Mucin 13 expression correlates with tumor development in hepatocellular carcinoma

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],

[1]Department of Immunology and Microbiology, School of Medicine, University of Texas Rio Grande Valley, McAllen, TX 78504, USA
[2] South Texas Center of Excellence in Cancer Research, School of Medicine, University of Texas Rio Grande Valley, McAllen TX 78504, USA
[3] Amity Institute of Biotechnology, Amity University, Noida, Uttar Pradesh 201313, India
[4] Department of Biotechnology, Hamdard University, New Delhi, 110062, India
[5] Center for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi 110025, India.

Abstract

Background: Hepatocellular carcinoma (HCC) has a poor prognosis due to ineffective therapeutic modality and lack of early diagnostic marker. Accumulating studies have shown that elevated expression of mucin 13 as potential oncogene and predictive biomarker for various cancer. However, very little is known about its expression and function for development and progression of HCC

Objective: To investigate mucin 13 expression in chemically induced hepatocellular carcinoma model.

Methodology: Diethyl nitrosamine (DEN) and 2-Acetylaminofluorene (2-AAF) induced method was employed for the development of hepatocellular carcinoma in Male Wistar rats. Serum and tissues were collected at regular interval of time and routinely validated for liver cancer stages. Immunohistochemistry and *in situ* hybridization were performed on formalin-fixed, paraffin-embedded tissues. Molecular docking studies were performed to study the interaction of mucin 13 and DEN.

Results: Our results demonstrate hepatocellular adenoma as observed by histopathological analysis. Biochemical analysis showed a progressive increase in the levels of serum ALT, AST and ALP, suggesting the development and progression of hepatocellular damage. Notably, mucin 13 expression gradually elevated during consecutive stages of hepatocellular carcinoma. Interestingly, an increase in nuclear localization of mucin 13 was observed in treated group as compared to control group. *In situ* hybridization analysis showed that a decrease in miR-132 and miR-145, which are inversely related with mucin 13 expression. Moreover, DEN efficiently binds mucin 13 with high affinity and thus stabilize it as demonstrated by molecular docking analysis.

Conclusion: These results suggest that mucin 13 expression is closely associated with hepatocarcinogenesis and could serve as a predictive candidate biomarker for HCC.