Stelic Institute & Co a Tokyo-based bioventure company specializing in regenerative medicine, has announced the development of a new treatment method for acute liver failure. The company’s stem cell dynamism research team has shown that a protein called chemokine CXCL10 directly affects hepatic cells, regulating their replication and proliferation. “Hepatic cell replication has great potential as an alternative to current methods of treating liver damage, such as transplants and cellular therapy,” said Stelic chairman Hiroyuki Yone yama. By administering an effective dose of a specific neutralizing agent for chemokine CXCL10, and thus promoting the histological and functional repair of hepatic cells.

It is particularly difficult to save the lives of patients with acute liver failure caused by damage to the hepatic cells, and until now a liver transplant was considered the only treatment method capable of improving the probability of survival. The long-term use of immuno suppression for infection is high cost and unknown side effects, however, are problems that have yet to be solved, meaning that the quality of life (QOL) of patients is markedly reduced.

For these reasons, recent years have seen a rise in the development of treatment methods based on regeneration of the liver by using growth factors, cytokines and treatments employing stem cells. The mechanism of action within the body of the factors first reported as inducing the regeneration of hepatic cells has yet to be fully analyzed, however, as have the factors involved in the creation of hepatic cords during the regeneration process and the maintenance of their function.

Results of Research

Stelic’s Stem Cell Dynamism Research Team has shown that hepatic cord regeneration in acute liver cell damage is regulated at the in vivo level by a protein called chemokine CXCL10. The research team discovered that in chronic hepatitis B or mouse models of liver damage, CXCL10 is strongly expressed within the damaged liver, especially within hepatic cells.
Initially, the research team used a mouse model of liver damage for drug-induced acute liver failure, administering a neutralizing antibody to inhibit the activity of CXCL10 in order to investigate how this would modify damage to the liver. As a result, in mice administered the anti-CXCL10 neutralizing antibody the serum alanine transferase (ALT3) level was significantly lower, and histologically too the area of necrotized hepatic cells was strikingly reduced. From this they deduced that anti-CXCL10 antibody would also result in a striking improvement in clinical findings for liver damage associated with drug-induced acute liver failure.

They then analyzed the uptake of the proliferative cell marker 5-bromo-2-deoxyuridine (BrdU4, also known as brominated deoxyuridine), with the objective of elucidating the mechanism of anti-CXCL10 antibody in hepatic regeneration. Accordingly, they showed that anti-CXCL10 antibody not only promotes replication of damaged hepatic cells, but also plays a role in rebuilding functional structures in the liver.

An investigation of these results using human hepatic cell lines in vitro found that recombinant CXCL10 protein inhibits the proliferation of hepatic cells, whereas anti-CXCL10 antibody promotes it. The research team thus demonstrated that CXCL10 directly affects hepatic cells, regulating their replication and proliferation.

**Future Possibilities**

Restoring hepatic cell damage and functional impairment related to liver tissue damage is still problematic by means of today’s liver transplants or cellular therapy, and has its limits. Accordingly, attempts to regenerate the liver via the promotion of hepatic cell replication is a vital issue in achieving effective treatment for liver damage. Stelic believes that administration of an effective dose of a specific neutralizing agent for chemokine CXCL10 will offer a new treatment by means of promoting the histological and functional repair of hepatic cells.

**About Stelic Institute & Co**

Stelic Institute & Co was established in November 2004 to pursue research to uncover the dynamics of somatic stem cells *in vivo*, and to carry out R&D in regenerative medicine on the basis of a completely innovative business model never before seen in a bioventure enterprise. Stelic is placing top priority in its patent strategy to the patenting of somatic stem cell therapeutic concepts, in addition to expanding the scope of associated patents with the objective of achieving a unique market expansion.

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