pro-fibrogenic processes are key in tumor development. On the other hand, Pirfenidone (PFD) has anti-inflammatory and antifibrogenic properties useful to counteract hepatocarcinogenesis; however, the effects of this drug on SIRT1, and histone H3 regulation in this disease are unknown.

The objective this work is evaluate PFD effects on SIRT1 translocation, and histone H3 lysines 9 and 14 (H3K9 and H3K14) deacetylation in an experimental model of HCC.

Materials and Patients: Fischer-344 rats were divided into three groups: CTL: control group, HCC: group damaged with diethylnitrosamine (DEN), 50 mg/kg and 2-aminofluorene (2AAF), 25 mg/kg/p.o. HCC/PFD group: damage group and with PFD (300 mg/kg/day) for 16 weeks. Histological and molecular analyzes were performed evaluating patterns of protein acetylation, fibrosis, and malignancy.

Results: Normal liver architecture is disturbed by dysplastic nodules formation surrounded by extracellular matrix and fibrosis, also an increase in cells with anaplasia and steatotic foci was observed in liver tissues of HCC group. PFD administration was effective to prevent these changes. Immunohistochemistry reveals an overexpression of GPC3 and α-SMA in damage group, which is correlated with malignant degeneration, these responses was prevented by PFD too. Finally, western blots evidence a SIRT1 overexpression in nuclear fraction of PFD group, triggering H3K9 and H3K14 deacetylation, in addition, a decrease in p300 acetylase expression in nuclear fractions. Notably, c-Myc was reduced and p53 increased significantly.

Conclusions: PFD treatment reduces fibrotic and malignant patterns development. Likewise, PFD induces SIRT1 expression and nuclear translocation, and H3K9 and H3K14 deacetylation, decompacting chromatin and possibly increasing tumor suppressor genes expression for example c-MYC. These results demonstrate for the first time the capability of PFD to regulate epigenetic hallmarks on histones.

Ethical statement

All the experiments were carried out in accordance with the guidelines approved by the Ethics, Research and Biosafety committees of the CUCS with approval number CI-03020.

Declaration of interests

None

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Bovine matrix scaffold implanted in rat liver improve regeneration in a partial hepatectomy model.

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Introduction and objectives: Liver transplant is the recommended therapeutic option for advanced liver damage in chronic liver disease. However, the biocompatibility and low donation rates significantly reduce the chances of performing a successful transplant. The use of inert biomaterials such as collagen matrix scaffolds (CMS) has been suggested as a promising option to restore the function of organs, including liver. The objective was to evaluate the biocompatibility and liver restoration after partial hepatectomy and the implant of bovine matrix scaffold in a rat model.

Materials and Patients: Three groups of Wistar rats were evaluated: Sham, Partial hepatectomy (PH) (40%, left lobe) and PH + Collagen Matrix (CM). After surgical procedure the animals were monitored and the exploratory laparoscopy and histological analysis at 14 and 30 days was performed. The liver function was also compared in the three animal groups. The study was approved by the ethics committee of the School of Medicine at the *Universidad Nacional Autónoma de México* (*UNAM*). All procedures were performed according to official Mexican policy (*SAGARPA*, 1999). Our institution fulfills all technical specifications for the production, care, and use of laboratory animals and is certified by national law (*NOM*-062-ZOO-1999).

Results: The biomaterial showed evidence of reabsorption, the animals did not display signs of infection or systemic alterations. Moreover, the histopathological evaluation showed abundant hepatocyte proliferation and angiogenesis near to the site of CM implantation. An incipient inflammation or exacerbate macrophages, Langhans-type, and foreign-body giant cells were observed; these findings strongly suggest not rejection at 30 days. Furthermore, no statistical differences in albumin, bilirubin, cholesterol, triglycerides, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase were observed at day 14 in sham, PH and PH + CM.

Conclusions: Bovine collagen matrix showed great compatibility with the liver and was bioabsorbable. The incorporation of this biomaterial does not interfere with liver function and promotes the proliferation of hepatocytes and vessels, showing typical arrangement of the hepatic parenchyma. The use of the biomaterial could be beneficial to reduce the current limitation of organ transplant.

Ethical statement

This study was approved by the ethics committee of the School of Medicine at the Universidad Nacional Autónoma de México (UNAM). All procedures were performed according to official Mexican policy SAGARPA, 1999). Our institution fulfills all technical specifications for the production, care, and use of laboratory animals and is certified by national law (NOM-062-ZOO-1999).

Declaration of interests

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