J Liver 2016, 5:2(Suppl)
http://dx.doi.org/10.4172/2167-0889.C1.006

p38γ and p38δ reprogram liver metabolism by modulating neutrophil infiltration

Guadalupe Sabio
National Center for Cardiovascular Research, Spain

Nonalcoholic fatty liver disease (NAFLD) is a major health problem and the main cause of liver disease in Western countries. Although NAFLD is strongly associated with obesity and insulin resistance, its pathogenesis remains poorly understood. The disease begins with an excessive accumulation of triglycerides in the liver, which stimulates an inflammatory response. Alternative p38 mitogen-activated kinases (p38γ and p38δ), have been shown to contribute to inflammation in different diseases. Here we demonstrate that p38δ is elevated in livers of obese patients with NAFLD and that mice lacking p38γ/δ in myeloid cells are resistant to diet-induced fatty liver, hepatic triglyceride accumulation and glucose intolerance. This protective effect is due to defective migration of p38γ/δ-deficient neutrophils to the damaged liver. We further show that neutrophil infiltration in wild-type mice contributes to steatosis development by means of inflammation and liver metabolic changes. Therefore, p38γ and p38δ in myeloid cells provide a potential target for NAFLD therapy.

guadalupe.sabio@cnic.es

Genetic polymorphisms of APOBEC3A/B may influence the risk of HBV related HCC via affecting viral mutations: Key steps to interpret cancer Evo-Devo

Guangwen Cao
Second Military Medical University, China

The microenvironment of chronic inflammation promotes the evolution progression of *hepatitis B virus* (HBV) caused hepatocellularcarcinoma (HCC) by facilitating the generation and selection of viral and somatic mutation. We aimed to determine if that the family of apolioprotein B mRNA-editing enzyme catalytic polypeptide 3 (AOBEC3) bridge the chronic inflammation and HCC via inducing mutations. Three key single nuclear polymorphisms (SNPs) of APOBEC3A and B (rs2267401, rs5750717 and rs12628403) were genotyped in 1342 healthy controls, 330 HBV-clearance subjects, and 2846 HBV-positive subjects including 1182 HCC patients. HBV mutations in the previously defined genomic regions were determined by PCR amplification and sequencing. We found that rs2267401 (TG versus TT) significantly decreased HBV persistence. Variant genotypes of rs2267401 (TG+GG or TG versus TT), rs5750717 (all the variant genotypes versus wild type) and rs12628403 (CC versus AA) were associated with a decrease risk of HCC compared with healthy controls. rs5750717 variant genotypes significantly decrease the risk of HCC in the genotype B HBV infected subjects [GG versus AA: adjusted OR, 0.10; 95% CI,0.01-0.77] and the genotype C HBV infected subjects (AG versus AA: Adjusted OR, 0.45; 95% CI 0.28-0.72) compared with HCC free HBV infected subjects. AN rs5750717 were also related with the frequency of HCC telated HBV mutations (A1762T/G1764A). The interaction of rs2267401 variant genotypes with HBV preS1 start codon mutation and preS deletion significantly increased HCC risk in the genotype C HBV infected subjects. Thus, genetic polymorphisms of APOBEC3A/B may contribute to HBV clearance/persistence and affect HCC risk possibly via generating and interacting with the HCC related HBV mutations in Chinese populations.

gcao@smmu.edu.cn