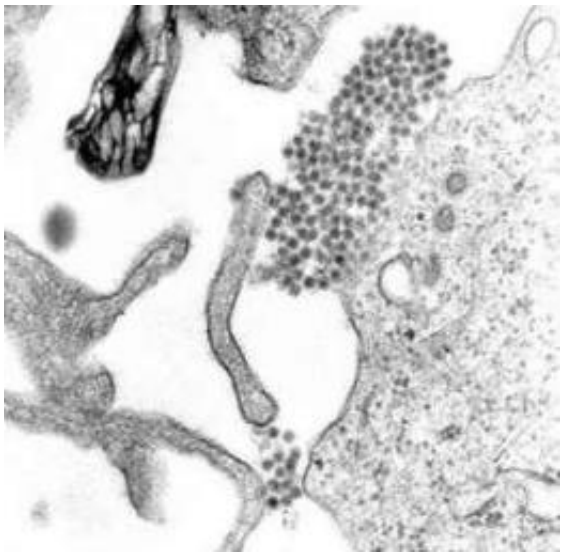
Researchers find T cells target dengue virus at the skin infection site

12 March 2015, by Bob Yirka



A TEM micrograph showing Dengue virus virions (the cluster of dark dots near the center). Image: CDC

(Medical Xpress)—A team of researchers working in Singapore has found that human T cells actually target dengue viral infections in the skin, which is the normal infection site. In their paper published in the journal *Science Translational Medicine*, the team describes how they found that T cells in patients were able to recognize the dengue virus and also expressed a marker that caused them to move to the skin.

Dengue (fever) is a mosquito borne tropical disease that strikes approximately 100 million people every year. It is characterized by fever, muscle and joint pain and headaches along with a skin rash. People stricken typically survive unless the disease develops into hemorrhagic fever. Though scientists have been working to find a cure for the disease for thousands of years, thus far, they have not found much success. Treatment typically focuses on relieving symptoms. In this new effort, the researchers focused on what T cells in the human body do once a mosquito deposits a viral load into the skin.

The team started by looking at tissue specific markers—ID tags that indicate where they are to go when the immune system is called into action. They found that certain T cells were dengue specific and to their surprise they were not indicators that would lead the cells to the GI track, which for patients, can be a viral hot spot (causing pain and bleeding). Instead, the markers led the T cells to the skin, which would be the site of the initial infection—and which would of course allow the T cells to combat the virus right from the get go.

The team was able to demonstrate that the T cells recognized the virus when their paths crossed and that they were capable of calling for an immune response when it happened, which typically meant attacking infected cells and making them burst. The findings by the team might eventually explain why patients develop a week-long rash—it could be the result of the battle between the virus and T cells raging shortly after the initial infection. The hope, however, is that the new findings might lead to a better vaccine, perhaps one that is directed at infections still confined to the skin.

More information: Virus-specific T lymphocytes home to the skin during natural dengue infection Sci Transl Med 11 March 2015: Vol. 7, Issue 278, p. 278ra35 . *Sci. Transl. Med.* DOI: 10.1126/scitranslmed.aaa0526

Abstract

Dengue, which is the most prevalent mosquito-borne viral disease afflicting human populations, causes a spectrum of clinical symptoms that include fever, muscle and joint pain, maculopapular skin rash, and hemorrhagic manifestations. Patients infected with dengue develop a broad antigen-specific T lymphocyte response, but the phenotype and functional properties of these cells are only partially understood. We show that natural

infection induces dengue-specific CD8+ T lymphocytes that are highly activated and proliferating, exhibit antiviral effector functions, and express CXCR3, CCR5, and the skin-homing marker cutaneous lymphocyte-associated antigen (CLA). In the same patients, bystander human cytomegalovirus –specific CD8+ T cells are also activated during acute dengue infection but do not express the same tissue-homing phenotype. We show that CLA expression by circulating dengue-specific CD4+ and CD8+ T cells correlates with their in vivo ability to traffic to the skin during dengue infection. The juxtaposition of dengue-specific T cells with virus-permissive cell types at sites of possible dengue exposure represents a previously uncharacterized form of immune surveillance for this virus. These findings suggest that vaccination strategies may need to induce dengue-specific T cells with similar homing properties to provide durable protection against dengue viruses.

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