Mucin 13 expression is an early indicator of hepatocellular carcinoma development

Malik S[1,2], Sikander M[1,2], Katare DP[3], Mishra S[3], Jain SK[4], Khan P[5], Chauhan SC[1,2], Jaggi M[1,2]

Background: Hepatocellular carcinoma (HCC) has a poor prognosis due to ineffective therapeutic modality and lack of an early marker for diagnosis. Studies show that increased mucin 13 (MUC13) expression as a possible oncogene and predictive biomarker for various cancers has been shown. But its expression and role in the development of HCC is very little known.

Objective: The aim of this study is to investigate the MUC13 expression in chemically induced hepatocellular carcinoma model.

Methodology: Male Wistar rats were subjected to a DEN and 2-Acetylaminofluorene (2-AAF) induced method for the development of hepatocellular carcinoma. Serum and tissues were collected at regular intervals and routinely validated for various stages of liver cancer. On formalin-fixed, paraffin-embedded tissues, immunohistochemistry and in situ hybridization were performed. The molecular interaction of mucin 13 and DEN were also performed using *in silico* analysis.

Results: Histopathological analysis of liver tissues revealed the development of hepatocellular carcinoma with successive stages in chemically induced model HCC. Moreover, biochemical analysis showed a progressive increase in serum ALT, AST, and ALP levels, indicating the development and progression of hepatocellular damage. Notably, mucin 13 expression gradually increased during the progression of hepatocellular carcinoma. The treated group showed an increase in nuclear localization of mucin 13 as compared to the control group. *In situ* hybridization analysis revealed a reduction in *miR*-132 and *miR*-145, both of which are inversely related to mucin 13 expression. Furthermore, molecular docking analysis showed that DEN efficiently binds mucin 13 with high affinity and thus stabilizes it.

Conclusion: These findings suggest that mucin 13 expression is linked to hepatocarcinogenesis and could be used as a candidate biomarker for HCC.