Arabinogalactan derived from Lycium barbarum fruit inhibits cancer cell growth via cell cycle arrest and apoptosis.

Related Articles
Arabinogalactan derived from Lycium barbarum fruit inhibits cancer cell growth via cell cycle arrest and apoptosis.

Int J Biol Macromol. 2020 Jan 25;:

Abstract
Previous studies have shown that crude polysaccharides from the Lycium barbarum fruit could inhibit cancer cell growth, but the major effective constituents are yet to be identified. In this study, we compared the effects of L. barbarum fruit polysaccharide fractions on the growth of hepatoma cells (SMMC-7721 and HepG2), cervical cancer cells (HeLa), gastric carcinoma cells (SGC-7901), and human breast cancer cells (MCF-7). LBGP-I-3 showed stronger inhibitory effects on MCF-7 cells (cell viability of 48.96%) than SMMC-7721 (cell viability of 78.91%) and HeLa cells (cell viability of 55.94%), and had no effect on HepG2 and SGC-7901 cells. In addition, LBGP-I-3 had no inhibitory effect on normal liver cells (L02, cell viability of 115.58%). Investigation of the underlying mechanism suggested that LBGP-I-3 inhibited the growth of cancer cells by cell cycle arrest and apoptosis. LBGP-I-3 arrested the cell cycle at the G0/G1 phase, altered mitochondrial function, activated oxidative stress, and regulated the MAPK signaling pathway to induce apoptosis. Thus, LBGP-I-3 may be a potential functional food ingredient for the prevention of cancer without toxicity to normal cells in vitro. These results could help further elucidate the structure-activity relationship of L. barbarum fruit polysaccharides and functional food development.

PMID: 31991207 [PubMed — as supplied by publisher]

Immune Modulation by Telomerase-Specific Oncolytic Adenovirus Synergistically Enhances Antitumor Efficacy with Anti-PD1 Antibody.

Related Articles
Immune Modulation by Telomerase-Specific Oncolytic Adenovirus Synergistically Enhances Antitumor Efficacy with Anti-PD1 Antibody.

Mol Ther. 2020 Jan 10;:

Abstract
The clinical benefit of monotherapy involving immune checkpoint inhibitors (ICIs) such as anti-programmed death-1 antibody (PD-1 Ab) is limited to small populations. We previously developed a telomerase-specific oncolytic adenovirus, Telomelysin (OBP-301), the safety of which was confirmed in a phase I clinical study. Here, we examined the potential of OBP-502, an OBP-301 variant, as an agent for inducing immunogenic cell death (ICD) and synergistically enhancing the efficacy of OBP-502 with PD-1 Ab using CT26 murine colon cancer and PAN02 murine pancreatic cancer cell lines. OBP-502 induced the release of ICD molecules such as adenosine triphosphate (ATP) and high-mobility group box protein 1 (HMGB1) from CT26 and PAN02 cells, leading to recruitment of CD8-positive lymphocytes and inhibition of Foxp3-positive lymphocyte infiltration into tumors. Combination therapy involving OBP-502 intratumoral administration and PD-1 Ab systemic administration significantly suppressed the growth of not only OBP-502-treated tumors but also tumors not treated with OBP-502 (so-called abscopal effect) in CT26 and PAN02 bilateral subcutaneous tumor models, in which active recruitment of CD8-positive lymphocytes was observed even in tumors not treated with OBP-502. This combined efficacy was similar to that observed in a CT26 rectal orthotopic tumor model involving liver metastases. In conclusion, telomerase-specific oncolytic adenoviruses are promising candidates for combined therapies with ICIs.

PMID: 31991110 [PubMed — as supplied by publisher]
Reevaluating the role of ferritin in the diagnosis of adult secondary hemophagocytic lymphohistiocytosis.

Related Articles

Reevaluating the role of ferritin in the diagnosis of adult secondary hemophagocytic lymphohistiocytosis.

Eur J Haematol. 2020 Jan 28;:

Authors: Naymagon L, Tremblay D, Mascarenhas J

Abstract

BACKGROUND: The standard diagnostic criteria for hemophagocytic lymphohystiocytosis (HLH) include hyperferritinemia to > 500ng/ml. This ferritin threshold is based on pediatric data, and evidence for its application among adults with secondary HLH is lacking.

OBJECTIVE AND METHODS: We conducted a retrospective study assessing the relationship between extreme hyperferritinemia and adult secondary HLH at our institution. All adult inpatients seen over a 10 year period, with serum ferritin >5,000ng/ml were included.

