PRESS RELEASE

Discovered the potential of a DNA regulator in the treatment of liver diseases

- Research led by CIC-BioGUNE has achieved the remission of the biliary cirrhosis phenotype by controlling the activity of an epigenetic regulator.

- The research, in which the University of California (UCLA) took part, was carried out using genetically modified mice.

(Bilbao, July 2015).- Center for Cooperative Research in Biosciences CIC bioGUNE is leading a study which has enabled the discovery of the therapeutic potential of using inhibitors that control the activity of an epigenetic regulator relating to serious liver diseases such as primary biliary cirrhosis, fibrosis or liver cancer.

The study, published by the prestigious journal Hepatology and headed by Doctor in Biology, Mª Luz Martínez Chantar, has found that the use of a natural anti-inflammatory drug, known as parthenolide, manages to keep the activity of histone deacetylase 4 (HDAC4) - a DNA modifier whose dysfunctionality is related to serious liver diseases - under control.

The research, which began a few years ago, has shown that the primary biliary cirrhosis phenotype which damages liver cells and can lead to cancer, disappears in mice when they are treated with parthenolide, an inhibitor under clinical trials which acts on the HDAC4.

The results of this important study have opened the doors to new therapeutic approaches for dealing with diseases of the liver which currently do not have definitive treatments.

Prohibitin 1, a key protein

The starting point of the research is the observation of prohibitin 1, a mitochondrial protein which appears in very low levels in adults with morbid obesity and in patients with various liver conditions.

“Prohibitin levels appear to be diminished in various liver diseases, therefore we think that this was a good model for understanding the development of these illnesses", explains Martínez Chantar.

To carry out the study, Dr. Martínez's team, in collaboration with Dr. José María Mato and Dr. Shelly Lu of the University of California, developed a mouse model from which the prohibitin 1 was eliminated using genetic modification. The animal developed fibrosis and subsequently liver cancer.

The research team tried to discover the mechanisms through which the disease was triggered and observed that the absence of the protein is involved in the loss of control of the activity of HDAC4.

“Prohibitin regulates energy factors such as HDAC4. In healthy patients, prohibitin combines with HDAC4 and prevents alterations of DNA. Whenever this protein disappears, histone deacetylase 4 loses control, begins to act in an aberrant way and incorrectly modifies the genetic code of the liver cells", specified the expert.

Following this finding, treatment was begun on mice with the parthenolide inhibitor in order to block the incorrect activity of HDAC4. The result was that the biliary cirrhosis phenotype remitted.

“The objectives of this research were to find the mechanism by which the prohibitin blocked the activity of HDAC4 and secondly to consider new treatments based on controlling the action of this epigenetic regulator in order to analyse its therapeutic capacity", the scientist added.

The next step is to try to prove the possibilities for carrying out this clinical treatment in patients.

In addition to CIC bioGUNE and the University of California (UCLA), the Hospital de Módena (Italy) and hospitals Clínic of Barcelona and La Paz of Madrid also participated.

About CIC bioGUNE

The Center 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 into the interface

between structural, molecular and cell biology, focusing specifically on the study of the molecular bases of disease, to be used in the development of new diagnostic methods and advanced therapies.

Study references

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