Bone marrow plays critical role in enhancing immune response to viruses: study

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Researchers at Mount Sinai School of Medicine for the first time have determined that bone marrow cells play a critical role in fighting respiratory viruses, making the bone marrow a potential therapeutic target, especially in people with compromised immune systems. They have found that during infections of the respiratory tract, cells produced by the bone marrow are instructed by proteins to migrate to the lungs to help fight infection. The data are published in the current issue of *Cell Host & Microbe*.

Led by Carolina Lopez, PhD, Assistant Professor of Microbiology at Mount Sinai School of Medicine, the research team evaluated the immune response to influenza infection in the lung and blood of mice. The team found that in the days following infection the lung became inflamed and produced interferons, or infection-fighting proteins, a message that alerted bone marrow cells of the presence of the virus and signaled them to prepare to fight the infection. The researchers determined that many new cells generated in the bone marrow enter the infected lung to help fight infection.

Previous studies of the immune response against respiratory viruses focused on the regulation of specific immune cells that acquire a specific function in the lymph nodes of the infected animals. These adaptive cells develop relatively late during infection, but are important for the clearance of the virus and for protection against reinfection with the same virus. This study is the first to show that the immune response also involves the earlier activation of cells in the bone marrow, and that

this earlier response is also critical for the efficient clearance of the virus.

"Our research shows that in addition to the regulation of the development of cells, the immune response is regulated at a much earlier stage by influencing cells in the distal bone marrow and that this regulation of what is known as the innate immune response is important for the efficient clearance of the infection," said Dr. Lopez. "Very limited research has been done to evaluate bone marrow's response to a virus infection. Our study is the first to determine the pivotal role bone marrow cells play in fighting a respiratory infection. This discovery has broad-reaching implications in boosting protection against viruses."

After the mice were infected, researchers analyzed the inflammatory response daily by measuring the level of immune cells present in the lung, blood and bone marrow. They noticed that interferons, or anti-viral proteins, and cytokines, a type of immune cell, were produced exclusively by the infected lung but cells in the bone marrow responded to the infection with the expression of a number of anti-viral proteins known to be induced by interferons. Further analysis showed that cells from the bone marrow of infected mice were protected from the virus and were able to produce higher levels of cytokines upon exposure to a virus. The analysis showed that the bone marrow supplies the lung with infection-fighting cells, and that acute infection of the lung is sensed by bone marrow cells, cuing them to be prepared to fight the virus.

"The findings may be especially significant for people with compromised immune systems, including transplant and HIV patients," said Dr. Lopez. "These patients are treated with anti-viral drugs to help them avoid infection or reactivation of chronic viruses, as these types of infections are especially dangerous and could become systemic in people with suppressed immune systems. This new discovery may open new avenues for prevention and treatment of lethal infections."

Provided by The Mount Sinai Hospital