Telomeres tell on cancer cells

By Life Scientist Staff | Posted in Genetics on 25 August, 2014

The discovery that the DNA sequence of telomeres in cancer cells is different to normal cells may unravel how these cells maintain their ability to multiply unchecked.

Telomeres are notoriously difficult to read because of their tandemly repeated DNA sequence. Using state-of-the-art whole genome sequencing, Dr Hilda Pickett and colleagues at the Children's Medical Research Institute in Sydney successfully sequenced the DNA of telomeres in normal and cancer cells and found critical differences in particular variant repeat sequences.

In normal cells, telomeres shorten every time a cell divide and naturally shorten with ageing. In cancer cells the opposite can occur - telomere length is maintained, allowing for uncontrolled cell division and tumour growth.

CMRI researchers have been intensively studying telomeres and discovered a process called alternative lengthening of telomeres (ALT), which prevents telomere shortening in about 10% of cancers - including some incurable brain and bone tumours.

The team's latest work builds on these previous results and explains how these variant repeats may cause an ALT.

Cancer cells use one of two possible mechanisms for telomere maintenance. The most common involves activation of the enzyme telomerase, which adds DNA sequence repeats to the telomere region of a chromosome. The other is the ALT pathway, which enables telomere extension.

The researchers observed different patterns and types of variant repeats between cancer cells that use each mechanism.

The researchers have also identified that many of the steps in the ALT process are orchestrated by a molecular mechanism involving a number of different proteins, called the NuRD complex.

They found that one protein, ZNF827, is key to this process and the function of all the proteins in the complex can potentially be disrupted if ZNF827 is obstructed.

New drugs designed to block telomere lengthening in cancer cells are currently in clinical development, and these results have exciting implications for potential new therapeutics aimed at preventing cancer growth.

The study has been published in *Nature Structural & Molecular Biology*.