not express RBMY, a marked immune-positive signal of RBMY was identified upon metastasis. Importantly, HCC patients harboring cytoplasmic RBMY generally showed early metastasis (<15 months after primary tumor resection, p<0.01). Conclusion: RBMY is a novel onco-
protein. Its regulatory roles in facilitating malignant hepatic steatosis and tumor metastases are identified in this study. Because of its absence from normal human tissues except testis, RBMY represents a feasible therapeutic target for the selective eradication of HCC cells in male patients.

Sui1461

CIRCULAR RNA SLC3A2 PROMOTES HEPATOCELLULAR CARCINOMA GROWTH AND INVASION BY SPONGING MIR-490-3P AND UPREGULATING PPM1F/AKT/GSK3β/CATENIN SIGNALING PATHWAY

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Background: Non-coding RNAs (ncRNAs) have been shown to regulate gene expression involved in tumor progression of multiple malignancies. Previous studies indicated that protein phosphatase Mg2+/Mn2+ dependent 1F (PPM1F) plays a critical role in metastasis. But, the underlying mechanisms by which ncRNAs modulate PPM1F expression in hepatocellular carcinoma (HCC) remain undefined. Methods: The association between PPM1F and has-miR-490-3p (miR-490) expression and the clinicopathological characteristics and prognosis of HCC patients was analyzed by TCGA RNA-sequence data. A novel circular RNA SLC3A2 (circSLC3A2) was identified to sponge miR-490 by circRNA expression profile and bioinformatic analysis. The binding site of miR-490 with PPM1F or circSLC3A2 was validated by dual luciferase assay and RNA immunoprecipitation (RIP) assay. The expression and localization of circSLC3A2 in HCC tissue cases were investigated by fluorescence in situ hybridization (FISH). MT, colony formation, Wound healing and Transwell assays were performed to assess the effects of miR-490 or circSLC3A2 on cell proliferation and invasion, and Western blotting analysis was conducted to evaluate their effects on PPM1F and AKT signaling pathway. The expression of circSLC3A2 in HCC tissues represented an independent prognostic factor for overall survival of HCC patients. Conclusion: Circ-SLC3A2 may act as an oncogenic factor and a potential biomarker in HCC.

Sui1462

TARGETED DELIVERY OF EPIGALLOCATECHIN GALLATE AND ANTI-MIR-221 REGRESSED INTRAHEPATIC TUMORS IN ATHYMIC MICE

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Background and Aims: Hepatocellular carcinoma (HCC) is a primary malignant hepatic tumor and highly resistant to chemotherapy. Current treatment methods for HCC are not effective due to lack of efficient and targeted drug delivery. Here we employed milk-derived nanovesicles (MN) for targeted delivery of anticancer agents, epigallocatechin gallate (EGCG) and anti-miR221. Methods: Nanovesicles ranging from 100–200 nm were isolated from commercial skim milk using ultracentrifugation, purified, and characterized with nanoparticle tracking analysis (NTA). EGCG and anti-miR221 were introduced into MNVs using lipofectamine 2000, purified in a second ultracentrifugation, and further characterized. The MNVs were injected in athymic nude mice with surgical implantation of PLC/PRF/5 HCC cells stably transfected with EGCG- or anti-miR221. The proliferation and growth of HCC cells were determined by transwell assay. The growth and metastatic capacity of HCC cells in vivo were evaluated by murine hepatic orthotopic implantation and pulmonary metastatic model. Results: The mRNA and protein expressions of AS1G in human HCC tissues were markedly increased. The inhibition of AS1G in PLC/PRF/5 HCC cells increased cell apoptosis and induced epithelial-to-mesenchymal transformation (EMT) of the HCC cells. Conclusion: AS1G inhibitor or AS1G shRNA inhibited the extracellular acidity-induced proliferation, migration, invasion, and EMT of HCC cells. AS1G shRNA in HCC cells significantly inhibited HCC cell growth in the liver and pulmonary metastasis in mice. AS1G expression level in human HCC tissues was significantly correlated with the stage and prognosis of HCC patients. Conclusion: AS1G mediated extracellular acidity signals mediates extracellular acidity-induced proliferation, migration and invasion of HCC cells, and promotes the progression of HCC, indicating that AS1G can be used as a prognostic marker and a therapeutic target for HCC.

