

## PRESS RELEASE

## New pharmacological therapies for treating the most aggressive form of porphyria

- Research led by the Center for Cooperative Research in Biosciences seeks to obtain effective methods for changing the stability of the enzyme that causes development of congenital erythropoietic porphyria.
- The research, which has received financial assistance from the multinational pharmaceutical company, Merck Serono, is focused on the use of pharmacological chaperones.

(Bilbao, July 2015).- A research project carried out by the Center for Cooperative Research in Biosciences CIC bioGUNE explores the therapeutic potential of using pharmacological molecules for modifying the activity of enzymes involved in the development of Günter's disease or congenital erythropoietic porphyria (CEP), an extremely aggressive illness which belongs to the group of rare diseases.

This project will have financial support from the multinational pharmaceutical company Merck Serono.

CEP, or Günther's disease, of which there are only 300 known cases throughout the world, is a metabolic pathology caused by the mutation of an enzyme, with symptoms exhibited during the first few months of life.

The first warning sign is red-coloured urine in babies. Patients suffer from extreme sensitivity to sunlight manifested by lesions on the skin which may lead

to epidermal atrophy, scleroderma and the gradual destruction of bone and cartilage.

The study, led by scientist Oscar Millet, aims to develop selective molecules pharmacological chaperones - which enable modulation of the action of uroporphyrinogen III synthase (UROIIIS), the enzyme whose alteration causes this pathology.

The disease occurs because this enzyme participates in the formation of the heme group, a molecular group which performs vital functions for the body such as storing, transporting and setting the oxygen level in the blood, and is also responsible for its red colour.

The generation of this molecular group that is so crucial to life takes place through a process of biosynthesis which occurs due to the intervention of an enzyme chain responsible for transforming some molecules into others until the group is finally created. If any of the enzymes, which function as links in a chain, show any alterations, the whole heme production process will be compromised.

This fact has severe consequences for the body and, depending on the enzyme that has failed in the production chain, may lead to one kind of porphyria or another. Günther's disease is the most serious variant of this family of diseases.

For this reason, the Center for Cooperative Research in Biosciences is focusing its efforts on the screening of thousands of molecules with the aim of isolating those which show activity with the maximum selectivity, that is, that they return stability to the mutated enzyme without affecting other proteins in the body.

The enzyme chain responsible for producing the heme group is like a house of cards. If one of the cards is unstable this will compromise the stability of the entire house. We are searching for pharmacological chaperones in order to restore the mutated enzyme's stability and guarantee that the house "does not fall", explained the expert.

The team, led by Oscar Millet has been working on research into therapeutic methods for eight years in order to combat porphyria and for two years on pharmacological chaperones.

## Funding from Merck Serono

The multinational company Merck Serono, which every year calls for applications for an aid programme for research in various fields, has just granted the financial allocation for the 2015 call for this work, which aims to continue moving forward in the search for therapeutic strategies against porphyria.

## About CIC bioGUNE

The Centre for Cooperative Research in Biosciences CIC bioGUNE, with headquarters in the Bizkaia Science and Technology Park, is a biomedical research organisation that conducts innovative research on the interface between structural, molecular and cell biology, focusing especially on the study of the molecular bases of disease, to be used in the development of new diagnostic methods and advanced therapies.