Background Primary hepatocellular carcinoma (HCC) is one of the most common malignancies all over the world. However, the mechanism of HCC initiation and development remains unclear. In our previous work, high-throughput microarray assay in HCC samples followed by bioinformatic analysis suggested that Metallothionein1G (MT1G) might be one of the key factors in HCC. In this study, we aim to clarify the biological function of MT1G and validate its potential to be utilised as a biomarker in HCC.

Methods We detected the MT1G expression in paired HCC samples and cell lines by both RT-qPCR and Western blot. MSP (Methylation specific PCR) and BGS (Bisulfite genomic sequencing) were performed to evaluate methylation status of MT1G in HCC. TCGA (The Cancer Genome Atlas) data analysis was used to validate the results from our samples. The functional significance of MT1G was investigated by overexpression or knockdown *in vivo* and *in vitro*. Kaplan-Meier survival analysis was performed using TCGA data to estimate the clinical value of MT1G expression and methylation status in HCC.

Results MT1G was inactivated in 4 of 6 HCC cell lines. The expression of MT1G was downregulated in cancer tissues compared with the adjacent non-tumour tissues ($p < 0.001$). The gene expression of MT1G was closely correlated to the promoter methylation status. The MT1G expression in silenced HCC cell lines could be restored by demethylation agent. Ectopic re-expression of MT1G by stable transfection in SMMC7721 and Hep3B cells inhibited colony formation ($p < 0.001$), suppressed cell motility and invasiveness ($p < 0.05$), accompanying with up-regulation of E-cadherin; and down-regulation of PCNA, MMP2, MMP13 and Vimentin. Xenograft tumour assay in nude mice also revealed that MT1G could markedly decrease tumour weights and volumes *in vivo* ($p < 0.001$). Survival analysis revealed that hypermethylation of MT1G predicts good outcomes of HCC patients.

Conclusions Our results demonstrate that MT1G promoter methylation directly mediates the transcription down-regulation and commonly occurs in HCC. MT1G gene can act as a functional tumour suppressor in liver carcinogenesis by playing an important role in the depression of cell proliferation, migration and invasion.

IDDF2018-ABS-0140 THE CROSSTALK OF MTORC1 AND DNA METHYLATION IN HEPATOCELLULAR CARCINOMA

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10.1136/gutjnl-2018-IDDFabstracts.51

Background Metabolic reprogramming in cancer cells is likely to interact with the epigenetic landmarks, which may modulate tumorigenesis. However, the exact mechanism is still largely unknown. In our previous study, inhibition of activity of mechanistic target of rapamycin (mTORC1), a nutrient sensor that affects cellular metabolism, was able to attenuate the DNA methylation level. In this study, we aim to clarify the correlation between the metabolism and DNA methylation and evaluate their interactive roles in the pathogenesis of hepatocellular carcinoma (HCC).

Methods We treated HCC cell lines with rapamycin to inhibit mTORC1 activity and performed immunofluorescence (IF) and Enzyme-linked immune sorbent assay (ELISA) to detect the

levels of 5-methylcytosine (5-mC). Western-blot and IF assays were used to detect the protein levels of DNA methyltransferases (DNMTs) and RT-PCR was performed to test transcription of DNMTs. Cycloheximide was used to suppress the protein translation. Moreover, MG132 and BafA1 were used to inhibit the functions of ubiquitin-proteasome and autophagy-lysosome respectively to evaluate the effect of posttranslational modification for DNMTs degradation. Finally, we selected twenty liver cancer cell lines and combined western-blot and CCK8 assays to observe the association between mTORC1 inhibition-induced DNMTs degradation and cell viabilities.

Results Rapamycin treatment reduced 5 mC levels in HCC cell lines. In parallel, mTORC1 inhibition attenuated the expressions of DNMT1. The subsequent experiments revealed that transcriptional regulation and posttranslational modification is not likely to participate in the process of DNMT1 degradation induced by mTORC1 inhibition. However, cycloheximide half-life assay indicated that mTORC1 might adjust the expression DNMT1 through regulating initial translational efficiency. We found that mTORC1-mediated DNMT1 degradation is closely linked to cell proliferation.

