PE-145
Kahweol Induces Cell Death through Caspase-Dependent Pathway and Autophagy Dysfunction in Hepatocellular Carcinoma Cell Line

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Background: Coffee is one of the most widely consumed pharmacologically active beverages in the world. Several studies showed that a daily intake of coffee has the protective effect of coronary heart disease, diabetes mellitus, nonalcoholic steatohepatitis and cancer. Recent research suggests that kahweol, a diterpene molecule founded in the coffee bean, has anti-carcinogenic, anti-tumor and anti-inflammatory properties. However, little is known about the anti-tumor mechanisms of kahweol. Here, we examined the anti-tumor effect of kahweol in HepG2 human hepatocellular carcinoma cells.

Methods: The effect of kahweol on apoptosis is determined by hoechst and propidium iodide (PI) staining analysis on cultured human hepatocellular carcinoma HepG2 cells. The expression of cleaved caspase-3, cleaved PARP, pAkt, pERK, LC3 and p62 were determined by western blot analysis. To investigate whether kahweol induced apoptosis is related with autophagy, autophagy inhibitor bafinomycin or autophagy related gene 7 siRNA (SiATG7) were treated.

Results: Kahweol increased nuclear condensation and PI staining positive cells and induced cleaved caspase-3 and cleaved PARP expression. In addition, kahweol inhibits insulin induced phosphorylation of Akt, ERK, STAT3. Kahweol also increased expression of LC3-II and p62, indicating inhibition of autophagy. When kahweol was treated with bafinomycin or siATG7, apoptosis was significantly enhanced.

Conclusion: This study shows that kahweol increases HepG2 cell apoptosis through caspase 3-dependent pathway and inhibition of autophagy. The present study suggest that kahweol has anti-tumor effect in hepatocellular carcinoma.

Keywords: Kahweol, Hepatocellular carcinoma, Caspase, Autophagy, Apoptosis

PE-146
The Difference of Ras Isoform in Liver Cancer

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Background/Aims: Activation of Ras proteins is a key oncogenic event in human carcinogenesis. Mutations affecting the three prototype Ras oncoproteins, Hras, Nras and Kras, show a high degree of tumor-type specificity. Kras and Nras are mutated in liver cancer, but mutations in Hras are rare. In this study, we have used the different Ras isoforms to determine whether they have different tumorigenic potentials in the liver.

Methods: Transgenic liver cancer mouse models expressing different Ras isoforms were developed using a hydrodynamic injection method and the Sleeping Beauty Transposon System. Transposon vectors, each encoding an oncogene (HrasG12V, KrasG12V, NrasG12V) or downregulating a tumor suppressor gene (shp53), were constructed. To induce liver cancer, 40 µg of the three plasmids, encoding the sleeping beauty transposase and two transposons, was diluted in 2.5 mL of 0.9% saline and injected into the lateral tail veins of 6week-old C57BL/6 mice. Mice were observed at 23 days post-hydrodynamic injection or near to death.

Results: Coexpression of H-, K-, N-RasG12V and shp53 resulted in a massive abdomen enlargement within 4 weeks after injection. Several nodular lesions emerged from the liver parenchyma, finally occupying most of the liver surface in 23 days after injection. The ratio of liver/ body weight in KrasG12V group increased significantly compared to the HrasG12V group (P=0.0005) or NrasG12V group (P=0.0181) individually. Although the ratio of NrasG12V group showed a mild increase compared to the HrasG12V group, but statistically it was not significant (P=0.3819). Survival curve of these groups corresponded to the ratio of liver/body weight. All mice became moribund by 36 days.

Conclusion: Coexpression of RasG12V and shp53 in the mouse liver promotes rapid hepatocarcinogenesis. In particular, we found that Kras was the most oncogenic in the liver among the Ras isoforms when co-expressed with shp53.

Keywords: Ras isoform, Liver cancer

PE-147
Knockdown of 14-3-3ζ Enhance the Radio-sensitivity and Radiation Induced Apoptosis in CD133+ Liver Cancer Stem-like Cells

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Background: Hepatitis B and C virus (HBV and HCV) infected patients with cirrhosis are under the risk of developing liver-cell carcinoma. The ratio of malignant transformation of liver is increased in patients with chronic liver diseases. Therefore, effective treatment is needed for the prevention and treatment of liver carcinoma. In the liver cells, the expression of effector molecule, 14-3-3ζ, has been increased. Thus, we hypothesized that 14-3-3ζ may have a role in the progression of liver carcinoma.

Methods: Human liver cancer cell line, HepG2, was transfected with 14-3-3ζ siRNA. The expression of 14-3-3ζ, cell proliferation, cell cycle, expression of cell death markers, and the expression of radiation response genes were measured.

Results: The expression of 14-3-3ζ was significantly downregulated by 14-3-3ζ siRNA transfection. The expression of cell death markers, caspase 3 and PARP, was increased. The expression of cell proliferation, cell cycle, and radiation response genes was decreased.

Conclusion: The knockdown of 14-3-3ζ enhances the radio-sensitivity and radiation induced apoptosis in CD133+ liver cancer stem-like cells.

Keywords: 14-3-3ζ, Liver carcinoma, Stem-like cells