Researchers mirror human response to bacterial infection and resolution in mice

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Imitating human diseases using an animal model is a difficult task, but Thomas Jefferson University researchers have managed to come very close.

Reporting in the Proceedings of the National Academy of Sciences, a team of Jefferson immunologists found that a specialized "human immune system" mouse model closely mimics a person's specific response and resolution of a tick-borne infection known as relapsing fever, caused by the bacteria Borrelia hermsii.

The response is so strikingly similar that it gives good reason for researchers to apply the strategy to a host of other infections to better understand how the immune system attempts to fights them— which could ultimately lead to precise treatment and prevention strategies.

"This is first time an interaction of an infectious agent with a host, the progression of the disease and its eventual resolution recapitulates what you would see in a human being," said Kishore R. Alugupalli, Ph.D., Assistant Professor of Microbiology and Immunology at Thomas Jefferson University and the Kimmel Cancer Center at Jefferson. "Our model is not only a susceptible model, but it actually tells us how the human immune system is functionally working. That is the big difference from the previous studies."

What really surprised the team is that the mouse physiological environment was able to facilitate the development of human B1-like

cells, which is specialized type of antibody producing systems used to fight infection due to a variety of bacterial pathogens, including Pneumococcus and Salmonella.

In the study, researchers transferred hematopoietic stem cells from human umbilical cord blood into mice lacking their own immune system. This resulted in development of a human immune system in these mice. These "human immune system" (HIS) mice were then infected to gauge response.

According to the authors, an analysis of spleens and lymph nodes revealed that the mice developed a population of B1b-like cells that may have fought off the infection. Researchers also observed that reduction of those B cells resulted in recurrent episodes of bacteremia, the hallmark of relapsing fever.

"The B1b cells in humans had been speculated, but never confirmed," said co-author Timothy L. Manser, Ph.D., Professor and Chair of the Department of Microbiology and Immunology at Jefferson. "We found that in mice, the B1b cell subset is critically important for resolution of this type of bacterial infection."

"This would indicate that there is a functional equivalent of the subset in humans that has not been previously recognized," he added.

The mouse model with relapsing fever recapitulates many of the clinical manifestations of the disease and has previously revealed that T cell-independent antibody responses are required to resolve the bacteria episodes. However, it was not clear whether such protective humoral responses are mounted in humans.

"It's an amazing platform that could be used to really study how the human B1 cells could work against a variety of bacterial and viral

infections," said Dr. Alugupalli.

More information: www.pnas.org/content/early/201 … 776109.full.pdf+html

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