RESULTS: Among 1055 patients with serum ferritin >5,000ng/ml there were 69 cases of HLH (HLH prevalence of 6.5%). Mean ferritin among HLH patients was 70,398ng/ml (SD 122,908), median 40,019ng/ml (IQR 16,051 — 68,326). The prevalence of HLH only reached 50% as serum ferritin approached 90,000ng/ml. A variety of conditions were contributory to hyperferritinemia, most commonly bacterial sepsis (33%), hematologic malignancy (29%), renal failure (24%), and liver injury (18%). The optimal cutoff ferritin for diagnosis of HLH was 16000ng/ml (sensitivity 79.4%, specificity of 79.2% , PPV 20.9%, NPV 98.2%).

CONCLUSIONS: The threshold ferritin levels used in diagnostic criteria for adult secondary HLH are too low to be clinically relevant and efforts should be undertaken to revise them upward. Similar reappraisals should be taken of the other criteria used to diagnose adult HLH.

PMID: 31990698 [PubMed — as supplied by publisher]

Prognostic Significance and Functional Relevance of Olfactomedin 4 in Early-Stage Hepatocellular Carcinoma.

Related Articles

Prognostic Significance and Functional Relevance of Olfactomedin 4 in Early-Stage Hepatocellular Carcinoma.

Clin Transl Gastroenterol. 2020 Jan 28;:

Authors: Ye L, Kriegl L, Reiter FP, Munker SM, Itzel T, Teufel A, Ziesch A, Török HP, Kirchner T, Gerbes AL, Guba M, Mayerle J, De Toni EN

Abstract

OBJECTIVES: Hepatocellular carcinoma (HCC) is a leading cancer-related cause of death. Unfortunately, recurrence is common even after curative treatment of early-stage patients, and no adjuvant treatment has yet been established. Aberrant expression of OLFM4 in human cancers has been reported; yet, its specific function during tumor development remains poorly understood, and its role in HCC is unknown. The purpose of this study is to examine the prognostic significance of OLFM4 and its functional relevance in determining recurrence in patients with early-stage HCC.

METHODS: Immunohistochemical staining to assess expression, cellular distribution, and prognostic significance of OLFM4 was performed in a tissue microarray comprising 157 HCC tissues and matched nontumor tissues. In addition, expression of OLFM4-coding mRNA was assessed in a separate patients’ cohort. The findings were validated by in vitro functional studies using siRNA directed against OLFM4 to assess its effect on cell motility and proliferation.

RESULTS: The fraction of HCC samples exhibiting positive OLFM4 staining was higher in comparison with that observed in hepatocytes from matched nontumor tissue (61% vs 39%). However, cytoplasmic-only staining for OLFM4 was associated with vascular invasion (P = 0.048), MMP-7 expression (P = 0.002), and poorer survival (P = 0.008). A multivariate analysis confirmed the independent significance of OLFM4 in determining patients’ outcome (5-year survival [58.3% vs 17.3%; HR: 2.135 {95% confidence interval: 1.135–4.015}; P = 0.019]). Correspondingly, inhibition of OLFM4 by siRNA modulated the expression of MMP-7 and E-cadherin, causing inhibition of cell proliferation, motility, and migration.

DISCUSSION: To the best of our knowledge, we provide the first report on the prognostic significance of OLFM4 in HCC and identify its mechanistic role as crucial mediator of MMP family protein and E-Cadherin in determining cell invasion and metastasis formation.

PMID: 31990698 [PubMed — as supplied by publisher]

Endocytosis of ATB0,+(SLC6A14)-targeted liposomes for drug delivery and its therapeutic application for pancreatic cancer.

Related Articles

Endocytosis of ATB0,+(SLC6A14)-targeted liposomes for drug delivery and its therapeutic application for pancreatic cancer.

Expert Opin Drug Deliv. 2020 Jan 28;:

**Overexpression of CFL1 in gastric cancer and the effects of its silencing by siRNA with a nanoparticle delivery system in the gastric cancer cell line.**

**Abstract**

Gastric adenocarcinoma, like other cancers, is a multifactorial genetic disease, and metastasis of cancer cells is one of the main features of this illness. The expression levels of the CFL1 gene have been modulated in this pathway. Using small interfering RNA (siRNA) in the treatment of gastric cancer is considered a hopeful gene therapeutic approach. The present study reported the level of CFL1 genes between tumor and margin and healthy tissue of gastric cancer. Also, the features of a cationic nanoparticle with a polymer coating containing polyacrylic acid and polyethyleneimine that were used in the delivery of CFL1 siRNA, were shown. Then the cytotoxicity, cellular uptake, and gene silencing efficiency of this nanoparticle were evaluated with CFL1 siRNA.

