Background Hepatocellular carcinoma (HCC) has become a prominent global health threat due to its occurrence, lethality and dismal survival rates. Increasing prevalence of obesity and diabetes-induced non-alcoholic fatty liver disease (NAFLD) and metabolic syndromes have been found culpable for the rise of HCC initiation, via disruption of liver microenvironment. Super enhancers, which are characterised by high density of transcription binding sites, high-level transcription regulation and response to external stimulation, determine cell fate during oncogenesis. Master transcription factors translate microenvironmental changes into super enhancer remodelling and activation, which subsequently changes the gene expression profile and define cell identity. This project aims at profiling the super enhancer status in the context of NAFLD-associated HCC and to unveil the master transcription factors responsible for diet-induced HCC progression.

Methods Nanoscale chromatin immunoprecipitation sequencing (nano ChIP-seq) against histone marks H3K27ac, H3K4me1 and H3K4me3 in 6 pairs of primary human NAFLD-HCC tumours and their adjacent non-tumour tissues revealed potential oncogenic super enhancers. Global mRNA expression was detected by RNA sequencing (RNA-seq) to support the enhancer-target gene transcription axis. Master transcription factor regulation of NAFLD-HCC super-enhancers was further supported by integrated bioinformatics analysis, including motif enrichment and signature transcription factor discovery. ChIP-seq data for the master transcription factors in HepG2 cells confirmed their occupancies on super enhancers controlling key oncogenic pathways.

Results Tumor-enabling super enhancers (averaged 553 and 484 per HCC tumour and non-tumour tissue, respectively) were profiled in primary human NAFLD-HCC tissues, and master transcription factors showed significant binding to NAFLD-HCC oncogenic super enhancers. Interestingly, tumor-enabling super enhancers co-bound by HCC-specific master transcription factors target critical genes involved in hepatic inflammation and NAFLD pathogenesis.

Conclusions Integrated analysis of chromatin profiling and transcriptome in primary human tissues provides insights into the trans-regulatory network involving oncogenic super enhancers and master transcription factors during the pathogenic process of metabolic syndrome-associated HCC.

Acknowledgement This work is supported by the RGC CRF (C4017-14G).

IDDF2018-ABS-0229

ENHANCING THE EFFICACY OF LIVER CANCER IMMUNOTHERAPY BY SPECIFIC INHIBITION OF HISTONE DEACETYLASE 8

¹Yu Feng*, ¹Weiqin Yang, ¹Jingying Zhou, ²Hanyong Sun, ²Stephen L Chan, ³Zhiwei Chen, ⁴Ka-Fai To, ¹Alfred Sze-Lok Cheng. ¹School of Biomedical Sciences, The Chinese University of Hong Kong, Hong Kong; ²Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong; ³AIDS Institute, The University of Hong Kong, Hong Kong; ⁴Theresa Chow Centre for Gastrointestinal Cancer, The Chinese University of Hong Kong, Hong Kong

10.1136/gutjnl-2018-IDDFbestabstracts.8

Background Recent clinical trials of inhibition of immune-checkpoints, programmed death-ligand 1 (PD-L1)/PD-1 axis, which elicits anti-tumour T-cell responses in various cancers, have also produced durable efficacy in a fraction of patients with advanced hepatocellular carcinoma (HCC). The heterogeneous responses to immune-checkpoint blockade therapy result from the

complicated interplay between cancer-cell-autonomous cues and the immunosuppressive tumour microenvironment. Our previous epigenomics and functional analysis have elucidated an oncogenic role of histone deacetylase 8 (HDAC8) in hepatic carcinogenesis (*Cancer Research* 2015;75:4803–16). In this study, we aimed to investigate the therapeutic potential of an HDAC8-specific inhibitor PCI-34051 in preclinical HCC model.

Methods To investigate the immune-modulatory and anti-tumour effects of PCI-34051, we established an orthotopic HCC mouse model via intrahepatic implantation of syngeneic Hepa1–6 hepatoma cells in immunocompetent C57BL/6 and immunodeficient nude mice. The mice have been treated with vehicle, PCI-34051, anti-PD-L1 antibody, or combined therapy for 2 weeks. The tumorigenicity was assessed by *in vivo* imaging and correlated with immune profiling.