Conclusions In conclusion, we demonstrated that mTORC1 could affect DNA methylation levels in HCC probably through regulating DNMTs expression. Besides, this interactive role seems to be closely linked to HCC cell viability. Investigation of the relationship between mTORC1 signalling and DNA methylation will deepen our insight on the pathogenesis of HCC and develop a novel therapeutic strategy for HCC patients.

IDDF2018-ABS-0165 CIRCULAR RNA CIRC5379-6 PERFORMS FUNCTIONS IN INHIBITING TUMORIGENESIS AND METASTASIS OF HEPATOCELLULAR CARCINOMA VIA THE REGULATION OF PPAR α

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10.1136/gutjnl-2018-IDDFabstracts.52

Background Circular RNAs (circRNAs) are considered as RNA molecules in loop structure and was reported as a potential novel biomarker for hepatocellular carcinoma (HCC). Peroxisome proliferator-activated receptor alpha (PPAR α) is a suppressor of HCC via direct targeting nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha (I κ B α) and nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) signalling pathway according to our previous study, whereas their relationship in the modulation of pathogenesis processes in HCC is still unclear. The aim of this study was to determine the circRNAs those perform functions in regulating the gene PPAR α and thereby regulate the pathogenesis processes in HCC.

Methods The candidate circRNAs were firstly validated in structure via the RNase R treatment, amplification of specific convergent and divergent primers, and Sanger sequencing. After over-expressing the circRNAs in HCC cell lines and further validation of the cell viability assay, the circRNA correlated to PPAR α was obtained. Functional analysis of the

candidate circRNA was performed *in vitro* and *in vivo*, including cell viability assay, colony formation assay, cell cycle analysis, apoptosis array and Matrigel migration and invasion assay. Differences between experimental groups and control groups were analysed using the paired t-test and Wilcoxon test.

Results Of the seven-candidate circRNAs, Circ5379-6 was verified to be correlated positively to PPAR α . Overexpression of circ5379-6 lead to up-regulation of PPAR α and it thereby suppressed the cell proliferation, inhibited the cell migration and invasion. The most obvious effect of circ5379-6 expression should be the induction of cell apoptosis in the HCC cell lines. Matrix metalloprotein 9 (MMP-9) was down-regulated expressed while Vimentin, N-Cadherin and E-Cadherin were up-regulated expressed in the tumour generated by the cells with circ5379-6 overexpression. Furthermore, the overexpression of circ5379-6 effectively inhibited the tumorigenesis and metastasis of HCC according to the *in vivo* studies in nude mice.

Conclusions Circ5379-6 acts as an effective tumour inhibitor of HCC via regulating the level of PPAR α . It suggests that induction of Circ5379-6 expression may utilise as a potential therapeutic method for HCC.

IDDF2018-ABS-0210 POKEMON OVER-EXPRESSION ACCELERATES THE PROGRESSION OF NAFLD VIA INCREASING LIPID DROPLET DEPOSIT IN HEPATOCYTE

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10.1136/gutjnl-2018-IDDFabstracts.53

Background Non-alcoholic fatty liver disease (NAFLD) is considered as the hepatic manifestation of metabolic syndrome and is characterised by the accumulation of lipid droplets. Pokemon (FBI-1/ZATB7A) is an important proto-oncogene which is involved in cancer development and adipogenic gene expression. The aim of our study is to explore the role of Pokemon in the development and progression of NAFLD.

Methods C57BL/6 mice were fed with normal chow (NC) or high-fat diet (HFD) for 16 weeks to induce NAFLD. Pokemon mRNA and protein were detected by RT-PCR and Western-blot as well as immunohistochemistry. NAFLD cell models were established by oleic acid, and si-Pokemon hepatic cancer cell lines were also constructed by plko lentiviral system.

