Researchers from CIC bioGUNE identify a risk gene that affects regeneration of the liver

- *This research project was carried out jointly with Keck School of Medicine (U.S.A.) and Vanderbilt University (U.S.A.).*

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Researchers from the Biosciences Co-operative Research Centre, CIC bioGUNE, and the Centre for Networked Biomedical Research into Hepatic and Digestive Diseases (CIBERehd) have discovered that the deficiency of the GNMT gene affects regeneration of the liver and causes uncontrolled proliferation, whilst causing greater susceptibility to liver damage. This discovery was recently published in the prestigious journal 'Hepatology'.

CIC bioGUNE's managing and scientific director, José M Mato, and the manager of Laboratory 2 of the Basque centre's Metabolomics Unit, Mari Luz Martínez Chantar, have found out that a deficiency of the GNMT gene increases the liver's susceptibility to damage caused by toxic agents such as alcohol or certain medicines. Thus GNMT deficiencies are found in steatosis (accumulation of fat in the liver), fibrosis (the stage prior to cirrhosis) and hepatocellular carcinoma (liver cancer).

This contribution to scientific knowledge is the outcome of research done jointly by the scientists from the Keck School of Medicine (U.S.A.), Vanderbilt University (U.S.A.) and CIC bioGUNE. The scientists developed, through genetic modification, a mouse model of GNMT deficiency, which is the gene identified by this team as the one chiefly responsible for hepatic metabolism of the SAMe (also known as *S*-Adenosyl methionine) molecule, whose job is to ensure consistent proliferation of the liver's cells. Controlled regulation of levels of SAMe prevents anomalous proliferation of liver cells, which would lead to the appearance of a tumour.

These results, together with those from an earlier study carried out by the same team and also published in the journal 'Hepatology' in 2008, demonstrate that chronic supraphysiological levels of SAMe alter the functionality of hepatocytes. This has two direct consequences: on the one hand, it causes uncontrolled proliferation of the liver, leading to the development of hepatocellular carcinoma; and on the other hand, this anomalous proliferation prevents the impaired liver from regenerating and makes it more susceptible to damage.