tissues of 37 HCC patients (20 MVI+ and 17 MVI-). We also investigated DNA methylation profiles of plasma samples from these 37 HCC patients and 30 normal individuals as controls to minimize the interference of random background DNA methylation signals. Tissue and plasma samples were prepared into DNA methylation library and sequenced on Illumina Hiseq X10 platform. Using methylation haplotype load (MHL) and unmethylation haplotype load (UMHL) as metrics, we quantified DNA methylation profiles on methylation haplotype blocks (MHBs) by computing the degree of linkage between methylated or unmethylated CpGs in HCC and adjacent normal samples to identify discriminatory markers. Grouping samples from our cohort into training and validation sets respectively, we employed two supervised machine learning algorithms, random forest (RF) and support vector machine (SVM) to train and cross-validate binary predictive models.

**Results** Supervised analyses identified 65 MHBs as classifiers for HCC tissues and adjacent normal liver tissues. Both RF- and SVM-built models were highly accurate in classifying HCC and normal liver tissues with AUC no less than 0.98 (AUC: 98%, CI: 97.3% – 98.8% for RF model; AUC: 99.9%, CI: 99.9 – 99.9% for SVM model). We applied the RF-trained classification model to differentiate HCC plasma DNA from those of healthy controls, with AUC of 96% (CI: 95.1% - 96.9%). We further identified 6 MHL-quantified MHBs and 5 UMHL-quantified MHBs as classifiers for MVI- and MVI+ samples. Combining the MHBs’ methylation scores as classifiers and applying RF method, we trained and cross-validated MVI- and MVI+ classification models. We found the AUC of these models is 85.9% (CI: 83.5% – 88.3%).

**Conclusions** These data showed that DNA methylation signatures can provide outstanding diagnostic accuracy for HCC and MVI.

**Methods**

**Results**

Mean body weight gains (approximately 4 g/day) were not significantly different between treatment groups. TAB extract did not affect average daily urine electrolyte concentrations (approximately 200 mg/dL). After 4 weeks, serum alanine aminotransferase levels of the ethanol group were increased nearly fourfold (110±16 IU/L) compared to control values (35±3 IU/L); this effect of ethanol was blocked by TAB extract (60±6 IU/L). Additionally, enteral ethanol caused severe fat accumulation, mild inflammation, and necrosis in the liver; TAB extract significantly blunted these changes. Increases in liver TNFalpha protein levels caused by ethanol were completely blocked by TAB extract. Further, ethanol significantly increased the accumulation of protein adducts of 4-hydroxynonenal, a product of lipid peroxidation serving as an index of oxidative stress; again this was counteracted by the addition of TAB extract.

**Conclusions** The result indicates that the TAB extracts exhibit the antioxidant activity through correction of oxidative stress and validates the traditional use of Terminalia arjuna to prevents early alcohol-induced liver injury.
anti-PD-L1 checkpoint blockade, leading to eradication of large tumor. More importantly, HDAC8 and PD-L1 co-blockade resulted in long-term survival (more than 1 year) with the induction of T cell memory responses.

**Conclusions** Our finding delineates that selective chromatin modifications by HDAC8 can augment the therapeutic efficacy of PD-L1 blockade therapy to fully unleash T cell responses, leading to long-term remission of HCC. This study highlights a new epigenetic target for immune potentiation in HCC, providing a rational combinatorial epigenetic immunotherapy.

**IDDF2019-ABS-0326** EVALUATION OF THE EFFECTS OF THE HYDROALCOHOLIC EXTRACT OF LIV.52 DS ON PARACETAMOL INDUCED LIVER TOXICITY AND OXIDATIVE STRESS IN RATS

Arun Gandhi*, Priya Kakkar. Faculty of Life Sciences, Maharishi Dayanand University, Rohtak, Haryana, India

10.1136/gutjnl-2019-IDDFAbstracts.111

**Background** Oxidative stress induced by toxicants is known to cause various complications in the liver. Herbal drug such as Liv.52 is found to have a hepatoprotective effect. However, the biochemical mechanism involved in the Liv.52 DS mediated protection against toxicity is not well elucidated using suitable in vivo models. Paracetamol causes oxidative stress and dysfunction of the liver.

This study was undertaken to evaluate the effects of the hydroalcoholic extract of Liv.52 DS on some biochemical and histopathological parameters of liver tissue in against paracetamol-induced hepatic damage in rats.

**Methods** Wistar rats were orally administered with 2 g/kg body weight Paracetamol. Vehicle (distilled water) and silymarin (50 mg/kg body weight) was used as the negative and positive control groups, respectively. Paracetamol-administered groups were treated with Liv 52 DS extract (100, 200, and 400 mg/kg). After 15 days of treatment, the blood specimens and liver samples were examined. Alteration in the levels of biochemical markers of hepatic damage like AST, ALT, ALP and lipid peroxides were tested, and phytochemical tests were also performed.

