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A common virus may help inform treatment planning for stem cell transplant patients

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Most healthy people barely notice infection with the human cytomegalovirus (hCMV), a form of the herpes virus that has evolved with humans over thousands of years and usually lays dormant in the body after initial infection. Now, in a study recently published in the journal *PLOS ONE*, a team of scientists from VCU Massey Cancer Center have shown a genetic relationship between the reactivation of hCMV and the onset of graft-versus-host disease (GVHD), a potentially deadly condition in which the immune system attacks healthy tissue following a bone marrow or stem cell transplant.

This new finding is the latest in a line of research led by physician-scientist, Amir Toor, M.D. Toor and his colleagues have been working to create computer models that simulate immune system recovery following stem cell transplantation in hopes of reducing complications such as GVHD and making transplantation an option for more patients. While the relationship between GVHD and hCMV has been described in medical literature since the 1980s, the connection was not well understood until one of Toor's mentees, Charles Hall, M.S., showed genetic similarities between the virus and tissue expressing GVHD.

"Until now, physicians have taken a 'wait and see' approach to antiviral therapies following transplantation," says Toor, a hematologist-oncologist in the Bone Marrow Transplant Program and member of the Developmental Therapeutics research program at VCU Massey Cancer Center as well as professor in the Division of Hematology, Oncology and Palliative Care at the VCU School of Medicine. "But, based on our data,

we believe there is a case for early intervention with personalized antiviral treatments following stem cell transplantation in order to suppress hCMV reactivation."

Toor and his team sequenced the DNA of 77 stem cell donors and their recipients. They found a significant number of patients (18) experienced hCMV reactivation and GVHD, and a majority (13) of those patients experienced hCMV reactivation prior to GVHD onset. Using the information they uncovered through DNA sequencing along with data from a new database established by the Center for the Study of Biological Complexity at VCU called Cross Reactive Open Source Sequence Database, developed by Charles Hall, M.S., and Vishal Koparde, Ph.D., the team uncovered a novel connection between the virus and GVHD.

The scientists found similarities in HLA-bound peptide sequences between human and hCMV genomes. The HLA (human leukocyte antigen) is a system of genes responsible for regulating immune responses, and peptides are short chains of amino acids that play key roles in regulating the activities of other molecules. It turns out that hCMV peptides are very similar to peptides expressed in GVHD-affected tissue.

"We developed a computer model that shows how the immune system can react to hCMV peptides to trigger a graft-versus-host response," explained Toor. "By sequencing the DNA of stem cell donors and recipients, we believe we can use computer modeling to further identify patients at risk and better personalize post-transplant care to decrease the potential for graft-versus-host disease."

Toor hopes to further explore the relationship between hCMV and GVHD. His team is currently working to secure funding to apply their model to larger patient data sets.

More information: Charles E. Hall et al. Sequence homology between HLA-bound cytomegalovirus and human peptides: A potential trigger for alloreactivity, *PLOS ONE* (2017). DOI: 10.1371/journal.pone.0178763