How blocking the 'Programmed Death 1' protein may treat or prevent sepsis and severe infection

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Scientists have made an important discovery that could lead to new drugs that reduce the severity of blood infections leading to sepsis. Research presented in the August 2010 issue of *Journal of Leukocyte Biology* shows how interfering with the function of the cell membrane protein called "Programmed Death 1" (PD-1) improves survival in a clinically relevant model of severe infection.

"Clinical trials of anti-PD-1 are currently underway in patients with cancer and in patients with hepatitis C," said Richard S. Hotchkiss, M.D., co-study author from the Department of Anesthesiology at Washington University School of Medicine in St. Louis, MO. "It is hoped that blocking PD-1 will lead to enhanced immune function and a resultant improved tumor elimination and viral eradication respectively."

To make this discovery, the researchers studied two groups of mice with a surgically induced severe infection that simulates a ruptured appendix in humans. One group of mice received an inactive antibody while the other group of mice received an antibody that blocked PD-1. The mice that received the PD-1 blocking antibody had a greater survival rate when compared to the mice that received the inactive control antibody. Results show that PD-1 inhibits the ability of the immune system to fight infection by suppressing the function of immune cells. Thus, blocking PD-1 can restore the ability of the host to combat infections, also helping to improve chances for survival.

"This research may lead to a new class of drugs that could treat severe bacterial infections, including those that are becoming increasingly resistant to today's antibiotics," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology, "This study is one of science's many steps to keep pace or a step ahead of the evolutionary progress that these microrganisms are making."

More information: Pavan Brahmamdam, Shigeaki Inoue, Jacqueline Unsinger, Katherine C. Chang, Jonathan E. McDunn, and Richard S. Hotchkiss Delayed administration of anti-PD-1 antibody reverses immune dysfunction and improves survival during sepsis. J Leukoc Biol 2010 88: 233-240. doi: 10.1189/jlb.0110037

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