

ERK Signaling-Mediated Molecules in the Progression of Liver Cirrhosis and Hepatocellular Carcinoma

Chiung-Fang Chang

Far Eastern Memorial Hospital, New Taipei City, Taiwan

Abstract

Liver cirrhosis is the fourteenth most cause of death worldwide. Aberrant apoptosis is associated with liver fibrosis and cirrhosis progression, even for the progression of hepatocellular carcinoma (HCC). The progression from long-term liver injury, liver cirrhosis to HCC is associated with liver damage, liver regeneration and immune responses. Targeting liver injury-dependent signaling pathways could help to alleviate liver cirrhosis and prevent HCC development. ERK signaling pathway plays an important role in cell proliferation, differentiation and regeneration. In this study, we investigate the role of ERK signaling pathway in the progression of liver cirrhosis and HCC in terms of hepatocytes as well as immune responses. Our results suggested that Erk2 deficient livers have less degree of liver cirrhosis than WT livers. However, the relative body weight and liver weight of WT and Erk2 deficient mice were similar. Cirrhosis-related genes such as alpha-SMA was down-regulated in Erk2 deficient livers. The enrichment GO and KEGG analysis of differential expression genes (DEGs) were identified for liver cirrhosis related events such as the calcium ion responses and ECM pathway.

In addition, inhibition of ERK signaling pathway could induce apoptosis but did not alter cancer stem cell marker CD133 in HCC cells. ERK downstream molecule Egr1 expressed highly and lowly in HCC cells were subjected to the DEG analysis. Genes involved in hepatic fibrosis or hepatic stellate cell activation in the top canonical pathway were identified. Therefore, ERK signaling plays an important role to regulate the molecules in the progression of liver cirrhosis and HCC.

INTRODUCTION

Cirrhosis, otherwise called liver cirrhosis or hepatic cirrhosis, is a condition wherein the liver doesn't work appropriately because of long haul damage. This harm is portrayed by the substitution of ordinary liver tissue by scar tissue. Typically, the sickness grows gradually over months or years. Early on, there are frequently no symptoms. As the illness exacerbates, an individual may get drained, powerless, bothersome, have expanding in the lower legs, create yellow skin, wound effectively, have liquid development in the mid-region, or create bug like veins on the skin. The liquid develop in the midsection may turn out to be suddenly infected. Other genuine intricacies incorporate hepatic encephalopathy, seeping from widened veins in the throat or enlarged stomach

veins, and liver cancer. Hepatic encephalopathy brings about disarray and may prompt unconsciousness.

Cirrhosis is most regularly brought about by liquor, hepatitis B, hepatitis C, and non-alcoholic greasy liver disease. Typically, more than a few mixed beverages for each day over various years are required for alcoholic cirrhosis to occur. Non-alcoholic greasy liver ailment has various causes, including being overweight, diabetes, high blood fats, and high blood pressure. Various less basic reasons for cirrhosis incorporate immune system hepatitis, essential biliary cholangitis, hemochromatosis, certain drugs, and gallstones. Diagnosis depends on blood testing, clinical imaging, and liver biopsy.

A few reasons for cirrhosis, for example, hepatitis B, can be forestalled by vaccination. Treatment mostly relies upon the basic cause, however the objective is regularly to forestall compounding and complications. Avoiding liquor is suggested in all instances of cirrhosis. Hepatitis B and C might be treatable with antiviral medications. Autoimmune hepatitis might be treated with steroid medications. Ursodiol might be valuable if the malady is because of blockage of the bile ducts. Other meds might be helpful for entanglements, for example, stomach or leg expanding, hepatic encephalopathy, and enlarged esophageal veins. In extreme cirrhosis, a liver transplant might be an option.

Cirrhosis influenced about 2.8 million individuals and brought about 1.3 million passings in 2015. Of these passings, liquor caused 348,000, hepatitis C caused 326,000, and hepatitis B caused 371,000. In the United States, a bigger number of men bite the dust of cirrhosis than women. The principal known depiction of the condition is by Hippocrates in the fifth century BCE. The term cirrhosis was created in 1819, from a Greek word for the yellowish shade of a sick liver.

Cirrhosis has numerous potential appearances. These signs and side effects might be either an immediate aftereffect of the disappointment of liver cells, or auxiliary to the resultant expanded weight in the veins in the hepatic entryway framework (gateway hypertension). A few indications of cirrhosis are vague, and furthermore happen in a few disconnected conditions. In like manner, the nonattendance of any signs doesn't preclude the chance of cirrhosis. Cirrhosis of the liver is moderate and continuous in its turn of events. It is normally very much progressed before its indications are observable enough to cause alert. Shortcoming and weight reduction might be early manifestations.

The accompanying highlights are as an immediate outcome of liver cells not working.

Creepy crawly angiomas or bug nevi are vascular sores comprising of a focal arteriole encompassed by numerous littler vessels (thus the name "bug") and happen because of an expansion in estradiol. One examination found that insect angiomas happen in around 1/3 of cases.

Palmar erythema is a blushing of palms at the thenar and hypothenar eminences likewise because of expanded estrogen.

Gynecomastia, or increment in bosom organ size in men that isn't harmful, is brought about by expanded estradiol and can happen in up to 2/3 of patients. This is not the same as increment in bosom fat in overweight people.

Hypogonadism, abatement in male sex hormones may show as feebleness, fruitlessness, loss of sexual drive, and testicular decay, and can result from essential gonadal injury or concealment of hypothalamic/pituitary capacity. Hypogonadism is related with cirrhosis because of liquor abuse or hemochromatosis.

Liver size can be broadened, typical, or contracted in individuals with cirrhosis.

Ascites, amassing of liquid in the peritoneal cavity (space in the mid-region), offers ascend to "flank bluntness". This might be obvious as an expansion in stomach girth.

Fetor hepaticus is a smelly breath scent coming about because of expanded dimethyl sulfide.

Jaundice, or icterus, is yellow staining of the skin and mucous films (with the white of the eye being particularly recognizable) because of expanded bilirubin (at any rate 2–3 mg/dl or 30 $\mu\text{mol/l}$). The pee may likewise seem dull.

BIOGRAPHY

Dr. Chiung-Fang Chang is a researcher at Far Eastern Memorial Hospital, Taiwan. She graduated from National Taiwan University. She received her Ph.D. degree in the Division of Biological Sciences at University of California, San Diego, USA. Her expertise includes immunology, cell biology and animal disease models. Her current research projects focus on the cancer stem cells and immune responses in hepatocellular carcinoma.