**METHOD:** In this study, the CFL1 gene expression was measured in 40 gastric adenocarcinoma, marginal and 15 healthy biopsy samples by a real-time polymerase chain reaction. Physicochemical characteristics, apoptosis, and inhibition of migration of the delivery of CFL1 siRNA by nanoparticle and lipofectamine were investigated in gastric cancer cells.

**RESULT:** The CFL1 expression was remarkably increased in gastric cancer tissues in comparison with the marginal samples and normal tissues \( (p < 0.05) \).

**CONCLUSION:** Our results demonstrated that CFL1 downregulation in AGS cells can interdict cell migration. Finally, our outcomes propose that CFL1 can function as an oncogenic gene in gastric cancer and would be considered as a potential purpose of gene therapy for gastric cancer treatment.

PMID: 31990240 [PubMed — as supplied by publisher]
Risk Factors for Postembolization Syndrome After Transcatheter Arterial Chemoembolization.

Related Articles

Risk Factors for Postembolization Syndrome After Transcatheter Arterial Chemoembolization.


Authors: Arslan M, Degirmencigolu S

Abstract
BACKGROUND: Transarterial Chemoembolization (TACE) is a minimally invasive treatment in managing unresectable liver primary neoplasms or liver metastases. Postembolization Syndrome (PES) is the most common adverse effect after TACE procedures.

OBJECTIVE: We investigate the risk factors for the development of PES after TACE therapy in patients with primary or metastatic liver tumors.

METHODS: In a retrospective analysis of 163 patients who underwent TACE between 01/01/2012 and 31/01/2018, patients that were given medication due to pain, fever, nausea or vomiting were evaluated and noted with PES. Analyses were made to evaluate factors such as age, gender, chemotherapy agent and dose, tumor size, tumor type, a particle used for embolization, multiple tumor treatments and selective application of the procedure, which may lead to PES after TACE.

RESULTS: In a total of 316 patients, PES was observed at a rate of 55 percent after TACE. Tumor size, number of tumors treated and adopting super selective fashion in the procedure were found to be related to the development of PES. No relationship was found between age, gender, presence of ascites, tumor type, size of embolic agent and drug type and the development of PES.

CONCLUSION: A treated tumor measuring >5 cm, treating more than one tumor, and the failure to perform the procedure in a super selective fashion increase the risk of PES development after TACE.

PMID: 31989907 [PubMed — in process]


Related Articles


Authors: Anysz-Grodzicka A, Podgorska J, Cieszanowski A

Abstract
BACKGROUND: Fibrolamellar Carcinoma (FLC) and Combined Hepatocellular– Cholangiocarcinoma (CHC) are rare primary liver tumours, which are related to different clinical settings. In both tumours, correlation with clinical data and laboratory tests are extremely important.

DISCUSSION: Typically, FLC is diagnosed in young patients without any chronic disease and with normal biochemical tests, whereas CHC arises in cirrhotic patients with elevated tumour markers: AFP and/or CA 19–9. The review describes epidemiology, aetiology, pathogenesis, radiological features and treatment of these tumours. Imaging features typical for FLC are: The presence of a single dominant mass located in the right lobe of the liver, with hypointense rim, and isointense to hypointense in the central part on T1-weighted images, and heterogeneous enhancement pattern on dynamic contrast-enhanced images. On T2-weighted images, the central part of the tumour shows hyperintense signal, whereas the peripheral part is hypointense. The ADC values of the tumour are lower than that of normal liver tissue.

CONCLUSION: The imaging features of FLC and CHC are distinctive, allowing for accurate preoperative diagnosis. The imaging features of these tumours can help in the differential diagnosis from other malignant liver tumours, especially hepatocellular carcinoma. The imaging features of FLC and CHC can aid in the selection of patients who may benefit from surgical resection or ablation therapy.

PMID: 31989904 [PubMed — in process]


Related Articles


Authors: Cieszanowski A, Anysz-Grodzicka A, Podgorska J, Jagielska B, Palucki J

Abstract
BACKGROUND: Primary Hepatic Epithelioid Haemangioendothelioma (HEHE) and Primary Hepatic Angiosarcoma (PHA) are rare mesenchymal tumours with different malignant potential. Whereas HEHE demonstrates low to intermediate malignant potential, PHA is an aggressive malignancy with poor prognosis. The knowledge of typical imaging features of these lesions may facilitate correct diagnosis; however, the ultimate diagnosis of HEHE and PHA is based on histopathologic examination.