Sui1464

ACYL-COA DEHYDROGENASE 11 INHIBITION SUPPRESSES PROLIFERATION AND GROWTH OF HEPATOCELLULAR CARCINOMA CELLS

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Background & Aims: Acyl-CoA dehydrogenase 11 (ACAD11) is a newly identified long chain acyl-CoA dehydrogenase that catalyzes the dehydrogenation of long chain acyl-CoA esters and participates in oxidations of long chain fatty acids. Recently, alteration of lipid metabolism has been increasingly recognized as a hallmark of cancer cells. It has been demonstrated that the reprogramming of lipid metabolism is critical for development and progression of hepatocellular carcinoma (HCC). Long chain fatty acids (LCFA) have been described as anoikis promoting source of energy and precursors of various lipid species in cells, such as the phospholipids essential for biomembrane synthesis. In this study, we wonder whether ACAD11 participates in development and progression of HCC. Methods: The mRNA and protein expressions of ACAD11 in human HCC tissues were analyzed by real time PCR and western blot. The activity of ACAD11 in native human HCC cells was measured by electron transfer flavoprotein fluorescence reduction assay. The proliferation and growth of HCC cells were evaluated by cell counting kit 8 (CCK8), S-Etynyl-2-deoxyuridine (EdU), growth curve assay, and hepatocellular carcinoma implantation model of nude mice. The mRNA expression levels of ACAD11 in human HCC tissues were markedly higher than those in pericarcinogenic liver tissues. The activity of ACAD11 in native human HCC cells was also significantly increased. The inhibition of ACAD11 by shRNA suppressed the survival of HCC cells under glucose deprivation in vitro, the proliferation and growth of HCC cell in vitro and the growth of HCC cells in nude mice. On the other hand, overexpression of ACAD11 in HCC cells increased the survival of HCC cells and promoted the proliferation and growth of HCC cell. Conclusions: ACAD11 inhibition suppresses the proliferation and growth of hepatocellular carcinoma cells, implying that ACAD11 may serve as a new therapeutic target for the treatment of HCC. The further study for the mechanisms of ACAD11 alteration and action is necessary.

Sui1465

THE ANTI-TUMOR EFFECTS OF A NOVEL MDY88 INHIBITOR TJ-M2010-5 ON HEPATOCELLULAR CARCINOMA GROWTH

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Objective: Compared with normal liver, MDY88 is highly expressed in hepatocellular carcino-
ma (HCC), promoting tumor proliferation and metastasis. In this study, we synthesized a novel MDY88 inhibitor, which is a small molecule derivative of aminothiazole, named as TJ-M2010-5 to explore its direct therapeutic effect on HCC. Methods: We found that H22 cells have higher expression level of MyD88 than normal liver cells. In vivo, the tumor growth in the inhibitor group was significantly slower in intradural tumor-bearing mice than that in the control group. TJ-M2010-5 was used to detect cell proliferation by CCK8 method at different concentrations. We revealed that TJ-M2010-5 inhibited the proliferation of H22 cells in a dose-dependent manner. To further elucidate the intrinsic mechanisms of TJ-M2010-5 on cell proliferation, we did cell cycle analyses and showed that G0/G1 phase H22 was 39.95% and 60.22% at the concentrations of 5 mmol/L and 10 mmol/L TJ-M2010- 5, whereas a greater proportion of G2/M phase was observed when H22 cells were treated with TJ-M2010- 5 could cause G0/G1 phase cell cycle arrest and thereby could inhibit the proliferation of H22 cells. Western blot analysis showed that TJ-M2010-5 downregulated the key factors involved in G1 to S phase transition, including cyclin D1, cyclin dependent kinases 6 (CDK6), cyclin E and CDK2. To confirm that TJ-M2010-5 could inhibit cell proliferation, the expression of both phospho-MEK1/2 (ser217/221) and phospho-ERK1/2 (Thr202/Tyr204) expression, suggesting that TJ-M2010-5 could modulate the Erk/MAPK signaling pathway which was recently found to be important for liver carcinogenesis. We observed a higher percentage of F4/80+CD11c+ macrophages is correlated with TJ-M2010-5. Interestingly, no difference was found in F4/80+CD11c+ macrophages between two groups in this setting. We demonstrated that TJ-M2010-5 led to decrease of MyD88 expression level in native human HCC cells was marked higher than those in pericarcinogenic liver tissues. The activity of ACAD11 in native human HCC cells was also significantly increased. The inhibition of ACAD11 by shRNA suppressed the survival of HCC cells under glucose deprivation in vitro, the proliferation and growth of HCC cell in vitro and the growth of HCC cells in nude mice. On the other hand, overexpression of ACAD11 in HCC cells increased the survival of HCC cells and promoted the proliferation and growth of HCC cell. Conclusions: TJ-M2010-5 can be a novel and potent inhibitor for HCC that inhibit cell growth and induce cell cycle arrest.