cadherin and Occludin was observed; conversely, mesenchymal-type features such as N-cadherin and Snail decreased with GDF11 treatment, confirming that this growth factor-induced a mesenchymal to epithelial transition. Furthermore, our group reported the effect of GDF11 in reducing lipid content, especially cholesterol and triglycerides. It was also confirmed that GDF11 reduced mevalonate pathway proteins in Huh7 and Hep3B liver cancer cell lines. Additionally, they reported that GDF11 was able to impair mitochondrial functionality and its structure. Moreover, GDF11 treatment induced an alteration of glycolytic capacity and oxygen consumption rate in these models.

Objectives General: To determine the sensitizing effect of GDF11 in the Hep3B cell line. Specific: To determine the capacity of GDF11 in the reduction of the EC50 of cisplatin.

Methods: We used the HCC cell line Hep3B (ATCC). A 72-h pretreatment with GDF11 or without was performed; then we treated the cells with cisplatin at various concentrations (0, 2.5, 5, 10, 15, 15, 25, 50, and 100 μM), incubated for 48 h, and cell viability assay was performed by crystal violet.

Results: In our experiments, GDF11 has shown an increased sensitivity of Hep3B cells to cisplatin treatment by significantly reducing the mean effective dose (EC50) from 22.26 μM to 8.11 μM this result was observed by crystal violet assay and by light microscopy.

Discussion: Results demonstrate that GDF11 has sensitizing effects against cisplatin treatment on the liver tumor cell line Hep3B. This agrees with previous results of our group where a detrimental impact in liver tumor cells is observed by the GDF11 treatment and contrast with other works where TGF-β family members have chemoresistance effects.

Conclusions: GDF11 pretreatment sensitizes the HCC cell line Hep3B by reducing the cisplatin EC50.

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HGF AND PROTECTIVE ROLL IN THE INTESTINAL COLLATERAL DAMAGE BY A-NAFTILISOTIOCIANATO- INDUCE CHOLESTASIS.

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Introduction and Objectives: he prevalence of cholestasis has been increasing in recent years; The excretion of bile acids via basolateral has been demonstrated to prevent the excessive accumulation in the hepatocyte, and the liver-intestine axis has been seen affected by enterohepatic circulation deregulation. The epithelial permeability loss caused by the tight junction ruptures leads to inflammation and reactive oxygen species (ROS) production. The hepatocyte growth factor is an essential cellular redox regulator and repair growth factor; it has been reported in its relevance in the intestinal mucosa regeneration and proliferative proprieties. This study aims to evaluate the protective effect of HGF in the intestine of animals subjected to cholestatic damage induced by ANIT. Material and methods: Twenty 10-12 weeks-old male CD-1 mice were used. ANIT (60mg/kg) was administrated at the beginning, 24 h later HGF (10 μg/kg) was injected, and 48 h later, the animals were subjected to euthanasia under anesthesia, and serum and intestines were collected. According to the National Institutes of Health of United Stated (NIH) guide, All mice have been cared for and the Norma Oficial Mexicana (NOM), NOM-062-ZOO-1999. The intestinal tissue was fixed and embedded in paraffin for the histological assessment, followed by routine H&E staining. The expression analysis of TNF- alpha, IL-1b and IL.6 were performed by RT-qPCR using a CFX96 Touch thermocycler with 5μg 2x SYBER Green, which included 1000ng of cDNA and 2μl of forward and reverse primers. The protein quantification was evaluated by Western Blot analysis; using 12% polyacrylamide gels, and the primary antibodies for anti-SOD-1, anti-GPx4, anti-Catalase were incubated. Data are presented as the average $\pm$ standard error media (SEM) using GrandPad (Prism 8) software. Variance analysis (ANOVA) was used for the statistical analysis and was considered $p<0.005$ to indicate a statistical significance.

Results and Discussion: Macroscopic changes reveal no apparent effect. Microscopic studies carried out by H&E staining showed a reduction of the intestinal lumen diameter in mice under ANIT treatment compared with Not treated control (NT). Interestingly, ANIT + HGF-treated group showed protective effects preserving lumen and tissue architecture. To corroborate the potential repair effect of HGF treatment to maintain the tissue and thus digestive process, the excreted stool for every group was addressed. The stools excretion level of ANIT- treated mice was significantly reduced compared with the control and co-treated mice. These results indicate that ANIT-cholestasis induce damage in the small intestine. However, results also found a vulnerability in the colon and ileum to cholestasis damage. To determine whether these sections received damage in ANIT- acute cholestasis model, by RT q-PCR, we examined the mRNA expression of inflammatory cytokines, which were increased in ANIT- treatment. By comparison, HGF co-treatment decreases inflammation like the control group. To check if this regulation of inflammation was for the HGF-induced redox regulation we evaluated, the protein expression of SOD-1, GPx4, and catalase. The treatment with HGF increased the expression of antioxidant enzymes of the intestine tissue. These results suggest that the damage in the intestine is supported by the regulation of ROS induced by cholestasis disease.

Conclusion: The current study demonstrated how HGF exerts a protective effect in the intestine triggered by ANIT. This effect seems to be the cellular redox regulation seen in the liver and renal tissue.

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IGFBP-1 TO 7 AS BIOMARKERS IN STAGES OF LIVER FIBROSIS DURING VIRAL HEPATITIS C

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