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Fatty liver and risk of dementia

NAFLD increases a risk of stroke

DPP-4 inhibitor-specific biomarkers in NAFLD

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Snapshot

Microbiome and metabolomics in alcoholic liver disease

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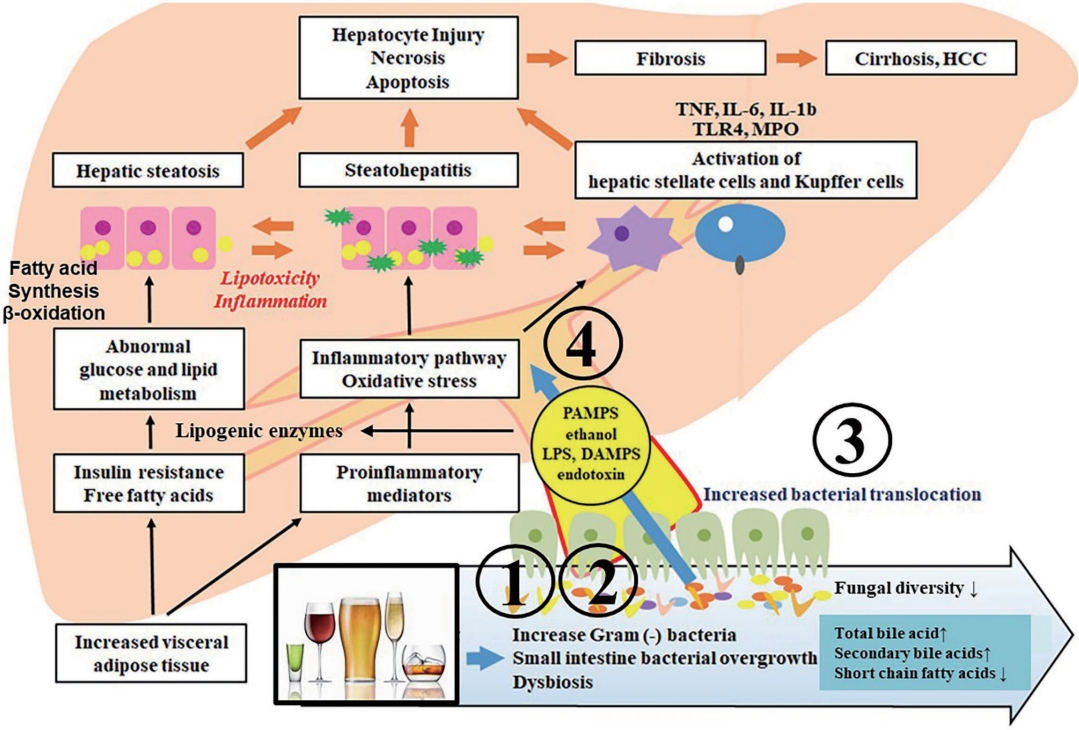

Identified microbial factor in the development of alcoholic liver disease

1. Small intestinal bacterial overgrowth (SIBO)
2. Alteration in the composition of microbiota (dysbiosis)
3. Bacterial translocation – leaky bowel
4. Direct effects of bacterial metabolites

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The gastrointestinal microbiome and metabolomics are the candidate biomarkers for alcoholic liver disease (ALD).[1] Alcohol-associated liver injury is characterized by oxidative stress, lipid peroxidation, steatosis, iron deposits, hepatocyte damage, and hepatocytes death. These features have been associated with liver inflammation, activation of Kupffer cells and hepatic stellate cells, liver fibrosis, and liver regeneration process. Alcohol use promotes a change in microbiome composition. Microbiota-host co-regulated metabolic pathways are promising targets for clinical needs.

Metabolite profiles such as lipids, fatty acids, carbohydrates, vitamins, proteins, enzymatic compounds, amino acids, and small-molecules profoundly affected host physiology and are being explored for their roles in ALD. The molecular families are shaped by the microbiome with short-chain fatty acids (SCFA; acetate, propionate, and butyrate), aromatic amino acid metabolites, indoles, complex polysaccharides, and host lipids such as sphingolipids and bile acids.[2,3] SCFA were found in human large intestine and involved in microbial fermentation. SCFA play intestinal homeostasis and potent immune regulators. SCFA indicate that gut-brain-liver axis could impaired by alcohol.[4,5]

Acetaldehyde is mainly expressed in hepatocytes and acts on hepatic stellate cells (HSCs) in a paracrine manner. Acetaldehyde directly increases expression of collagen-I in HSCs through transcription factors. Acetaldehyde reacts with metabolic components, which help maintain HSC activation. Ethanol increases fatty liver acid synthesis in hepatocytes via sterol regulatory element-binding protein-1c by increasing expression of lipogenic genes.[6] Interleukin (IL)-22 might be used treat to ALD patients because of its antioxidant, anti-apoptotic, anti-steatotic, anti-proliferative, and anti-microbial effects. Corticosteroids increased survival in patients with alcoholic hepatitis.

CXC chemokines such as CXCL12, CXCR4, and vascular endothelial growth factor have increased survival and the degree of hypertension. IL-8 and growth-related oncogene-alpha are parts of CXC chemokines family. These might be industrialized as a therapeutic drug for ALD.[7]

Anti-tumor necrosis factor (TNF)-α has an important role in the pathogenies of ALD in animal models. Pentoxifylline blocks transcription of TNF-α which can decrease serum level of TNF-α. S-adenosylmethionine (SAMe) acts as a methyl donor that has protect against ALD through antioxidant functions, and down regulation of TNF-α. SAMe plays as a safe drug for ALD. However, Cochrane report indicated that there have no evidences to support the use of SAMe in ALD patients.[8]

The time has come to develop the therapeutic biomarkers via gut-microbiome and metabolome in ALD. Patients with ALD show gut barrier dysfunction. Now, gut-microbiome-centered therapies are novel and associated metabolomics signature that plays a big platform for biomarkers discovery in ALD.

Authors' contribution

All authors wrote the manuscript and revised. Ki Tae Suk supervised and approved the manuscript for publication.

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Conflicts of Interest

The authors have no conflicts to disclose.

Abbreviations:

ALD, alcoholic liver disease; HSC, hepatic stellate cell; IL, interleukin; SAMe, S-adenosylmethionine; SCFA, short-chain fatty acids; TNF, tumor necrosis factor

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