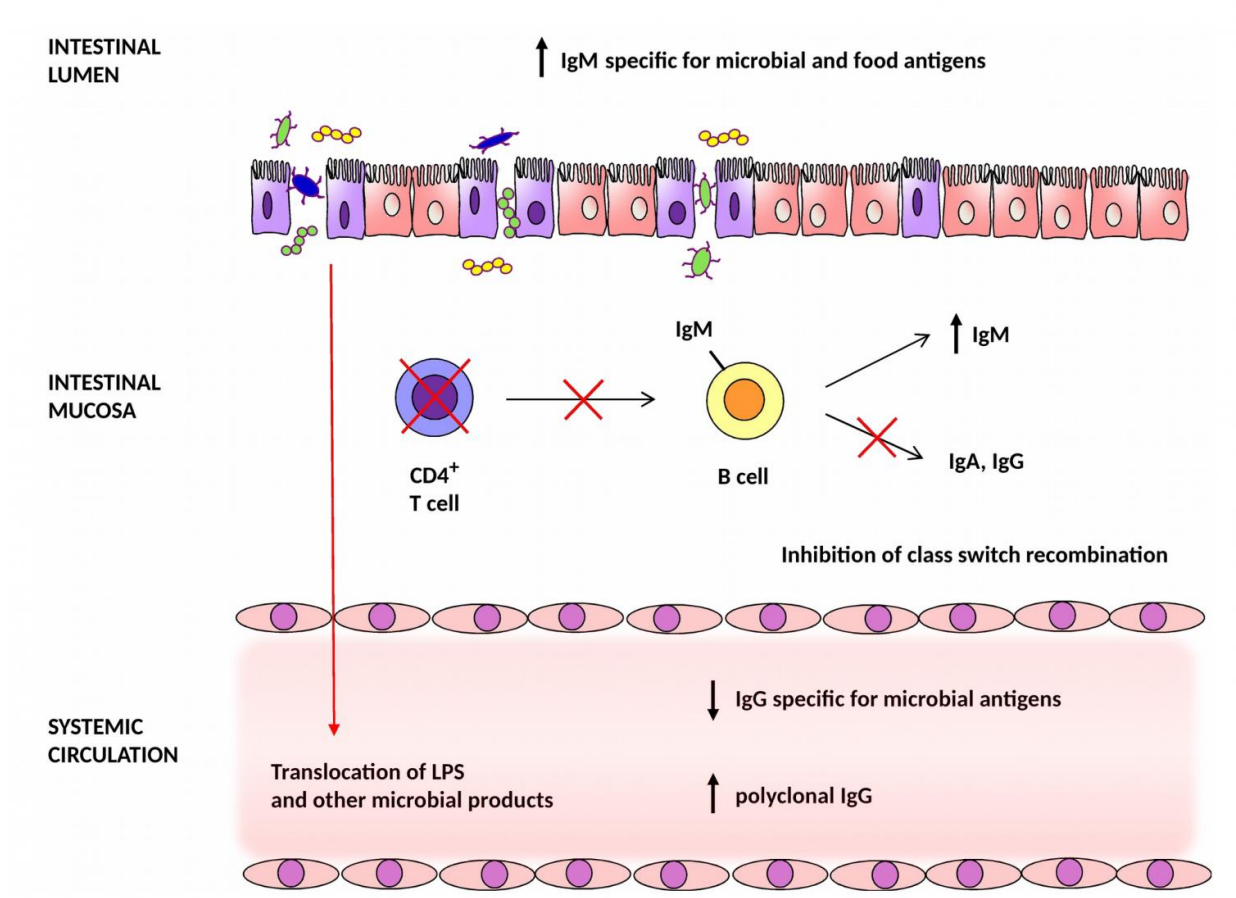
How the border guards fail in HIV infection

January 26 2017



Dysregulation of systemic and mucosal humoral responses to microbial antigens in HIV-1-infected individuals Credit: Hel, Z, et al (2017)

The barrier between the gut and the bloodstream is severely damaged in

the first few weeks of infection by HIV-1 virus. This can allow whole microbes in the intestine, as well as tiny pieces of bacteria, to enter the blood and provoke the inflammation that can lead to AIDS—even when replication of the virus is controlled by drug therapy.

Using a novel technique to analyze antibodies in fluid collected from intestines of 81 HIV-1-infected and 25 control individuals, University of Alabama at Birmingham researchers have found abnormal gut antibody levels in people infected with HIV-1. This antibody dysregulation, they say, may be an important factor contributing to the failure of the gut to prevent the inflammatory microbial invasion of the bloodstream.

The researchers, led by Zdenek Hel, Ph.D., associate professor in the UAB Department of Pathology, used a technique called protein microarray analysis. A total of 39 different protein antigens from gut bacteria—antigens that are known to elicit antibody immune responses in humans against those antigens—were used to bind antibodies from gut wash fluid. A variety of food antigen proteins were also used to bind antibodies. Researchers then could test what types of antibodies were produced in HIV-1-positive and HIV-1-negative subjects.

Hel and colleagues found that both infected and uninfected subjects made antibodies against these bacterial and food antigens. However, the two groups differed greatly in the types of antibodies produced.

People with HIV-1 had higher proportions of a less mature form of antibody called immunoglobulin M, or IgM, as compared with the antibody forms called IgG and IgA that are better at binding antigens. This suggests that immune system cells in the inner layer of the intestine, the mucosa, are unable to make the types of antibodies needed to prevent bacterial fragments from entering the bloodstream.

Further, the researchers say, accumulation of IgM in the gut mucosa may

form immune complexes that exacerbate inflammation.

It is well-known that antibody-producing cells switch from early production of IgM to later production of IgG and IgA in people with healthy immune systems. It is also well-understood that HIV-1 infections cause early and profound depletion of the immune memory cells in the mucosa that are indispensable for that immune-type switching.

Hel's finding that HIV-1 infection is associated with significant elevation of IgM levels and decreased ratios of IgG/IgM and IgA/IgM is consistent with the loss of those mucosal memory CD4+ T cells.

"This study involved a relatively small number of patients and did not include direct analysis of intestinal tract cells," Hel said. "Nonetheless, the findings could improve our understanding of how HIV-1 undermines the immune system and inform research into potential new treatments."

The paper, "Dysregulation of systemic and mucosal humoral responses to microbial and food antigens as a factor contributing to microbial translocation and chronic inflammation in HIV-1 infection," is published in *PLOS Pathogens*.

More information: Hel Z, Xu J, Denning WL, Helton ES, Huijbregts RPH, Heath SL, et al. (2017) Dysregulation of Systemic and Mucosal Humoral Responses to Microbial and Food Antigens as a Factor Contributing to Microbial Translocation and Chronic Inflammation in HIV-1 Infection. *PLoS Pathog* 13(1): e1006087. journals.plos.org/plospathogen … journal.ppat.1006087

Provided by University of Alabama at Birmingham