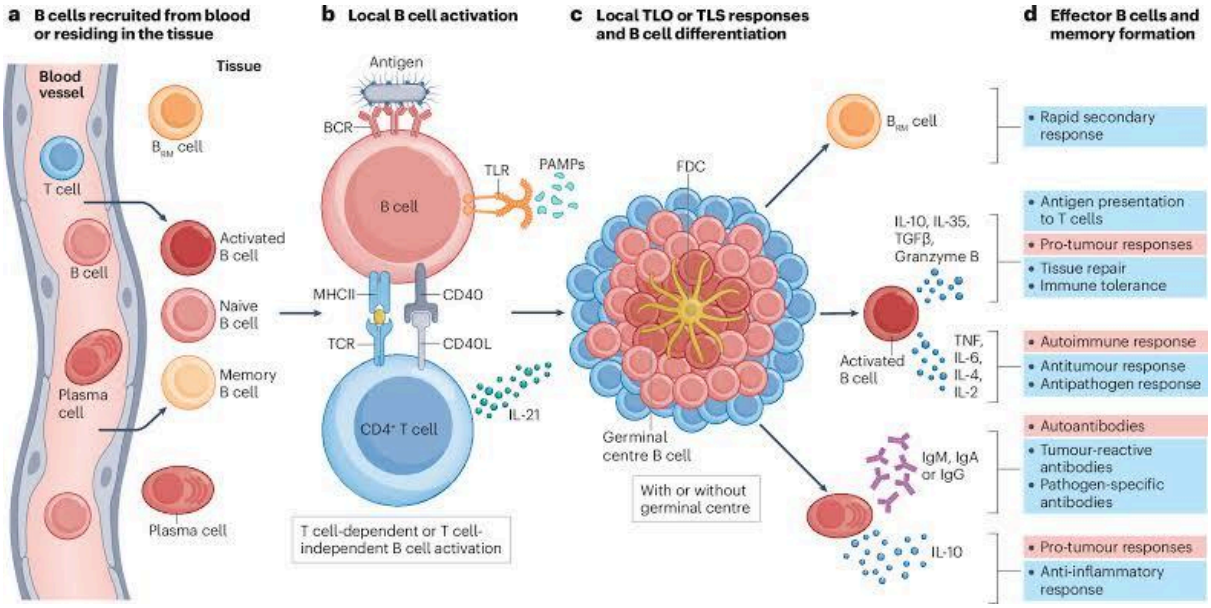
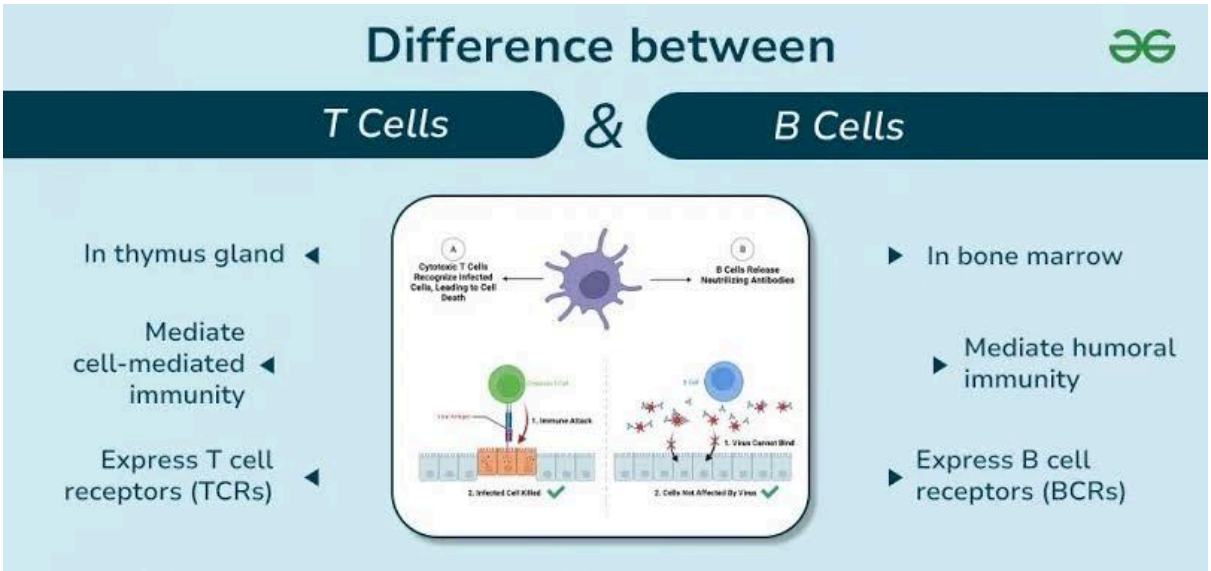