DISCUSSION: The most typical findings helpful in diagnosing HEHE are: Presence of multiple, confluent nodules located at the liver periphery (in young to middle-aged woman), retraction of the liver capsule, marked hyperintensity on T2-weighted images, “target-sign” appearance, progressive centrifugal contrast enhancement, and relatively high Apparent Diffusion Coefficient (ADC) values. More than ≥50% of nodules are hyper– or isointense on Hepatobiliary Phase (HBP) images.

CONCLUSION: The imaging features suggestive of PHA are: Occurrence of metastases (lungs, spleen) at the time of diagnosis, presence of a large dominant mass with smaller satellites, heterogeneity and areas of haemorrhage in a dominant mass, progressive contrast enhancement, slightly elevated ADC values as compared to other malignant liver tumours.

PMID: 31989907 [PubMed — in process]
Coenzyme Q10 attenuates rat hepatocarcinogenesis via the reduction of CD59 expression and phospholipase D activity.

Abstract

The current study aimed to test the profile of serum lipids, phospholipase D (PLD) activity, and CD59 expression pattern in rat hepatocellular carcinoma (HCC) after therapeutic treatment with Coenzyme Q10 (CoQ10). Three rat groups were allocated as normal control, untreated HCC, and treated HCC (HCC + CoQ10).

The levels of serum alpha-fetoprotein (AFP) and tumour necrosis factor (TNF)-alpha were assessed using enzyme-linked immunosorbent assay (ELISA), while proliferating cell nuclear antigen (PCNA) was detected using immunohistochemistry (IHC). Serum lipids, classical (CH50), and alternative (APH50) pathways of complement activation, the liver cell HMG-CoA reductase (HMGCR), and PLD activities were assayed colorimetrically. The protein expression of CD59, scavenger receptor class B type 1 (SRB1), B cell lymphoma-2 (Bcl2), and cleaved Caspase-3 (Casp-3) were detected using western blotting.

In the liver cell, CoQ10 decreased and increased PLD and HMGCR activities, respectively. In addition, reduction of liver CD59 and increased PLD and HMGCR activities was observed. Statistical correlation indicated an inverse relationship between CH50 and each of CD59 expression and PLD activity after treatment with CoQ10. In conclusion, CoQ10 could protect against rat HCC through increased lipids and the reduction of CD59 expression and PLD activity. SIGNIFICANCE OF THE STUDY: To our knowledge, this study is the first to describe the attenuating effect of antitumour natural product like Coenzyme Q10 (CoQ10) via the reduction of CD59 expression and phospholipase D (PLD) activity. This illustrates the important role of CD59 and PLD in relation to lipids in cancer prevention.

PMID: 31989878 [PubMed — in process]
CONCLUSIONS: This approach could discriminate GON with high accuracy, sensitivity, specificity, and AUC using color fundus photographs. It may provide a second opinion on the diagnosis of glaucoma to the specialist quickly, efficiently and at low cost, and assist doctors and the public in large-scale screening for glaucoma.

PMID: 31989285 [PubMed — as supplied by publisher]

Novel complementary antitumour effects of celastrol and metformin by targeting IkBκB, apoptosis and NLRP3 inflammasome activation in diethylnitrosamine-induced murine hepatocarcinogenesis.

Related Articles

Novel complementary antitumour effects of celastrol and metformin by targeting IkBκB, apoptosis and NLRP3 inflammasome activation in diethylnitrosamine-induced murine hepatocarcinogenesis.

Cancer Chemother Pharmacol. 2020 Jan 27;:

