in pre-clinical models, in another paper published this month by Professor Khachigian's team in the journal, Oncogene.

"This may be a 'one-size fits all' therapy, because it targets a master regulator gene called c-Jun which appears to be involved in all of these diseases," said UNSW Professor Levon Khachigian, of the Centre for Vascular Research (CVR), who is the senior author of the Nature Biotechnology paper.

"c-Jun is an important disease-causing gene," said Professor Khachigian, a molecular biologist. "It stands out because we don't see much of it in normal tissue but it is highly expressed in diseased blood vessels, eyes, lungs, joints, and in the gut – in any number of areas involving inflammation and aggressive vascular growth.

"Our experimental drug, Dz13, is like a secret agent that finds its target, c-Jun, within the cell and destroys it," he said. "It is a specific, pre-programmed 'molecular assassin'."

The paper in Nature Biotechnology shows the potential of c-Jun as a drug target in inflammation. It details tests in a variety of pre-clinical models showing how effective Dz13 is in problems such as eye disease and arthritis.

The next phase in the therapy's development would be a trial, involving up to 10 people with non-melanoma skin cancers. The tumours would be injected with the drug over an eight-week period.

"If such a trial were successful, it would be a significant development given the high rates of skin cancer and because the main treatment currently is surgical excision, which can cause scarring," said Professor Khachigian.

"Conventional anti-inflammatory drugs are associated with a whole host of side-effects. Our therapeutic may potentially avert some of these."

A third paper using the same technology, but focusing on a different master regulator, Egr-1, has also been published this month by Professor Khachigian's group in the Journal of Thrombosis and Haemostasis and shows that heart muscle damage is reduced by the drug after a heart attack.

Source: University of New South Wales