Results Mice fed with HFD for 16 weeks showed increased body weight, liver weight, liver-to-body weight ratio as well as increased lipid accumulation as shown by H and E staining and Oil Red O staining consistent with the establishment of NAFLD. The Pokemon mRNA as determined by RT-PCR and protein expression as determined by Western blot and immunohistochemistry were significantly increased in mice fed with HFD compared with the NC group ($p < 0.01$). The upregulated Pokemon was accompanied by increased serum TNF- α , IL-6, triglyceride, cholesterol and MDA levels in HFD group ($p < 0.01$). For *in vitro* study, Pokemon and SREBP-1 protein expression in HepG2 were increased in a concentration-dependent manner when treated with oleic acid ($p < 0.01$). SREBP-1 and FAS mRNA expression were also increased which could be counteracted by pokemon silencing. Knock-down pokemon by si RNA in HepG2 cells showed decreased lipid accumulation, triglyceride content, suppressed mRNA expression of lipogenic genes including FASN, SREBP, SCD-1,

HMGCR and genes related with oxidation metabolism including Cpt1 and Acadm.

Conclusions Pokemon promotes NAFLD progression via increasing lipid accumulation and repressing free acids oxidation.

IDDF2018-ABS-0216 ANTIDIABETIC EFFECTS OF SODIUM ORTHOVANADATE AND TRIGONELLA FOENUM GRAECUM SEED POWDER IN LIVER OF RAT MODEL

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10.1136/gutjnl-2018-IDDFabstracts.54

Background Diabetes has been considered as one of the fastest growing epidemic worldwide; the number of people with diabetes is estimated to increase from 381.8 million in 2013 to 591.9 million in 2030. Oxidative stress in diabetic tissues is accompanied by high level of free radicals and the simultaneously declined antioxidant enzymes status leading to cell membrane damage. In the present study, the effect of sodium orthovanadate (SOV) and Trigonella foenum graecum seed powder (TSP) administration has been studied on blood glucose and insulin levels, antioxidant enzymes, lipid peroxidation, lipofuscin and DNA degradation, distribution of glucose transporter (glut 2, glut4) in liver tissues of the alloxan-induced diabetic rats and to see whether the treatment with SOV and TSP is capable of reversing these effects.

Materials and methods Diabetes was induced by administration of alloxan monohydrate (15 mg/100 gm b.wt.) and rats were treated with 2IU insulin, 0.6 mg/ml SOV, 5% TSP in the diet and a combination of 0.2 mg/ml SOV with 5% TSP separately for 21 days. Control animals were given only the vehicle.

Results Diabetic rats showed hyperglycemia with almost four-fold high blood glucose levels. Hyperglycemia increases lipid peroxidation and DNA degradation, causing decreased activities of membrane-bound ATPases, antioxidant enzymes and glucose transporter expression with diabetes in the rat liver. Rats treated with a combined dose of SOV and TSP had glucose levels comparable to controls, similar results were obtained with the activities of antioxidant enzymes, membrane-bound ATPases, DNA degradation, lipid peroxidation and glucose transporter in the liver of diabetic rats.

Conclusions Our results showed that lower doses of vanadate (0.2 mg/ml) could be used in combination with Trigonella to effectively counter diabetic alterations without any toxic side effects. Therefore combined therapy can indeed be considered a better alternative to being explored further as a means of diabetic control.

IDDF2018-ABS-0232 WEARABLE TECHNOLOGY (MI BAND AND YU BAND) A BOON FOR PATIENTS WITH CHRONIC KIDNEY DISEASE

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10.1136/gutjnl-2018-IDDFabstracts.55

Background New wearable sensor networks together with smartphone applications are being examined and tested for their potential to monitor and manage patients with chronic kidney disease (CKD). To develop methods for analyses and