Authors: Saber S, Ghanim AMH, El-Ahwany E, El-Kader EMA

Abstract

One promising strategy for minimizing chemotherapeutic resistance in hepatocellular carcinoma (HCC) is the use of effective chemosensitizers. We studied the complementary multi-targeted molecular mechanisms of metformin and celastrol in mice with diethylnitrosamine-induced HCC to investigate whether metformin could augment the sensitivity of HCC tissue to the effect of celastrol. Simultaneous administration of celastrol (2 mg/kg) and metformin (200 mg/kg) improved liver function, enhanced the histological picture and prolonged survival. Additionally, combination therapy exerted anti-inflammatory activity, as indicated by the decreased levels of TNF-α and IL-6. This protective role could be attributed to inhibition of inflammasome activation. Herein, our data revealed downregulated NLRP3 gene expression, suppressed caspase-1 activity and reduced levels of the active forms of IL-1β and IL-18. Under this condition, pyroptotic activity was suppressed. In contrast, in the celastrol and celastrol + metformin groups, the apoptotic potential was amplified, as revealed by the increase in the caspase-9 and caspase-3 levels and Bax:Bcl-2 ratio. In addition to their repressive effect on the gene expression of NFXkBp65, TNFR and TLR4, metformin and celastrol inhibited phosphorylation-induced activation of IkBκB and NFXkBp65 and decreased IkBκ degradation. Combination therapy with metformin and celastrol repressed markers of angiogenesis, metastasis and tumour proliferation, as revealed by the decreased hepatic levels of VEGF, MMP-2/9 and cyclin D1 mRNA, respectively. In conclusion, by inhibiting NLRP3 inflammasome and its prerequisite NFκB signalling, simultaneous administration of metformin and celastrol appears to have additive benefits in the treatment of HCC compared to tela monotherapy. This effect warrants further clinical investigation.

PMID: 31989218 [PubMed — as supplied by publisher]

Infantile Hepatic Hemangioma: Avoiding Unnecessary Invasive Procedures.

Related Articles

Infantile Hepatic Hemangioma: Avoiding Unnecessary Invasive Procedures.


Authors: Ernst L, Grabhorn E, Brinkert F, Reinhagen K, Königs I, Trab J

Abstract

Infantile hepatic hemangioma, the most common vascular tumor of the liver in infancy, can occur with acute postnatal liver and congestive heart failure. Nevertheless, its course is often benign, and many children can be diagnosed and treated without surgical intervention. The distinction from malignant diseases is not always easy and it not clear whether invasive procedures for diagnosis and therapy should be performed. Here we report our experiences in our Center for Pediatric Liver Disease and postulate that large studies are needed to avoid unnecessary invasive procedures for these patients in the future.

PMID: 31988877 [PubMed]

PEGylated gold nanoparticles-ribonuclease induced oxidative stress and apoptosis in colorectal cancer cells.

Related Articles

PEGylated gold nanoparticles-ribonuclease induced oxidative stress and apoptosis in colorectal cancer cells.

Bioimpacts. 2020;10(1):27–36


Abstract

Introduction: Currently, drug-induced reactive oxygen species (ROS) mediating apoptosis pathway have extensively been investigated in designing effective strategies for colorectal cancer (CRC) chemotherapy. Bovine pancreatic ribonuclease A (RNase A) represents a new class of cytotoxic and non-mutagenic enzymes,
and has gained more attention as a potential anticancer modality; however, the cytosolic ribonuclease inhibitors (RIs) restrict the clinical application of this enzyme. Nowadays, nanotechnology-based diagnostic and therapeutic systems have provided potential solutions for cancer treatments. Methods: In this study, the gold nanoparticles (AuNPs) were synthesized, stabilized by polyethylene glycol (PEG), functionalized, and covalently conjugated with RNase A. The physicochemical properties of engineered nanobiomedicine (AuNPs-PEG-RNase A) were characterized by scanning electron microscope (SEM), dynamic light scattering (DLS), and UV-vis spectrum. Then, its biological impacts including cell viability, apoptosis, and ROS production were evaluated in the SW-480 cells. Results: The engineered nanobiomedicine, AuNPs-PEG-RNase A, was found to effectively induce apoptosis in SW-480 cells and result in a significant reduction in cancer cell viability. Besides, the maximum production of ROS was obtained after the treatment of cells with an IC50 dose of AuNPs-PEG-RNase A. Conclusion: Based on the efficient ROS-responsiveness and the anticancer activity of RNase A of the engineered nanomedicine, this nanoscaled biologics may be considered as a potential candidate for the treatment of CRC.

PMID: 31988854 [PubMed]

Programmed cell death-1 inhibitor-related sclerosing cholangitis: A systematic review.

Related Articles

Programmed cell death-1 inhibitor-related sclerosing cholangitis: A systematic review.

World J Gastroenterol. 2020 Jan 21;26(3):353-365


Abstract

BACKGROUND: Programmed cell death-1 (PD-1) inhibitor has been indicated for many types of malignancies. However, these inhibitors also cause immune-related adverse events. Hepatobiliary disorder is a phenotype of immune-related adverse event affecting 0%-4.5% of patients treated with PD-1 inhibitors. Recent studies have reported PD-1 inhibitor-related sclerosing cholangitis (SC); however, the associated clinical and pathological features are unclear.

