Methods of Inhibiting Caspase-6 for the Treatment Of Nash

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BACKGROUND

Nonalcoholic steatohepatitis (NASH), characterized by hepatic steatosis with inflammation and liver damage, has become the leading cause of transplant and liver associated death. Moreover, numerous studies suggest that hepatocellular death is the key event triggering progression to fibrosis and cirrhosis for NASH and perhaps other liver diseases. In normal liver, hepatocyte apoptosis plays a key role in liver homeostasis, maintaining equilibrium between the loss and replacement of hepatocytes. However, pathological conditions such as viral infection, alcoholic or nonalcoholic steatohepatitis and physical injury, lead to extensive hepatocyte apoptosis and liver damage. While inflammation contributes to the pericellular fibrosis at an early stage, sustained liver damage leads to scarring, bridging fibrosis and subsequent development of cirrhosis. Moreover, hepatocellular death is the major contributor to the pathogenesis of cirrhosis and hepatocellular carcinoma. Therefore, understanding the molecular mechanisms by which hepatocellular death is controlled may lead to new treatments for liver diseases.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed a method of preventing and/or treating hepatocellular apoptosis and liver damage in a liver disease, particularly NASH, by targeting the AMPK/caspase-6 axis to inhibit caspase-6 activity and/or activate AMPK activity. Hepatocellular death plays an essential role in the development of non-alcoholic steatohepatitis (NASH).The activity of the energy sensor AMP-activated kinase (AMPK) is repressed in NASH and nonalcoholic fatty liver disease (NAFLD). Liver-specific AMPK knockout exaggerates liver damage in several models of diet-induced NASH. Thus, the AMPK/caspase-6 axis regulates hepatocellular apoptosis and liver damage in NASH, suggesting AMPK and Caspase-6 may be attractive therapeutic targets.

APPLICATIONS

The invention provides a method of preventing and/or treating hepatocellular apoptosis and liver damage in a liver disease, particularly NASH, by targeting the AMPK/caspase-6 axis to inhibit caspase-6 activity and/or activate AMPK activity.

ADVANTAGES

This represents a new biological site for the therapeutic intervention for NASH.

STATE OF DEVELOPMENT

The current state of development is at the experimental data stage.

INTELLECTUAL PROPERTY INFO

The invention is patent-pending and is available for licensing and collaborations.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Caspase-6, hepatocellular apoptosis, Nonalcoholic steatohepatitis (NASH), apoptosis, cell death, liver homeostasis

CATEGORIZED AS

- **Medical**
  - Disease: Metabolic/Endocrinology
  - Therapeutics

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