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Introduction and Objectives: It has been shown that DNA methylation patterns and miRNA levels are effective markers for distinguishing different stages of liver fibrosis in European patients. A liquid biopsy allows the evaluation of ccfDNA methylation levels from hepatocytes damaged by necrosis/apoptosis, releasing degraded genomic DNA into the circulatory system, which reflects the gene changes present in hepatocytes. This study aimed to evaluate the potential association of specific miRNAs and the percentage of DNA methylation of genes linked with fibrosis in liver tissue and liquid biopsy from MEXICAN patients with various degrees of liver fibrosis and its severity.

Materials and Methods: Transjugular liver biopsies and liquid biopsies were collected from 23 patients with sustained viral response to HCV and residual fibrosis. The percentage of methylation in CpG islands of PPARα, gamma and δ gene promoters, as well as TGFβ1 and PDGFα, will be determined by pyrosequencing in DNA extracted from the liver and ccfDNA. Fibrosis was stratified according to Metavir. miR-21, miR-34, miR-122, miR181b, miR192, and miR-200a/b expression was evaluated.

Results: Higher methylation percentages were detected in antifibrotic gene promoters (PPARα and gamma) in patients with more severe degrees of fibrosis (F4), both in tissue and in liquid biopsy. TGFβ1 and PDGFα, profibrogenic genes, showed significant hypomethylation in their promoter regions, indicating hyperactivation. In addition, the overexpression of miRNAs evaluated was associated with the degree of fibrosis and severity.

Conclusions: Epigenetic mechanisms (DNA methylation and microRNA expression) regulate the expression of multiple genes and their measurement can be a biomarker associated with the degree of fibrosis. Liquid biopsy is an effective and accessible method for evaluating the degree of fibrosis in Mexican subjects and for monitoring clinical protocols.

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P- 78 DIETHYINITROSAMINE AND 2-ACETYLAMINOFLUORENE CHRONIC ADMINISTRATION LEADS TO BIOCHEMICAL, HISTOLOGIC AND GENETIC CHANGES RELATED TO HEPATOCELLULAR CARCINOMA IN WISTAR RATS

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Introduction and Objectives: Hepatocellular carcinoma (HCC) is one of the neoplasms with the highest mortality worldwide. The causes of the development of HCC have been related to hepatitis B virus and exposure to aflatoxin B1; however, chronic alcohol use, nonalcoholic fatty liver disease, and hepatitis C virus infection are the most important risk factors for developing HCC. The establishment of animal models of HCC is crucial for both basic and translational studies of hepatocellular carcinoma and is a valuable tool to identify alterations during the progression of the disease. This study aimed to analyze the biochemical, histological, and gene expression alterations produced in a model of chemical hepatocarcinogenesis by the chronic administration of diethylnitrosamine (DEN) and 2-acetylaminofluorene (2-AAF) in Wistar rats.

Materials and Methods: Twelve Wistar rats weighing 180 to 200 g were divided into control and damage groups: rats were treated with DEN (50 mg/kg/wk) i.p and an intragastric dose of 2-AAF (25 mg/kg/wk) for 18 weeks. Serum clinical biochemistry was performed on VITROS Chemistry System 350® equipment. Masson's trichrome and Hematoxylin-Eosin stains were performed on the liver tissue. Relative gene expression was performed by RT-qPCR in LightCycler®96.

Results: The damage group had significant increases in total cholesterol, HDL-C, AST, ALT, ALKP, and GGT. Furthermore, histological analysis showed the loss of normal liver architecture with nuclear pleomorphism in the hepatocytes, atypical mitosis, and fibrous septa distributed between portal triads and collagen fibers through the hepatic sinusoids. The expression of *TGFb1* was significantly increased ($p<0.05$); on the contrary, *ALB*, *CAT* and, *PPARα* were downregulated ($P<0.05$), *CPT1A* was downregulated too but without significance.

Conclusions: Chronic administration of DEN and 2-AAF induces characteristic alterations of hepatocellular carcinoma in Wistar rats. The uncontrolled proliferation of malignant cells requires a constant supply of energy and macromolecules. In this work, cancer cells reprogrammed their fatty acid oxidation pathway by downregulation of *PPARα* and *CPT1A*.

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P- 79 LIVER TRANSPLANTATION FOR HEPATOCELLULAR, LOOKING FOR THE BETTER SELECTION CRITERIA. RESULTS FROM THE URUGUAYAN LIVER TRANSPLANT PROGRAM

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Introduction and Objectives: Liver transplantation (LT) is an established therapeutic in hepatocellular carcinoma (HCC). Since 90' Milan's criteria have been the gold standard for the selection of the best candidate. In the last decade, new expanded criteria have been developed, like UCSF, Up to 7 and AFP Model, with the purpose of achieving a better selection of liver transplant candidates. This study aimed to describe the results of LT for HCC in our center, evaluate different selection criteria, and assess survival.