MedicalXpress

Understanding cancer onset

May 27 2015

Researchers in Malaysia have analysed the genomes of people with a rare genetic disorder to better understand their predisposition to cancer across generations.

Li-Fraumeni Syndrome (LFS) is one of the most variable forms of so-called "familial cancers", in which cancers occur in families more often than one would expect by chance. The development of cancer at an early age in multiple family members may indicate the presence of a gene mutation that increases the risk of cancer. Patients from families with LFS often carry a germ line mutation: a genetic change in the reproductive cells that becomes incorporated into the DNA of every cell in the body of offspring.

One germ line mutation of particular interest occurs in a tumour suppressor gene called TP53, the so-called "guardian of the genome". Normally, this gene repairs DNA and controls a cell's growth and division. A mutation in this gene impairs these functions. Previous studies on LFS have suggested that affected patients develop cancer more rapidly in successive generations, a phenomenon called "genetic anticipation".

To learn more about the genetic basis of LFS and how it occurs across generations, researchers analysed cancer patterns in a large database of LFS relatives and performed whole genome sequencing on 13 people with a family history of LFS across two generations. Professor Hany Ariffin and colleagues from the University of Malaya's Cancer Research Institute conducted the study in collaboration with researchers in France

and the United States.

Using human data and mouse models, the researchers proposed a novel hypothesis, called genetic regression, to explain their findings: germ line TP53 mutation carriers who develop cancer at a late age may have an inherent genetic resistance to early cancer onset. Following from this work, Professor Ariffin and her collaborators will investigate the genetic evolution of primary and secondary cancers in patients with LFS.

Provided by University of Malaya