PRESS RELEASE

Research published in the journal *Gastroenterology*

LKB1: Friend or foe?

- *Researchers from CIC bioGUNE have found that LKB1* protein*, which is commonly used to inhibit the* proliferation *of breast, lung and cervical cancers, stimulates the growth of liver cancers in mice.*

- *This discovery may lead to therapeutic applications in the fight against this type of cancer, which is one of the most dangerous and difficult to treat.*

(Bilbao, 10 December 2012).- Researchers from the Metabolomics Unit at CIC bioGUNE, led by Dr. María Luz Martínez Chantar, have discovered that LKB1 protein, which is well known in oncology to inhibit the growth of breast, lung and cervical tumours, has the opposite effect in hepatocellular carcinomas (HCCs), in some cases inducing their malignant transformation in mice.

The study, which was published in the prestigious US journal Gastroenterology lately, has revealed a previously unknown molecular mechanism involved in the development of HCC by showing that the malignancy of this disease may be related to the increased activity of a protein known as liver kinase B1 (LKB1).

As noted by Dr. Martínez Chantar, "in the field of oncology, LKB1 is generally thought to act by inhibiting tumour growth. And this is precisely one of the key discoveries of this research, as in the case of hepatocellular carcinoma, activation of LKB1 appears to stimulate the oncogenic pathways that result in the proliferation of anomalous cells and induce malignant transformation".

HCC, which is responsible for around 90% of all liver cancers, is the fifth most common cancer in the world and the third cause of cancer-related death after lung and gastric cancer. This tumour has a very poor prognosis, even in developed countries, and its incidence is similar to its mortality rate, thus meaning that most patients die within a few months despite recent diagnostic and therapeutic breakthroughs. Furthermore, as it is a very heterogeneous tumour the scientific community has renewed its efforts to establish very precise and personalised therapeutic targets.

Conventional oncological treatment options for HCC are limited as this strongly chemoresistant tumour often develops in cirrhotic livers. Approximately 40% of patients are diagnosed with HCC in an advanced stage and as such have a life expectancy of one year in 29% of cases and two years in 16% of cases.

This cancer is unique in oncology as, despite its high incidence and poor prognosis, until recently there was no effective therapy available. A possible explanation for this fact is the high heterogeneity of the molecular mechanisms involved in the development of this tumour.

“Now we have discovered that LKB1 may play a key role in the development and progress of HCC, our next step will involve a comprehensive study of its potential therapeutic applications”, concludes Martínez Chantar.

Reference of the study:

‘Hepatoma cells from mice deficient in glycine N-methyltransferase have increased RAS signaling and activation of liver kinase B1’

http://www.ncbi.nlm.nih.gov/pubmed/22687285

Martínez-López N, García-Rodríguez JL, Varela-Rey M, Gutiérrez V, Fernández-Ramos D, Beraza N, Aransay AM, Schlangen K, Lozano JJ, Aspichueta P, Luka Z, Wagner C, Evert M, Calvisi DF, Lu SC, Mato JM, Martínez-Chantar ML. Gastroenterology. 2012 Sep;143(3):787-98.e1-13. doi: 10.1053/j.gastro.2012.05.050. Epub 2012 Jun 8.