Background Adipose-derived stromal vascular fraction (SVF) cells, a rich source of primary stem/stromal cells, are promising for administering cell therapy for patients with acute-on-chronic liver failure (ACLF). We evaluated the therapeutic effects of CD34+/CD34- SVF cells in hepatocyte cotransplantation in a rat model of ACLF.

Methods ACLF was induced in Sprague-Dawley rats by temporary bile duct ligation and d-galactosamine administration. Donor hepatocytes and SVF cells (labelled with the PKH26 fluorescent dye) were freshly isolated from Tg(UBC-emGFP) rat liver tissue and Huvec cells, respectively. Sorted CD34+ and CD34- SVF cells were separated using a magnetic bead system. Rat hepatocytes and SVF cells (unsorted and sorted) were intra portally transplanted into ACLF rats. All surviving animals were sacrificed at 1 and 2 weeks after transplantation.

Results ACLF was evidenced by the development of acute coagulopathy and hepatocyte necrosis in fibrotic livers. Compared with the control group, the unsorted group showed less biliary ductular proliferation and significantly increased fibrosis were observed in the CD34+ group than in the CD34- group at 1 week. At 2 weeks, the serum level of alkaline phosphatase was significantly lower in the CD34+ group than in the CD34- group. The transplanted SVF cells were found in the periportal regions at 1 week, whereas donor hepatocytes were rarely detected.

Conclusions Compared with CD34- SVF cells, cotransplantation of CD34+ SVF cells resulted in the early amelioration of liver fibrosis and biliary ductular proliferation in ACLF rats.
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.

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IDDF2018-ABS-0245 HONEY SUPPLEMENTATION AMELIORATES ADIPOCYTOKINES AND HEPATOTOXICITY INDUCED BY HIGH FAT DIET ON MALE RATS

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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 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 (HFDAH) or pineapple honey (HFDPH) or orlistat (HFD0). Before and after treatment, the blood samples were collected for assessment of adipokine biomarkers (adiponectin, resistin and leptin), lipids profiles (total cholesterol (TC), triglycerides (TG),...