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Suppressing tumour growth via telomerase

By Susan Williamson | Posted in Genetics on 18 July, 2014

Over 90% of cancers express the telomerase enzyme, which is required for their survival, but researchers have had little success in targeting this enzyme to suppress tumour growth - until now.

A recent collaborative study involving Dr Jeremy Henson from the Children's Medical Research Institute at Westmead in Sydney has found that simultaneously suppressing another gene, the cyclin-dependent kinase inhibitor 1A or p21 gene, makes targeting telomerase much more effective.

Telomerase is a specialised reverse transcriptase that maintains telomere length by synthesising and adding DNA sequence repeats to the ends of chromosomes. This noncoding telomere DNA protects the ends of chromosomes preventing the loss of more important coding DNA when a chromosome is copied.

The expression of telomerase distinguishes cancer cells from normal cells. Cancer cells rely on telomerase for their survival because it enables them to bypass normal cellular senescence and continue to divide, to become immortalised. Hence, why this enzyme is such an ideal target for cancer therapies.

Although genetic or pharmacological inhibition of telomerase suppresses the growth of cancer cells, telomerase inhibitors alone have so far failed to provide any significant clinical benefit.

The tumour suppressor protein p53 mediates cellular responses to telomere shortening and telomerase inhibition, effectively preventing cancer. Inhibition of this protein in mice promotes tumour growth.

In this study, researchers showed that loss of the p21 gene, the expression of which is tightly controlled by p53, following telomerase inhibition increases apoptosis in a variety of cancer cell lines and mouse xenografts. The combined genetic or pharmacological inhibition of telomerase and p21 synergistically suppressed tumour growth.

The researchers also found that simultaneous inhibition of telomerase and p21 also suppressed growth of tumours containing mutant p53 when used with therapies that restore the function of mutant p53; thus, identifying a genetic vulnerability that could be exploited to treat tumours containing wild-type or mutant p53.

This study was published in *PNAS*.