Results We demonstrated that PCI-34051 significantly reduced HCC tumorigenicity in C57BL/6 ($p < 0.01$) but not nude mice. Immune profiling revealed a specific reduction in tumor-infiltrating regulatory T cells (Tregs; $p < 0.05$), associated with significant increase in CD8+T cells ($p < 0.05$). The functional significance of Tregs was demonstrated by adoptive transfer, which completely abrogated PCI-34051-induced tumour growth inhibition. Notably, PCI-34051 treatment significantly enhanced the efficacy of anti-PD-L1 therapy ($p < 0.01$). More importantly, combined PCI-34051 and anti-PD-L1 treatment resulted in complete tumour eradication in all co-treated mice, which exhibited significantly better survival rate than single treatment groups ($p < 0.05$). Moreover, the combination therapy promoted long-term survival (> 300 days), which was associated with elevated CD8+T memory cells.

Conclusions Our data suggest that selective chromatin modifications by HDAC8 alter the tumour immune surveillance program and demonstrate the potential of rational combinatorial epigenetic immunotherapy to fully unleash T-cell responses, leading to long-term remission of HCC.

IDDF2018-ABS-0245

HONEY SUPPLEMENTATION AMELIORATES ADIPOCYTOKINES AND HEPATOTOXICITY INDUCED BY HIGH FAT DIET ON MALE RATS

¹Suhana Samat*, ¹Francis Kanyan Enchang, ¹Zolkapli Eshak, ²Wan Iryani Wan Ismail. ¹Universiti Teknologi MARA (UITM), Puncak Alam Campus, Selangor, Malaysia; ²Universiti Malaysia Terengganu (UMT), Kuala Terengganu, Terengganu, Malaysia

10.1136/gutjnl-2018-IDDFbestabstracts.9

Background Nowadays, obesity has become a serious problem worldwide and the cause of many diseases. Honey has been used since the dawn of human civilization contains various ingredients that contribute to its medicinal properties and health-beneficial effects. For this reason, honey could be considered as a potential traditional remedy for various illnesses plaguing mankind. This study was conducted to investigate the protective role of honey supplementation in modulating the hepatic damage and obesity biomarkers associated with obesity on *in vivo* model.

Methods Animals were induced obesity by feeding high-fat diet for eight weeks. Then, they were divided into different groups which received normal diet (NC); fed with high-fat diet (HFD) alone or with the treatment of Acacia (HFDAC) or pineapple honey (HFDPH) or orlistat (HFDO). Before and after treatment, the blood samples were collected for assessment of adipocytokines biomarkers (adiponectin, resistin and leptin), lipid profiles (total cholesterol (TC), triglycerides (TG),

high and low density lipoprotein (HDL and LDL) and liver function profiles (Alanine aminotransferase (ALT), alkaline phosphatase (ALP) and Aspartate aminotransferase (AST)). Hepatoprotective activity, Hepatosomic Index (HI) and histopathological changes in liver tissues were also evaluated.

Results Animals administered with honey showed significant ($p<0.05$) decrease on TC, TG, LDL and significant increase ($p<0.05$) of HDL when compared to HFD. Interestingly, honey supplementation exhibited a hepatoprotective effects as indicated by reduced ALT and AST levels and HI index. Adipocytokines were markedly ameliorated in HFDPH compared to HFD. Adiponectin levels significantly increased in HFDAH and HFDPH (8.13 and 8.22 $\mu\text{g/mL}$ respectively) compared to HFDO (6.07 $\mu\text{g/mL}$). Leptin level ($p<0.05$) decreased from 8.08 to 5.68 ng/mL for the HFDPH compared to HFD. Histopathological changes were observed in the liver tissue of HFD and HFDO treated group. The honey supplementation restored all the biochemical parameters significantly ($p<0.05$), especially the liver function parameters and histopathological changes when compared to HFD or orlistat.

Conclusions In conclusion, honey supplementation has positive effects on modulating several biochemical pathways of adipocytokine excretions, lipid profiles as well as hepatoprotective which may potentially be applicable for suppression of obesity and its metabolic complications.

Clinical Gastroenterology

IDDF2018-ABS-0026 PERSISTENCE AND ADHERENCE OF ANTI-TUMOUR NECROSIS FACTOR (TNF) BIOLOGICS FOR INFLAMMATORY BOWEL DISEASE (IBD) IN AUSTRALIA

¹Li-Chin Wang*, ²Rupert Leong. ¹Faculty of Medicine, University of Sydney, Australia; ²Concord Repatriation Hospital, Gastroenterology and Liver Services, Australia

10.1136/gutjnl-2018-IDDFbestabstracts.10

Background Infliximab (IFX) and adalimumab (ADA) induce and sustain IBD clinical remission, but their adherence and persistence are yet to be characterised in the Australian population. These markers are surrogates for treatment efficacy and determinants of cost-effectiveness. We analysed real-world dispensing of IFX and ADA for IBD in Australia using national Pharmaceutical Benefits Scheme (PBS) data.

