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A few cells could prevent bone marrow transplant infections

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Bone marrow transplantation is a life-saving therapy for patients with blood cancers like leukemia or lymphoma. However, the depletion of the patient's immune system prior to transplantation can put patients at risk of for an infection by a virus called cytomegalovirus (CMV) that can be life threatening in these immune-compromised individuals. Now, researchers have found that a very small subset of anti-viral immune cells, transplanted along with a donor's blood stem cells, could be enough to fight and even prevent the disease caused by CMV, in research conducted in mice and published Jan 16th in the *Journal of Immunology*.

Anywhere between 50-80 percent of adults in the United States are infected with CMV, although the virus is kept under control by a healthy immune system. In patients with weakened immune systems, however, CMV can become reactivated and can cause life-threatening pneumonia, among other symptoms. Current treatment includes antiviral medication, but these are not always well tolerated by patients and they also harm the very cells that bone marrow transplantation aims to replenish.

"We know that re-establishment of anti-viral immunity in these patients is critical to fully control cytomegalovirus in bone marrow transplant recipients," says senior author Christopher Snyder, Ph.D., an Assistant Professor of Microbiology and Immunology at Thomas Jefferson University. "Our study suggests that, in addition to infusing stem cells that restore the bone marrow, life-long anti-CMV immunity may be rapidly restored by also infusing a subset of anti-viral immune cells that have stem cell-like properties."

Currently, investigators around the world are experimenting with restoring the immune cells responsible for keeping CMV in check by transplanting those specific anti-viral cells from healthy donors - a type of immunotherapy. "The problem," says Dr. Snyder, "is that current methods for selecting anti-viral immune cells may inadvertently limit the ability of those cells to restore life-long immunity."

To date, researchers have focused on developing anti-CMV immunotherapy around the "fighter" cells - called CD8 T effector cells - that attack and kill virally-infected host cells. These cells are selected and expanded in the lab to increase their numbers, but this process may limit their life-span and ability to divide.

Dr. Snyder and colleagues found that CMV-specific fighter T cells divided poorly in response to CMV infection or reactivation in mouse models. They hypothesized that a different type of CD8 T cells - one that acts more like a stem cell - could help control the infection long term. His group showed that a small number of stem-cell like CD8 T cells -called "memory" cells -were enough to produce and repeatedly replenish all of the T-effector cells needed to fight the disease. The infused memory cells became major contributors to the recipient anti-viral immune response, persisting for at least 3 months of time and producing the "fighter" cells at a steady stream.

In order to survey whether these cells have counterparts in humans, the researchers compared the genomic fingerprint - the profile of genes that were turned up or down - of mouse and human memory T cells that were specific for CMV and found that the two had similar profiles. "This suggested that human and mouse CMV-specific memory T cells are very similar populations. Therefore infusing similar cells into humans could improve on immunotherapeutic methods for controlling CMV infection," said first author Michael Quinn MD/PhD student in the Department of Microbiology and Immunology at Thomas Jefferson

University. "This may be a valuable approach to keep the disease from emerging in people."

"Our data argue for developing new clinical trials focused specifically on using these T memory cells, in order to determine if it would indeed be better than current therapeutic options," said Dr. Snyder.

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