AIM: To evaluate the clinical and pathological features of PD-1 inhibitor-related SC through a systematic review of the literature.

METHODS: The review, conducted using electronic databases in PubMed, was restricted to the period from January 2014 to September 2019 and focused on case reports/series on PD-1 inhibitor-related SC published in English. We scanned the references of the selected literature to identify any further relevant studies. Six cases previously studied by us, including three that have not yet been published, were included in this review.

RESULTS: Thirty-one PD-1 inhibitor-related SC cases were evaluated. Median age of patients was 67 years (range, 43-89), with a male to female ratio of 21:10. The main disease requiring PD-1 inhibitor treatment was non-small cell lung cancer. Agents that caused PD-1 inhibitor-related SC were nivolumab (19 cases), pembrolizumab (10 cases), avelumab (1 case), and durvalumab (1 case). The median number of cycles until PD-1 inhibitor-related SC onset was 5.5 (range, 1-27). Abdominal pain or discomfort (35.5%, 11/31) was the most frequent symptom. Blood serum tests identified liver dysfunction with a notable increase in biliary tract enzymes relative to hepatic enzymes, and a normal level of serum immunoglobulin G4. Biliary dilation without obstruction (76.9%, 20/26), diffuse hypertrophy of the extrahepatic biliary tract (90.5%, 19/21), and multiple strictures of the intrahepatic biliary tract (30.4%, 7/23) were noted. In 11/23 (47.8%) cases, pathological examination indicated that CD8+ T cells were the dominant inflammatory cells in the bile duct or peribiliary tract. Although corticosteroids were mainly used for PD inhibitor-related SC treatment, the response rate was 11.5% (3÷26).

CONCLUSION: Some clinical and pathological features of PD-1 inhibitor-related SC were revealed. To establish diagnostic criteria for PD-1 inhibitor-related SC, more cases need to be evaluated.

PMID: 31988594 [PubMed — in process]

Idarubicin vs doxorubicin in transarterial chemoembolization of intermediate stage hepatocellular carcinoma.

Related Articles

Idarubicin vs doxorubicin in transarterial chemoembolization of intermediate stage hepatocellular carcinoma.

World J Gastroenterol. 2020 Jan 21;26(3):324-334

Authors: Roth GS, Teyssier Y, Abousalihac M, Seigneurin A, Ghelfi J, Sengel C, Decaens T

Abstract

BACKGROUND: Liver cancer is the fifth most common cancer and the second cause of cancer-related deaths worldwide. Transarterial chemoembolization (TACE) is the best treatment of intermediate hepatocellular carcinoma (HCC). Doxorubicin is the most commonly used drug despite a low level of evidence.

AIM: To compare the objective response rate of idarubicin-based TACE (Ida-TACE) against doxorubicin-based TACE (Dox-TACE) in intermediate stage HCC.

METHODS: Between January 2012 and December 2014, all patients treated with TACE at our academic hospital were screened. Inclusion criteria were patients with Child-Pugh score A or B, a performance status below or equal to 1, and no prior TACE. Either lipiodol TACE or drug-eluting beads TACE could be performed with 10 mg of idarubicin or 50 mg of doxorubicin. Each patient treated with idarubicin was matched with two doxorubicin-treated patients. The TACE response was assessed by independent radiologists according to the mRECIST criteria.

RESULTS: Sixty patients were treated with doxorubicin and thirty with idarubicin. There were 93% and 87% of cirrhotic patients and 87% and 70% of Child-Pugh A in the doxorubicin and idarubicin
Median number of HCC per patient was two in both groups with 31% and 26% of single nodules in doxorubicin and idarubicin groups, respectively. Objective response rate after first TACE was 76.7% and 73.3% (P = 0.797) with 41.7% and 40.0% complete response in doxorubicin and idarubicin groups, respectively. Progression-free survival was 7.7 mo in both groups, and liver transplant-free survival was 24.9 mo and 21.9 mo in doxorubicin and idarubicin groups, respectively. Safety profiles were similar in both groups, with grade 3–4 adverse events in 35% of Dox-TACE and 43% of Ida-TACEs.

CONCLUSION: Ida-TACE and Dox-TACE showed comparable results in terms of efficacy and safety. Ida-TACE may represent an interesting alternative to Dox-TACE in the management of patients with intermediate stage HCC.

