Medical Xpress

Researchers link cancer to failures in chromosome protection for the first time

March 19 2013

A study published today in the journal *Nature Genetics* explores a new mechanism that may contribute to the development of several tumours, including Chronic Lymphocytic Leukaemia, a type of cancer that affects more than a thousand new patients in Spain each year.

This work, led by researchers Carlos López-Otín, from the University Institute of Oncology at the University of Oviedo; Elías Campo, from the Hospital Clínic/University of Barcelona; and María Blasco, the Director of the Spanish National Cancer Research Centre (CNIO), represents a significant milestone for the Spanish Consortium in the study of the Chronic Lymphocytic Leukaemia Genome.

"Chronic Lymphocytic Leukaemia is the most frequent leukaemia in Western countries," says López-Otín, adding that, "Once the most frequent genetic and epigenetic changes in its development have been decoded, it's necessary to discover the biochemical mechanisms altered by those changes, in order to be able to improve the diagnosis and treatment of this disease."

Thus, continuing the work from previous studies led by Campo and López-Otín published in *Nature* and *Nature Genetics* over the past two years, the researchers concentrated on the mutations affecting POT1, one of the genes involved in the protection of the ends of chromosomes, the telomeres.

This is the first time that a gene with this function has appeared mutated

in a human cancer. Blasco says: "We have been studying telomere biology for a long time, given that alterations in telomere maintenance are associated with cancer and ageing. Although the mechanisms used by tumour cells to alter their telomeres have been identified, POT1 mutations reveal yet another, previously unknown route."

Each chromosome has, at its extremes, in its telomeres, a protective hood made up of proteins, and POT1 is the staple that fixes it in place, joining it to the telomeric DNA. All of the mutations discovered in POT1 prevent this gene from fulfilling its function. The DNA at the end of the chromosome is therefore left without its protective cover. The study of the biochemical pathway that leads from these abnormalities to the uncontrolled growth of B lymphocytes can provide important clues for the understanding of chronic lymphocytic leukaemia and cancer in general.

One of the most frequently mutated genes in leukaemia

Furthermore, after analysing the genome of 341 chronic lymphocytic leukaemia patients —comparing for each case the genes from normal healthy cells with those of tumour cells—, researchers have discovered that POT1 is one of the most frequently mutated genes in this illness.

Prior results from the Spanish Consortium for the study of the Chronic Lymphocytic Leukaemia Genome had already shown that more than a thousand mutations are involved in this disease, and that each patient has a unique combination of hundreds of them. One of the most unexpected findings of the Consortium's studies is the wide genetic and molecular diversity of the disease. The different mutated genes identify relatively small subgroups of patients with diverse disease characteristics. In fact, the most frequently-repeated mutations are only present in 15% of

patients. Despite that, identifying them represents a great advance, because it is a step towards the goal of personalised therapies, adapted to the genetic profile of each individual tumour.

In the study published today, the researchers have found that 3.5% of patients with chronic lymphocytic leukaemia show POT1 mutations, but this figure rises to 9% in a subgroup of patients suffering from an especially aggressive form of the disease. In this way, the study identifies POT1 as one of the most important genes for this disease.

As Campo concludes, "Patients with POT1 mutations belong to the group that has the worst prognosis. Therapeutic intervention affecting this pathway could, therefore, help treat a group of patients whose clinical outcome is currently very poor."

Provided by Centro Nacional de Investigaciones Oncologicas (CNIO)

Citation: Researchers link cancer to failures in chromosome protection for the first time (2013, March 19) retrieved 21 May 2024 from https://medicalxpress.com/news/2013-03-link-cancer-failures-chromosome.html