

differentiation and senescence. Specific HBV mutations or distinct HBV genotypes are associated to higher risks factors for HCC or hepatic complications leading to HCC. In summary, active HBV replication potentially disrupts

gene integrity, may lead to oncogenic activation through several parallel mechanism, and the role of each of these mechanism may vary with the molecular diversity of viral genotypes.

Hepatocellular carcinoma (HCC) biomarkers in Colombia

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The hepatocellular carcinoma (HCC) account for 70 to 85% of primary liver cancer worldwide. SouthEast Asia and sub-Saharan Africa represent the areas with the highest incidence; instead Europe and North America correspond to low incidence areas. The data available for Latin American countries show a low incidence (<3.3/100.000 inhabitants) in most of the countries including Colombia. The rate of incidence is <5.6/100.000 in Central America, Peru and Argentina and <10/100.000 in Chile and Brazil.

Major risk factors associated with HCC are chronic Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infection, dietary aflatoxin B1 (AFB1) exposure and intake of alcohol. In fact, alcohol abuse represents a leading cause of cirrhosis, the end-stage liver disease that precedes most cases of HCC.

The prevalence of HBV and HCV infection among cirrhosis and HCC cases varies considerably within and between regions and mirrors the patterns of HBV and HCV endemicity. The World Health Organization estimates that globally, 57% of cirrhosis were attributable to either HBV (30%) or HCV (27%) infection and 78% of HCC was attributable to HBV (53%) or HCV (25%) infection. According to the 2002 worldwide mortality report, approximately 929.000 deaths from cirrhosis (446.000) and HCC (483.000) were likely due to chronic viral hepatitis infections.

In Latin America, 31% of cirrhosis cases were attributable to HBV (8%) and HCV (23%) infection and 64% of HCC cases was attributable to these chronic viral infections (HBV 43%, HCV 21%).

In Colombia, the mortality registry shows 1300 cases of liver tumors per year, which correspond to a rate of inci-

dence of 3.18/100.000 inhabitants. Additionally, there are not data available of HCC cases attributed to each one of the well-recognized risk factors. However this data does not match the number of primary hepatic tumor and cirrhosis cases expected. The prevalence of HBV infection is moderate is most part of the country, but there are some high prevalence regions. The prevalence of HCV infection in general population is unknown but some studies has been described a high prevalence in population at risk. On the other hand, the intake of alcohol beverages in the Colombian population and the evidence of contamination with AFB1 in human and animal food consumption predict a higher rate of incidence of hepatic cirrhosis and HCC cases in this country

Since 2005 we are performing the first biomarkers study in cirrhosis and HCC in Colombia. The first part of the project consisted of a retrospective study of 2000-2004 of cases of HCC diagnosed at 4 hospitals in Bogota, Cali and Medellin. The second one is a cross-sectional study of cirrhosis and HCC at a hospital in Medellin through 2005-2007.

The study will us to determine the frequency of biomarkers corresponding to two main risk factors for cirrhosis and HCC: HBV infection, HCV infection, and a third risk factor for HCC, the AFB1 exposition, in a group of patients from the three principal cities in population, infrastructure, health coverage, and technology of Colombia.

The biomarker of HBV infection (Core Ag (HBcAg)) is being evaluated by immunochemistry in paraffin embedded of HCC cases using the monoclonal antibody (Ab) NCL-HBcAg-506 (Novo-Castra®) and the kit ultravision

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LP detection System HRP Polymer & DAB Plus Chromogen (Lab Vision corporation).

The first assays of biomarker of HCV infection detection were performed by using the human monoclonal Ab anti-Core B12.F8 (gift from Dr. Mario Mondelli, University of Pavia, Italy). However the technique is under standardization and another antibody is being considered.

The evidence of exposition to AFB1 are being assessed by the detection of DNA-AFB1 adducts in HCC paraffin embedded hepatic tissues using the monoclonal antibody 6A10 (kindly donated by Dr. Regina Santella, Columbia University, USA), which recognizes the imidazole ring in the open guanine adduct DNA. The DNA adducts-albumin complexes will also be detected in the serum sample obtained from the patients diagnosed in the period 2005-2007. This detection method corresponds to a competitive ELISA using policlonal antiserum.

Additionally, the mutation in the third base of p53 gene codon 249, associated with exposure to AFB, is being evaluated by PCR of exon 7 p53 and its flanking introns, and by restriction analysis with the enzyme HaeIII.

This study will contribute to the understanding the importance of these three risk factors in hepatic cirrhosis and HCC in a Latin-American country. The results of the study are essential for the instauration of public health policies aimed to reduce the incidence of hepatic cirrhosis and HCC. It will also facilitate the transfer of technology for the implementation of techniques on HCC's risk factors.

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Epidemiology of hepatocellular carcinoma

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INTRODUCTION. The incidence of hepatocellular carcinoma (HCC) has increased both due to the world-

wide increase on the virus C infection and to the increase on the survival rate of patients with chronic liver disease.

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