PMID: 31988592 [PubMed — in process]

Fibroblast growth factor signaling in non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: Paving the way to hepatocellular carcinoma.

Related Articles

Fibroblast growth factor signaling in non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: Paving the way to hepatocellular carcinoma.

World J Gastroenterol. 2020 Jan 21;26(3):279-290
Authors: Ocker M
Abstract
Metabolic disorders are increasingly leading to non-alcoholic fatty liver disease, subsequent steatohepatitis, cirrhosis and hepatocellular carcinoma. Fibroblast growth factors and their receptors play an important role in maintaining metabolic homeostasis also in the liver and disorders in signaling have been identified to contribute to those pathophysiologic conditions leading to hepatic lipid accumulation and chronic inflammation. While specific and well tolerated inhibitors of fibroblast growth factor receptor activity are currently developed for (non-liver) cancer therapy, treatment of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis is still limited. Fibroblast growth factor-mimicking or restoring approaches have recently evolved as a novel therapeutic option and the impact of such interactions with the fibroblast growth factor receptor signaling network during non-alcoholic fatty liver disease/non-alcoholic steatohepatitis development is reviewed here.

PMID: 31988589 [PubMed — in process]

Lipid desaturation-associated endoplasmic reticulum stress regulates MYCN gene expression in hepatocellular carcinoma cells.

Related Articles

Lipid desaturation-associated endoplasmic reticulum stress regulates MYCN gene expression in hepatocellular carcinoma cells.

Cell Death Dis. 2020 Jan 27;11(1):66
Authors: Qin XY, Su T, Yu W, Kojima S
Abstract
Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related deaths worldwide due to its high rate of recurrence, in part because of cancer stem cell (CSC)-dependent "field cancerization". Recently, we identified that the oncogene v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN) marked CSC-like subpopulations in heterogeneous HCC and served as a therapeutic target and prognostic marker for HCC. In this study, we explored the molecular basis of upregulated MYCN gene expression in HCC cells. Liquid chromatograph time-of-flight mass spectrometry-based metabolome analysis demonstrated that the content of unsaturated fatty acids was increased in MYCN high expression (MYCNhigh) CSC-like HCC cells. Inhibition of lipid desaturation using either the chemical inhibitor or siRNA/shRNA against stearoyl-CoA desaturase-1 (SCD1) suppressed cell proliferation as well as MYCN gene expression in MYCNhigh HCC cells, grown as both monolayer and spheres. Further mechanistic study using RNA-seq based transcriptome analysis revealed that endoplasmic reticulum (ER) stress related signaling networks such as endocannabinoid cancer inhibition pathway were under the control of SCD1 in MYCNhigh HCC cells. Furthermore, the expression of ER stress-inducible transcription suppressor cyclic AMP-dependent transcription factor (ATF3) was downregulated in MYCNhigh CSC-like HCC cells and CSC-rich spheroids, which was upregulated by inhibition of lipid desaturation or treatment with acyclic retinoid (ACR). Lipid profiling using NMR spectroscopy revealed that the ACR dramatically reduced the content of unsaturated fatty acids in HCC cells. The chemical inducer of ER stress inhibited MYCN gene expression, while the chemical inhibitor of ER stress or knockdown of ATF3 gene expression partially rescued the suppression of MYCN gene expression by ACR in MYCNhigh HCC cells. These data suggested that lipid desaturation-mediated ER stress signaling regulates MYCN gene expression in HCC cells and serves as a promising therapeutic target for the treatment and prevention of HCC.

PMID: 31988297 [PubMed — in process]
LncRNA AC093818.1 accelerates gastric cancer metastasis by epigenetically promoting PDK1 expression.

Related Articles

LncRNA AC093818.1 accelerates gastric cancer metastasis by epigenetically promoting PDK1 expression.

