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 533 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.

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Clinical Gastroenterology

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

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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.

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

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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 16s 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...