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Finding hiding place of virus could lead to new treatments

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Discovering where a common virus hides in the body has been a long-term quest for scientists. Up to 80 percent of adults harbor the human cytomegalovirus (HCMV), which can cause severe illness and death in people with weakened immune systems.

Now, researchers at Wake Forest Baptist Medical Center's Institute for Regenerative Medicine report that stem cells that encircle blood vessels can be a hiding place, suggesting a potential treatment target.

In the *American Journal of Transplantation* (online ahead of print), senior scientist Graca Almeida-Porada, M.D., Ph.D., professor of regenerative medicine at Wake Forest Baptist, and colleagues report that perivascular stem cells, which are found in bone marrow and surround blood vessels in the body's organs, are a reservoir of HCMV.

The virus, which is part of the herpes family, is unnoticed in healthy people. Half to 80 percent of all adults in the U.S. are infected with HCMV, according to the Centers for Disease Control and Prevention. In people with weakened immune systems, including those with HIV, undergoing chemotherapy, or who are organ or bone marrow transplant recipients, the virus can become re-activated.

Once re-activated, HCMV can cause a host of problems – from pneumonia to inflammation of the liver and brain – that are associated with organ rejection and death.

"There are anti-viral medications designed to prevent HCMV from re-activating, but HVMC infection remains one of the major complications after both organ and bone marrow transplants," said Almeida-Porada. "The question scientists have been asking for years is, 'Where does the virus hide when it is latent?' Maybe if we knew, we could target it."

Scientists have previously shown that one hiding place is hematopoietic stem cells, which give rise to blood cells. "There has been research on and off looking for the other hiding places," said Almeida-Porada. "Identifying the cells that can harbor the virus and are responsible for its re-activation could potentially lead to development of novel targeted therapies."

Almeida-Porada's team hypothesized that cell populations in the body's tissues may be able to harbor the virus and suspected that perivascular cells that surround blood vessels were a likely culprit. Their suspicions were confirmed when testing revealed that perivascular cells are susceptible to HCMV infection and that the virus can grow within these cells.

The team compared the susceptibility of perivascular cells from the liver, brain lung and bone marrow to the virus and found the highest rate of HCMV infection in lung perivascular cells.

"This may explain why pneumonia is the primary manifestation of the HCMV infection in bone marrow transplant recipients," said Almeida-Porada.

To further test their hypothesis about perivascular cells, the team evaluated the bone marrow of 17 healthy individuals who tested positive for HCMV and detected the virus in the marrow of nine of them. Bone marrow was selected to test because it is very vascular tissue and is a rich source of perivascular cells.

"We have found another source of cells that can harbor HCMV virus," said Almeida-Porada. "Knowing the identity of the cells opens the possibility of targeting treatments to stop its re-activation."

Provided by Wake Forest University Baptist Medical Center