Methods 10 year national PBS data obtained (2005–2015). Non-persistence defined as no ADA and IFX prescriptions for 6 and 7 months respectively. Kaplan-Meier analysis conducted with Cox regression adjusting for age, gender and state. Adherence defined as mean possession ratio (MPR) >0.8 , with yearly MPR and Chi-squared analysis. Initiation and maintenance phases determined by PBS codes with dose-intervals corrected.

Results Persistence for IFX and ADA: 77% and 79% (6 months), 68% and 69% (12 months), and 50% and 52% (3 years) respectively (IDDF2018-ABS-0026 Figure 1. Kaplan meier curve of persistence for ifx-and ada); no statistical differences in persistence observed (hazard ratio [HR]: 1.03, 95% CI: 0.75–1.43, $p=0.84$, table 1). Those younger than 20 (HR: 2.08, 95% CI: 1.15–3.74, $p=0.02$) and older than 61 (HR: 1.99, 95% CI: 1.11–3.59, $p=0.02$) had double discontinuation risks than reference age (41–50). Patients in Victoria had greater persistence than New South Wales (HR: 0.65,

95% CI: 0.43–0.99, $p=0.04$). Maximal discontinuation within first 1–6 months (IFX 23%, ADA 17%). IFX had higher MPR than ADA (IDDF2018-ABS-0026 Figure 2. Mean yearly mpr for ifx and ada): year 1: 0.92, 0.79 ($p<0.001$); year 2: 0.93, 0.86 ($p=0.012$), year 3: 0.99, 0.94 ($p=0.047$). 65% and 84% of patients were adherent for ADA and IFX respectively ($p<0.001$); differences driven by initiation therapy.

Abstract IDDF2018-ABS-0026 Table 1 Cox Regression Analysis for Persistence P 0–05

	Univariate analysis	Multivariate analysis
IFX (ref= ADA)	HR 1.03 (0.75–1.43)	HR 1.03 (0.74–1.44)
Male (ref= F)	HR 1.24 (0.90–1.72)	HR 1.18 (0.85–1.64)
Age (ref 41– 50)		
0– 20	HR 2.08 (1.15 –3.74) *	<30: HR 1.47 (0.92–2.36)
21– 30	HR 1.41 (0.86–2.32)	
31– 40	HR 1.31 (0.77–2.23)	HR 1.28 (0.75–2.19)
41– 50	1	1
51– 60	HR 1.53 (0.79–2.94)	HR 1.47 (0.76–2.85)
61+	HR 1.99 (1.11 –3.59) *	HR 1.95 (1.08 –3.52) *

Conclusions Persistence and adherence for anti-TNFs among Australian IBD sufferers are suboptimal, with better adherence for IFX than ADA. There was comparable persistence between the biologics, with poorer persistence in the elderly suggesting its use as bridging therapy for surgery to avoid long-term immunosuppression. Discontinuation was determined by the first six months, with geographical heterogeneity identified. Personalised interventions should be developed to improve adherence through anti-TNF selection, education, empowerment and follow-up.

IDDF2018-ABS-0041 STRUCTURAL CHANGES IN THE HUMAN GUT MICROBIOME FOLLOWING TRIPLE THERAPY USING A POTASSIUM-COMPETITIVE ACID BLOCKER IN HELICOBACTER PYLORI-INFECTED JUNIOR HIGH-SCHOOL STUDENTS

¹Takuji Gotoda*, ²Chika Takano, ¹Chika Kusano, ¹Sho Suzuki, ¹Hisatomo Ikehara, ³Satoshi Hayakawa, ⁴Akira Andoh. ¹Division of Gastroenterology and Hepatology, Department of Medicine, Nihon University School of Medicine, Japan; ²Department of Pediatrics and Child Health, Nihon University School of Medicine, Japan; ³Division of Microbiology, Department of Pathology and Microbiology, Nihon University School of Medicine, Japan; ⁴Division of Gastroenterology, Department of Medicine, Shiga University of Medical Science, Japan

10.1136/gutjnl-2018-IDDFbestabstracts.11

Background *Helicobacter pylori* eradication is imperative to prevent gastric cancer before the development of gastric atrophy and/or intestinal metaplasia. However, there is no clear consensus on the optimal age for *H. pylori* eradication, and changes in the gut microbiota after eradication and their potential future impacts remain unknown. Our aim was to assess gut microbiome changes after *H. pylori* eradication in children.

Methods Changes in the gut microbiota before and after *H. pylori* eradication was prospectively investigated in 8 students without any underlying diseases by 16 s rRNA genes using next-generation sequencing. A total of 24 stool samples were collected, and operational taxonomic unit analysis was performed. As secondary analyses, alpha and beta diversity were