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Novel potential approach to prevent infection in patients with liver failure

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Findings published in the American Association for the Study of Liver Diseases journal, *Hepatology*, indicate that infection, the commonest cause of mortality in patients with acute liver failure (ALF), may be decreased by inhibiting the activity of a protein found in saliva called SLPI (secretory leukocyte protease inhibitor). New research has found that this protein, produced by the body in response to injury, plays a vital role in patients with ALF.

Acute liver failure occurs when there is rapid death of liver cells (hepatocytes). According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) drug-induced liver injury, particularly acetaminophen (Tylenol®) overdose, is the most common cause of acute liver failure in the U.S. and other developed countries. Previous studies have demonstrated that infection is the commonest complication in liver failure and is the leading cause of premature death in over 50% patients.

"Infection, namely sepsis, in patients with acute liver failure may be linked to an inadequate response of the body's immune system," explains Dr. C.G. Antoniades, an MRC Clinician Scientist from Imperial College London and King's College London. "Our study is the first to investigate the role of this particular protein in liver failure patients."

A team of scientists and clinicians at King's College London, King's College Hospital NHS Foundation Trust and Imperial College London studied 98 patients with liver failure as well as 24 healthy volunteers.

Results show that patients with ALF had elevated levels of this key molecule (SLPI) in the liver and circulating round the body, that impaired the ability of immune cells, monocytes/macrophages, to combat infection. When researchers blocked the activity of the SLPI molecule the function of monocytes/macrophages was restored, similar that seen in healthy individuals. When SLPI protein was added to healthy immune cells, it rendered them poorly responsive to infectious organisms that are commonly encountered in patients with liver failure.

"Our findings indicate that SLPI is a critical mediator of excessive anti-inflammatory responses in ALF which explains the susceptibility to sepsis/infection in these patients," concludes Dr. Antoniades. "Further study of therapeutic options to inhibit the activity of SLPI in the management of sepsis in liver failure are needed."

More information: "Secretory Leukocyte Protease Inhibitor: A Pivotal Mediator of Anti-Inflammatory Responses in Acetaminophen Induced Acute Liver Failure." Charalambos Gustav Antoniades, Wafa Khamri, Robin D Abeles, Leonie S Taams, Evangelos Triantafyllou, Lucia A Possamai, Christine Bernsmeier, Ragai R Mitry, Alistair O'Brien, Derek Gilroy, Robert Goldin, Michael Heneghan, Nigel Heaton, Wayel Jassem, William Bernal, Diego Vergani, Yun Ma, Alberto Quaglia, Julia Wendon and Mark Thursz. *Hepatology*; (DOI: 10.1002/hep.26933).

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