MedicalXpress

A study shows that 'mosaicism' is gaining ground in cancer research

June 12 2012

A study recently published in *Nature Genetics* provides new evidence that the genetic makeup of the embryo may cause the appearance of tumors in adult life. These results bear out the growing theory that some tumors may have an extremely early origin, tracing to the individual's embryonic development, while offering new clues to understand the genetic causes of certain kinds of cancer, and their prevention and treatment.

Researcher Francisco X. Real, head of the Epithelial Carcinogenesis Group at the Spanish National Cancer Research Centre (CNIO) took part in the study, which was led by Christian Hafner of the University of Regensburg, Germany.

A cell, when it divides, generates two other identical cells with the same characteristics and genetic material. Genetic mutations – alterations in the genes – can occur during the embryo's development, and will then be passed to the daughter cells in the division process. The result is an individual whose cells differ genetically. It has long been suspected that this phenomenon, known as mosaicism, could be linked to several types of cancer, but the scientific community has little information on the genetic alterations that underlie it.

The authors of the paper conducted an exhaustive genetic study of 67 patients with a number of congenital skin lesions leading to tumours (nevus sebaceous, NS). They also studied the Schimmelpenning syndrome (SS), in which tissues like the brain or eye are also affected.

Biopsies of these patients' lesions found for the first time mutations in genes of the RAS family (97% in cases of NS and 100% in SS) which encode proteins of key importance in cell division regulation, while analyses of lesion-free tissues, like cells of the mouth mucous, blood leukocytes, etc. found their gene sequence to be normal. Further, all the patients that developed tumours were also mosaic for this gene family.

The above results, and those of previous studies led by the CNIO group, show that these mutations, which are confined solely to the cells of the affected skin and, as congenital conditions, arise during embryonic development, are the genetic cause of these anomalies and predispose to the formation of tumours.

Analysing the genome of 57,000 people

A complete analysis of the genome of over 57,000 individuals, also published this week in Nature Genetics, lends weight to the theory that mosaicism of distant origin is more widely present in patients with tumours than cancer-free individuals.

This second study drew on the combined efforts of 189 researchers worldwide, including Francisco X. Real and fellow CNIO researcher Núria Malats, head of the Genetic and Molecular Epidemiology Group, under the leadership of scientists at the U.S. National Cancer Institute and Pompeu Fabra University in Barcelona.

It is from this variability in the genetic makeup of cells from the same individual that we get the idea of personal genomes, in the plural. "Some of these mutations imply an increased risk of cancer, so certain patients should have more frequent examination to check how their lesions are progressing," explains Real.