**Results** In Paracetamol-treated group, the levels of serum urea, high-density lipoprotein (HDL), and liver superoxide dismutase (SOD), catalase (CAT), and vitamin C significantly decreased (p<0.05) compared to control. Also, in this group, serum triglyceride (TG), total cholesterol (TC), very low-density lipoprotein cholesterol (VLDL), protein carbonyl (PC), malondialdehyde, tumor necrosis factor-α (TNF-α), and TNF-α gene expression significantly increased (p<0.05) as compared to the control (vehicle-treated rats). Treatment with Liv. 52 DS extract in a significant increase (p<0.05) in CAT, SOD, vitamin C, HDL, and a significant decrease (p<0.05) in the level of urea, MDA, PC, TG, TC, VLDL, TNF-α protein, and the gene expression of TNF-α compared with the test without treatment group. Histopathological evidence demonstrated that treatment with Liv.52 DS extract could decrease liver lymphocyte infiltration.

**Conclusions** The present study suggests that Liv. 52 DS extract possesses hepatoprotective activity. It could be an effective and promising preventive agent against Paracetamol-induced hepatotoxicity.

**IDDF2019-ABS-0334** CLINICAL ESCHERICHIA COLI NF73–1 ISOLATED FROM A PATIENT WITH NONALCOHOLIC STEATOHEPATITIS INDUCES LIVER INJURY THROUGH IMPAIRING INTESTINAL BARRIER FUNCTION AND INDUCING INFLAMMATORY RESPONSES OF HEPATOCYTES

Yang Song*, Zhe Wu, Jun Xu, Yujing Chi, Yifan Zhang, Yulan Liu. Peking University People’s Hospital, China

10.1136/gutjnl-2019-IDDFAbstracts.112

**Background** Gut microbiota plays critical roles in nonalcoholic fatty liver disease (NAFLD). We have previously isolated and identified one clinical Escherichia coli (E. coli) strain from the intestinal mucosa of a nonalcoholic steatohepatitis (NASH) patient, and named it as E. coli NF73-1. Our aim is to investigate the role of E. coli NF73-1 in the development of NAFLD in a high-fat diet (HFD) mice.

**Methods** Conventional (CV) mice, plus mice treated with antibiotics (AB) to deplete gut microbiota, were fed with HFD for 12 weeks. At the 10th week, mice were treated daily with oral gavage of LB, live-NF73-1, or pasteurized-NF73-1 (pas-NF73-1) for 2 weeks. AB mice were treated in drinking water containing 1 g/L ampicillin, 500 mg/L vancomycin, 1 g/L neomycin, and 1 g/L metronidazole for 4 weeks, starting at 6th week. In vitro bacterial translocation and transepithelial permeability assay was performed. Primary hepatocytes from NAFLD mice were cocultured with NF73-1 to evaluate inflammatory responses.

**Results** Live-NF73-1 group developed severer liver pathology than LB and pas-NF73-1 groups in both CV and AB mice, verified by increased NAFLD activity (NAS) score. Besides, intestinal permeability was higher in live-NF73-1 group than that in LB and pas-NF73-1 groups of both CV and AB mice, supported by decreased expression of ZO-1 and Occludin in the colon. In vitro bacterial translocation and transepithelial permeability assay indicated that HT-29 cells treated with live-NF73-1 developed a higher concentration of translocated bacteria and FITC fluorescein than LB and pas-NF73-1 groups. Interestingly, live-NF73-1 decreased mRNA levels of ZO-1, Occludin and Claudin2 in Caco2 cells, and downregulated mRNA expression of Claudin2 and E-cadherin in HT-29 cells compared with LB and pas-NF73-1 groups. NF73-1 also induced inflammatory responses of primary hepatocytes, supported by increased IL-6 expression.

**Conclusions** Clinical E. coli NF73-1 aggravates liver injury in NAFLD mice, through impaired intestinal integrity and inflammatory responses in hepatocytes. These findings provide new insights on management using specific bacterial strain.

**Clinical Gastroenterology**

**IDDF2019-ABS-0013** CELIAC CRISIS IN AN ADULT TYPE 1 DIABETES MELLITUS PATIENT PRESENTING WITH DIARRHEA, WEIGHT LOSS AND HYPOGLYCEMIC ATTACKS- A RARE ENTITY

Shivam Shivaum*, Pratibha Nadig, Vijaya Sarathi, Manohar KN. Vidyarthi Institute of Medical Sciences and Research Centre, India

10.1136/gutjnl-2019-IDDFAbstracts.113

**Background** Type 1 diabetes mellitus (T1DM) is an autoimmune disease, characterized by loss of insulin-producing beta