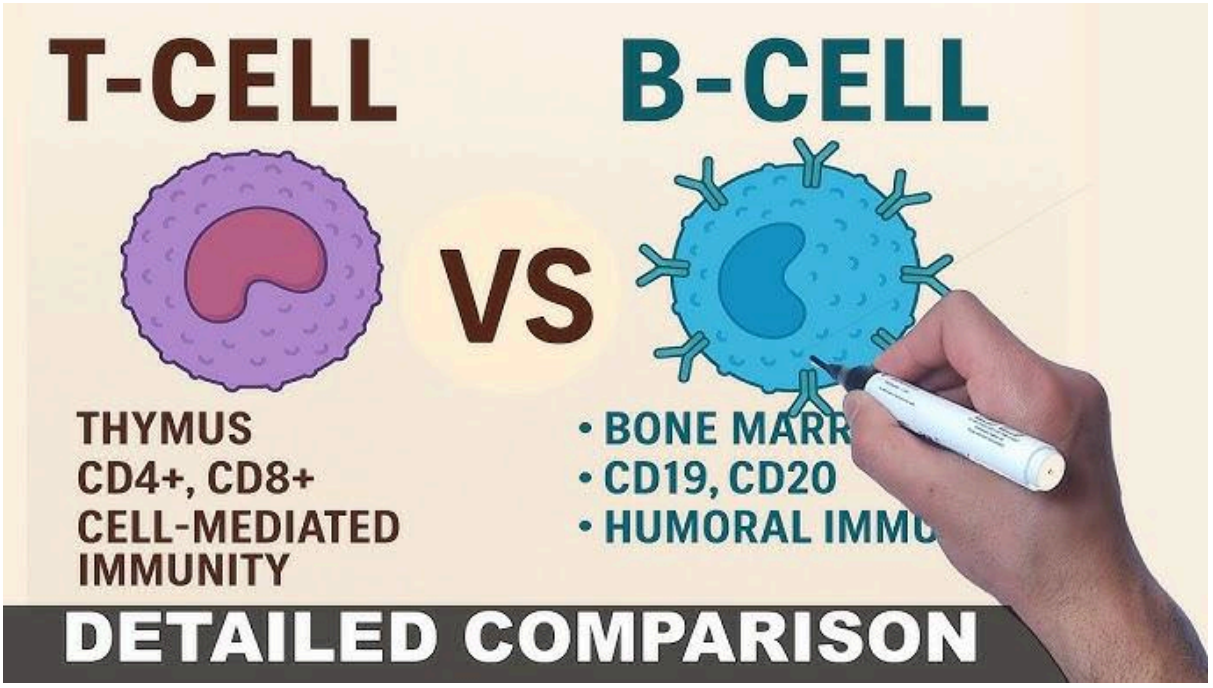
Dengue virus infects memory B cells to evade immune defenses. 7/ 26/2026



