



A revolutionary new way of reversing certain cancers

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Australian and American scientists have found a way of shrinking tumours in certain cancers – a finding that provides hope for new treatments.

The cancers in question are those caused by a new class of genes known as ‘microRNAs’, produced by parts of the genome that, until recently, were dismissed as ‘junk DNA’. While much is still unknown about microRNAs, it is clear that they can interfere with how our genes are ‘read’.

The current finding identifies one particular microRNA (microRNA 380) that appears to disable the king of tumour suppressors, the P53 gene. So important is P53, that it is known as the ‘guardian of the genome’. In order for a cell to become cancerous, P53 must either be mutated or otherwise disabled.

Dr Alex Swarbrick, from Sydney’s Garvan Institute of Medical Research, Dr Susan Woods from Brisbane’s Queensland Institute of Medical Research and Dr Andrei Goga from The University of California San Francisco chose to study neuroblastoma, a childhood cancer of the nervous system in which 99% of patients do not have mutations of the P53 gene.

The researchers found instead that neuroblastomas disable p53 by over-producing microRNA 380. When they blocked the microRNA, P53 production resumed, cancer cells died and tumours became much smaller. Their results are reported in the prestigious international journal *Nature Medicine*, online today.

“The revolutionary thing about this finding is that it’s the first time anyone has blocked the growth of a primary tumour by the simple delivery of a microRNA inhibitor,” said Swarbrick.

“By that, I mean we delivered the microRNA inhibitor in a way we might give it to a person – as a twice-weekly injection – not using some genetic trick. It’s the closest thing to a clinical result that’s yet been published.”

“That, of course, makes this microRNA a potential therapeutic target for all cancers that depend on it.”

“The other good news is that you don’t find this microRNA in normal adult cells. It’s very active while we are developing embryos, when cells need to divide very quickly, but after that it appears to get switched off. So by blocking it, you’re effectively returning cells to normal.”

“We still don’t know why it gets switched on again in certain cancers. Apart from neuroblastomas, we often see it in brain tumours and in melanomas that don’t have mutations in P53.”

So how exactly does it work?

When a gene is transcribed or “read”, in this case P53, a copy of the gene is made in RNA. In a normal cell, that P53 RNA carries the instructions to make P53 proteins, which in turn carry out the tumour suppressor function in cells.

“MicroRNAs act to control the production of proteins – the molecules that do the work in cells,” explained Swarbrick.

“In the cancers we are discussing, our microRNA binds with P53 RNA, preventing it from making proteins. That effectively reduces the number of P53 proteins in a cell and allows the tumour to grow.”

“Understanding that certain cancers appear to be regulated like this gives us a new avenue to explore in their treatment.”

While this finding is at an early research stage, it holds much promise for the future treatment of early childhood neuroblastomas and other microRNA- induced cancers.

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 nearly 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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