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New Advances in Genetic Studies of Fanconi Anaemia Patients

A consortium of thirty-two researchers worldwide, led by Dr Jordi Surrallés, professor of UAB, genetically and clinically characterised almost all Spanish patients suffering from Franconi anaemia and studies the clinical impact of the mutations. Published online in *Blood*, the journal of the American Society of Hematology, the study describes over 130 pathogenic mutations and the origins and world distribution of some of the most frequent mutations.

Fanconi anaemia is a rare disease affecting one in every 500,000 persons and is characterised by severe anaemia in children, congenital malformations and a high predisposition to cancer. One hundred people in Spain suffer from Fanconi anaemia; 80% of these with mutations in the FANCA gene. In the research, 90% of these patients were studied, as well as patients in Brazil, Mexico, Argentina, Peru, United States, United Kingdom, Portugal, Germany, Pakistan and Nigeria.

The study, led by Dr Jordi Surrallés, professor of the Department of Genetics and Microbiology

and member of the Centre for Biomedical Network Research on Rare Diseases (CIBERER), includes characterisation of over 130 pathogenic mutations in the FANCA gene, present in two of every three cases in almost all of the countries analysed, as well as the study of the origin and world distribution of some of the most frequent mutations. The mutation predominating in Spain and in the rest of countries is an ancestral mutation of Indo-European origin which spread throughout Europe thousands of years ago and which reached America across the Atlantic, producing founder effects in areas such as La Palma, with a high prevalence of the disease, and Brazil, where half of all patients share the same gene mutation.

Finally, researchers analysed the effects of the genetic mutations and their clinical impacts. Results indicate that these mutations provoke the absence or dysfunction of the FANCA protein, which prevent it from reaching the cell nucleus and activating a DNA repair pathway necessary for genomic stability. This in turn brings about cell death - producing anaemia and abnormal tissue functions - or causes them to develop into tumours. For this reason the study of genes involved in Fanconi anaemia is essential to understand the factors which protect the general population from cancer.

Researchers verified that the fact that mutation produces protein absence or dysfunction does not determine the clinical evolution of anaemia or the severity of the malformative syndrome.

Dr Jordi Surrallés highlights the importance of the study carried out given that results will have significant applications in the diagnosis, prognosis and evolution of this rare disease. For example, several of the mutations described in the article served to carry out prenatal and even pre-implant diagnoses followed by the selection of healthy and compatible embryos, with the aim of using blood from the umbilical cord for bone marrow transplants to cure siblings.

Participating in the research were eleven hospitals in Spain and Portugal, two of which are UAB-affiliated hospitals (Sant Pau Hospital and Vall d'Hebron University Hospital) and several national and international research and university centres: CIEMAT (Centre for Energetic, Environmental and Technological Research), CNIO (National Cancer Research Centre), CIBERER, University of Wurzburg, The Rockefeller University, New York, and VU University Medical Center, Amsterdam.

Through its Genome Instability and DNA Repair Group, directed by Dr Jordi Surrallés, UAB has become a worldwide leader in research carried out into Fanconi anaemia. In recent years it has contributed greatly to the further understanding of genetic mechanisms involved in the disease, to the improvement of diagnoses and advances in new therapies, both independently and with the collaboration of institutions such as CIEMAT, CIBERER and CRMB (Centre of Regenerative Medicine in Barcelona).

About Fanconi Anaemia

Fanconi anaemia is a rare hereditary disease which mainly affects the bone marrow and causes it to produce less blood cells. Treatment includes transplanting healthy blood stem cells from the bone marrow or umbilical cord of a compatible donor, if possible, a relative. Unfortunately, few patients can find a healthy and compatible donor.

It is however a crucial disease to biomedical research since it is associated with vital functions such as embryonic development, blood production and genetic predisposition to cancer.

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