Researchers at the University of Vermont Robert Larner, M.D. College of Medicine and Upstate Medical University in Syracuse, NY, have discovered that dengue virus can infect and replicate inside memory B cells, immune cells traditionally understood to help protect the body from infection. The findings, *published July 20 in the Journal of Virology*, reveal a previously unrecognized way the virus may evade immune defenses and point toward new strategies for treating a disease that threatens 40 percent of the world's population, including parts of the southern US.The study was conducted by researchers in the laboratories of Sean Diehl, Ph.D., professor of Microbiology and Molecular Genetics at the University of Vermont, and Adam Waickman, Ph.D., associate professor of Microbiology and Immunology.

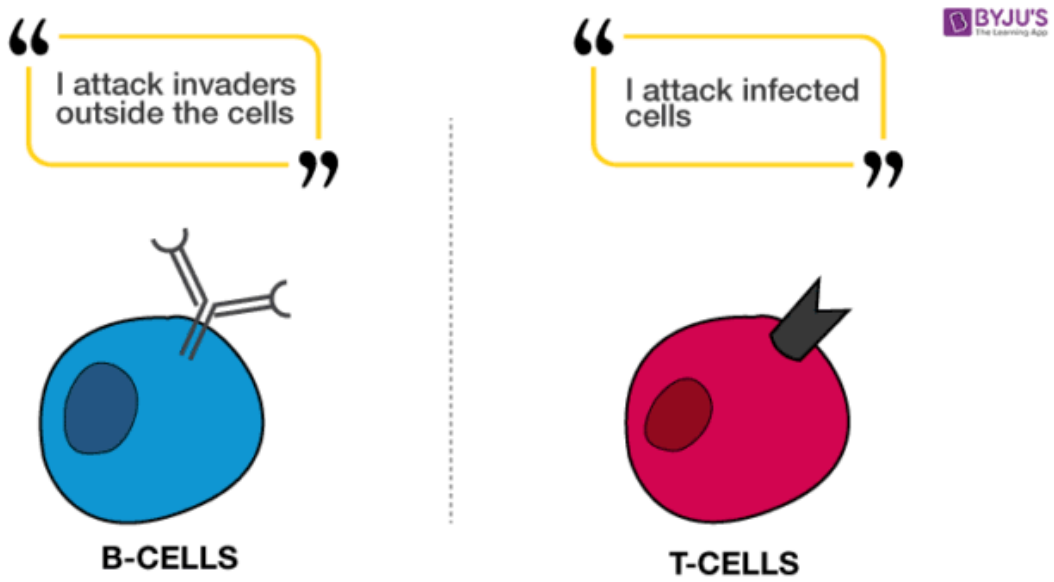


Four different dengue viruses (DENV1-4) are transmitted by tropical mosquitoes, infecting an estimated 100 million people each year worldwide. More than four billion people live in regions where dengue-carrying mosquitoes are present. Symptoms can include high fever, severe headaches, muscle and bone pain, and, in severe cases, life-threatening complications caused by damage to blood vessels and dangerously low blood pressure.



Scientists have long known that a previous dengue infection can sometimes make a later infection with a different dengue virus strain more severe, a phenomenon known as antibody-dependent enhancement (ADE). In ADE, antibodies generated during a first infection bind to a second dengue strain but fail to neutralize it, instead helping the virus enter certain immune cells.

Previous work from the Diehl and Waickman laboratories identified another possible pathway. The researchers showed that dengue virus could enter B cells - the cells that make antibodies - through the B cell receptor, a molecule on the cell surface responsible for recognizing pathogens. The team named this process B cell receptor-dependent enhancement (BDE).



In the new study, co-led by UVM Cellular, Molecular, and Biomedical Science graduate student Gaby Madrigal and Upstate staff scientist, and recent PhD graduate Chad Gebo, the team demonstrated for the first time that dengue-specific memory B cells can become infected by all four dengue virus types and produce infectious virus. Memory B cells are generated following an initial infection and persist for years, making them likely targets during subsequent exposure to a different dengue strain.

Using advanced microscopy techniques, in collaboration with Menelaos Symeonides, Ph.D., assistant professor of Microbiology and Molecular Genetics at UVM, the team was able to visualize dengue virus entering these cells and identify potential vulnerabilities in the process by targeting molecular signaling pathways activated by the B cell receptor that are required for infection.

> *It is a high bar to show something genuinely new in dengue research and I am very proud of this high-quality data produced by our trainees who rose to the occasion." (Sean Diehl, Ph.D., Professor of Microbiology and Molecular Genetics, University)*

The findings could have important therapeutic implications. There are currently no approved drugs that specifically target dengue virus, and vaccines continue to face challenges related to broad implementation and effectiveness across different populations. In contrast, several drugs that target B cells are already approved for treating cancers and autoimmune diseases, raising the possibility that similar approaches could be adapted for dengue treatment.

Researchers say future strategies might also include therapies designed to selectively eliminate or modify high-risk memory B cells after an initial dengue infection, potentially reducing the risk of severe disease following later exposure.

"This work challenges existing assumptions about how dengue interacts with the immune system," said Diehl. "By revealing a previously unrecognized route of infection, it opens new avenues for understanding dengue disease and developing interventions to prevent or treat it."

The researchers believe the discovery represents an important advance in understanding how dengue virus subverts immune defenses and may help guide the development of future therapies aimed at reducing the global burden of the disease.

Journal reference: Madrigal, G., *et al*. (2026). Molecular and biophysical requirements for B cell receptor-dependent enhancement of dengue virus infection. *Journal of Virology*. DOI: 10.1128/jvi.02216-25. https://journals.asm.org/doi/10.1128/jvi.02216-25

Advances in the diagnosis and treatment of dengue-associated ocular diseases
QIU Suo, Eye Science, 2025