Cell Death Dis. 2020 Jan 27;11(1):64

Authors: Ba MC, Ba Z, Long H, Cui SZ, Gong YF, Yan ZF, Lin KP, Wu YB, Tu YN

Abstract

Gastric cancer (GC) is a highly prevalent type of metastatic tumor. The mechanisms underlying GC metastasis are poorly understood. Some long noncoding RNAs (lncRNAs) reportedly play key roles in regulating metastasis of GC. However, the biological roles of five natural antisense lncRNAs (AC093818.1, CTD-2541M15.1, BC047644, RP11-597M12.1, and RP11-40A13.1) in GC metastasis remain unclear. In this study, the expression of these lncRNAs was measured by quantitative reverse transcription-polymerase chain reaction. Migration and invasion were evaluated by wound-healing and the Transwell assay, respectively. Stable cells were injected into the tail veins of nude mice. Sections of collected lung and liver tissues were stained using hematoxylin and eosin. Protein expression was analyzed by western blot. RNA immunoprecipitation (RIP) assay was used to verify whether the STAT3 and SP1 transcription factors bound to AC093818.1 in GC cells. Expression levels of the five lncRNAs, especially AC093818.1, were significantly upregulated in metastatic GC tissues relative to those in nonmetastatic GC tissues. AC093818.1 expression was correlated with invasion, lymphatic metastasis, distal metastasis, and tumor-node-metastasis stage. AC093818.1 expression was highly sensitive and specific in the diagnosis of metastatic or nonmetastatic GC. AC093818.1 overexpression promoted GC migration and invasion in vitro and in vivo. AC093818.1 overexpression increased PDK1, p-AKT1, and p-mTOR expression levels. AC093818.1 silencing decreased these expressions. AC093818.1 bound to transcription factors STAT3 and SP1, and SP1 or STAT3 silencing could alleviated the effect of AC093818.1 overexpression. The data demonstrate that lncRNA AC093818.1 accelerates gastric cancer metastasis by epigenetically promoting PDK1 expression. LncRNA AC093818.1 may be a potential therapeutic target for metastatic GC.

PMID: 31988283 [PubMed — in process]

Polyphyllin II inhibits liver cancer cells proliferation, migration and invasion through down-regulated cofilin activity and AKT/NF-κB pathway.

Related Articles

Polyphyllin II inhibits liver cancer cells proliferation, migration and invasion through down-regulated cofilin activity and AKT/NF-κB pathway.

Biol Open. 2020 Jan 27::

Authors: Pang D, Yang C, Li C, Zou Y, Feng B, Li L, Liu W, Luo Q, Chen Z, Huang C

Abstract

The morbidity and mortality of primary liver cancer is one of the highest among all the cancers. Deficiency of effective treatment and characteristics of cancer metastasis are believed to be responsible for this situation, thus a great demand is required for new agents developing. Polyphyllin II (PP2), an important steroidal saponin extracted from Rhizoma Paris, has emerged as a potential anticancer agent, but the effects of PP2 in liver cancers and its underlying mechanisms remain unexplored. In our study, we found that PP2 could remarkably suppress the proliferation of two liver cancer cell lines–HepG2 and BEL7402 cells, resulting from significant cell death. Besides, low dose of PP2 has displayed the property to inhibit cellular motility and invasion of liver cancer cells. In addition, we have found that PP2-mediated cofilin activity suppression was implicated in the inhibition of liver cancer cells motility. And, decreased expressions of two major hydrolytic enzymes (MMP2/MMP9), through the AKT/NF-κB signaling pathway, may be also responsible for this process. Rescue experiment either done with non-phosphorylatable mutant cofilin-1 (S3A) transfection or an activator of AKT pathway significantly reversed the inhibition effects of PP2 on liver cancer cells. Taken together, we reported a potential agent for liver cancer treatment and revealed its underlying mechanism.

PMID: 31988091 [PubMed — as supplied by publisher]

Socioeconomic status in relation to risks of major gastrointestinal cancers in Chinese adults: a prospective study of 0.5 million people.

Related Articles

Socioeconomic status in relation to risks of major gastrointestinal cancers in Chinese adults: a prospective study of 0.5 million people.
BACKGROUND: Low socioeconomic status (SES) is associated with higher risk of certain gastrointestinal (e.g. colorectal, pancreatic, and liver) cancers in Western populations. Evidence is very limited in China where correlates and determinants of SES differ from those in the West.

METHODS: The prospective China Kadoorie Biobank recruited 512,715 adults (59% women, mean age 51 years) from 10 (5 urban, 5 rural) regions. During 10 years of follow-up, 27,940 incident cancers (including 3061 colorectal, 805 pancreatic, and 2904 liver) were recorded among 510,131 participants without prior cancer at baseline. Cox regression was used to estimate adjusted hazard ratios (HRs) for specific cancers associated with area-level (e.g. per capita gross domestic product, disposable income) and individual-level (e.g. education, household income) SES.

RESULTS: Area-level SES and household income showed positive associations with incident colorectal and pancreatic cancer and inverse associations with liver cancer (p for trend