PRESS RELEASE

“New non-invasive test for fatty liver disease diagnosis developed”

- *Researchers at Biogune, in collaboration with OWL Genomics, CIBERehd and eleven hospitals and research centres from Spain, France and United States, have developed the first metabolome-based serum test for the non-invasive diagnostic of non-alcoholic fatty liver disease or NAFLD*

- *Diagnosis for NASH, an advanced NAFLD disease, is presently done trough a liver biopsy, an invasive, subjective procedure with potential complications*

(Bilbao, May 23th, 2012).- Researchers at Biogune in collaboration with OWL Genomics, CIBERehd and eleven hospitals and research centres from Spain, France and the United States, have developed the first metabolome-based serum test for the non-invasive diagnostic of nonalcoholic fatty liver disease or NAFLD.

NAFLD is a progressive disease that ranges from the simple accumulation of fat (steatosis), to nonalcoholic steatohepatitis or NASH (inflammation around the fat). NAFLD is the most common liver disease in Europe and the United States and its prevalence is increasing in many other parts of the world, such as Asia and India. The prevalence of steatosis and NASH in Western adults is around 30% and 3%, respectively. NASH is the most serious form of NAFLD, about 20% of NASH patients develop cirrhosis in 10 years, and more than one-fourth of these patients group develop hepatocellular carcinoma or HCC (cancer of the liver) in 10 years.

NASH diagnosis is presently done histologically and requires a liver biopsy. Liver biopsy is an invasive, subjective procedure with potential complications (risk of death about 0.01%) and prone to sample error. Imaging techniques, such as MRI and ultrasound imaging (ecography), perform as well as liver biopsy for fat measurement, but cannot distinguish simple steatosis from NASH. Because these limitations of liver biopsy and imaging techniques, NAFLD patients will benefit from this new noninvasive metabolome-based NASH predictor.

The study analyzed 467 biopsied individuals with normal histology (n=90) or diagnosed with NAFLD (steatosis n=246; NASH=131). Analysis of around 700 serum metabolites (including amino acids, glycerolipids, phospholipids, sphingolipids, fatty acids, acyl carnitines and bile acids) was

performed using ultra-performance liquid chromatography coupled to mass spectrometry (UPLC-MS). “The analysis of this massive metabolomic information reveals”, says José Mato from Biogune, “that NAFLD metabolic signature is dependent on the patients’ body-mass index (BMI), indicating that the NAFLD pathogenesis mechanism may be quite different depending on the individual’s level of obesity”.

A BMI-stratified multivariate model based on the NAFLD serum metabolic signatures was generated to separate patients with and without NASH. This metabolome-based NASH predictor, which presently is commercialized by the Basque company OWL Genomics under the trademark *owlliver*, correctly established NASH in 94% of the patients.

- **Metabolomics**

Metabolomics is a branch of “omics” research focused in the high-throughput identification and quantification of small sized (< 1500 Da) compounds. While in other “omics” fields, such as genomics, transcriptomics, and proteomics, thousands of targets are routinely identified and quantified at a time few studies have identified and/or quantified more than 30 metabolites simultaneously. Over 4,600 different compounds (http://www.serummetabolome.ca) have been identified in human serum, of which more than 75% are lipids being the majority phospholipids (over 2,000 different molecular species) and glycerolipids (over 1,000 different triglycerides and diglycerides). Using proprietary technology OWL Genomics, in collaboration with Biogune, has introduced the first in vitro serum based diagnostic for steatosis and NASH.

References for the study:

- *Obesity dependent metabolic signatures associated with nonalcoholic fatty liver disease progression.* Journal of Proteome

J. Barr†, J. Caballería, I. Martínez-Arranz†, A. Domínguez-Díez, C. Alonso, J. Muntané, M. Pérez-Cormenzana, C. García-Monzón, R. Mayo, A. Martín-Duce, M. Romero-Gómez, O. Lo Iacono, J. Tordjman, R. J. Andrade, M. Pérez-Carreras, Y. Le Marchand-Bruste, A. Tran, C. Fernández-Escalante, E. Arévalo, M. García-Unzueta, K. Clement, J. Crespo, P. Gual, M. Gómez-Fleitas, M. L. Martínez-Chantar, A. Castro, S. C. Lu, M. Vázquez-Chantada, and J. M. Mato