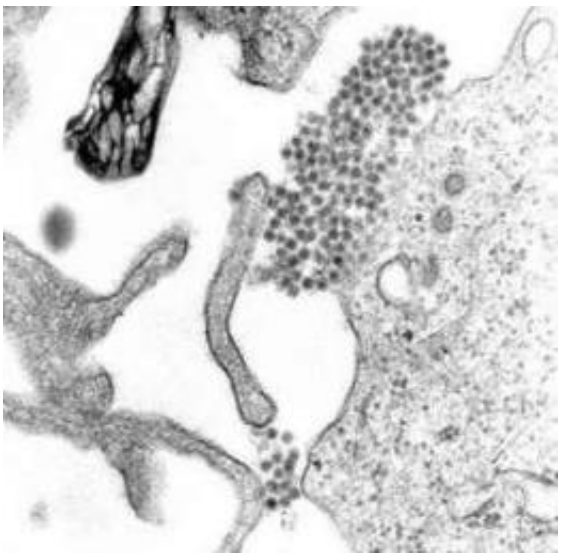
# Interaction between two immune cell types could be key to better dengue vaccines, study shows

February 7 2019



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

Researchers at Duke-NUS Medical School have demonstrated for the first time a physical interaction between two types of immune cells that plays an important role in the early fight against dengue virus infection.

Dengue virus is widespread in the tropics and is transmitted by mosquitos. Dengue virus infection incidence has grown dramatically in recent years, with estimates suggesting 390 million infections annually. It

manifests as a severe, flu-like illness with high fever, and can in some cases develop into a life-threatening condition. No treatments exist for dengue fever. A vaccination does exist but is only recommended for use in people who have had dengue at least once before.

"We need much better vaccinations for dengue and for related viral pathogens that are injected into the skin by mosquitoes," said Dr. Ashley St. John, Assistant Professor of Duke-NUS' Emerging Infectious Diseases (EID) Signature Research Programme and corresponding author of the study.

Very little is known about how the immune system first recognizes viruses, such as dengue virus, in the skin, she explains. Understanding how this happens could help design better vaccines for this and similar viruses.

Dr. St. John and study co-author Dr. Chinmay Mantri, a Research Fellow in the EID Programme, investigated the role played by a type of immune cell, called a mast cell, which patrols the skin to guard against infections. Mast cells are largely known for recruiting other types of immune cells through the release of special attracting chemicals. Much is understood about how mast cells react in the presence of bacteria and parasites, but investigations into their roles with viruses have only recently begun.

The researchers analysed how the dengue virus reacted in an animal model without any mast cells and compared the responses to animals with normal numbers of mast cells in order to determine which reactions were dependent on the presence of mast cells.

They found that mast cells attracted several types of immune cells to the site of infection. One of these is called gamma delta (γδ) T cells. Not only were γδ T cells attracted to the infection site, they also physically interacted with the mast cells, something not previously observed in viral

infections. The γδ T cells bound to a receptor present on the mast cells called the endothelial protein C receptor. This so-called 'immune synapse' led to the T cells activating, proliferating, and producing interferon gamma, which initiated their role in killing cells infected with dengue.

"These [immune synapse] structures of cells in the process of communication were very exciting and visually striking to us when we first made this observation, and provide a glimpse into the ways that cells must work together to fight infection," said Dr. St. John.

Professor Patrick Casey, Senior Vice Dean of Research, Duke-NUS Medical School, commented, "According to recent news, the number of dengue cases in Singapore since the start of 2019 have been at their highest in over two years. This timely study is all the more important as an example of how we develop insights from outstanding basic research that can one day lead to clinical innovations to protect against such diseases."

The study authors next plan to use the results of their research to work toward the development of better vaccines for viruses, like dengue, that are spread by mosquitoes.

**More information:** Mantri CK, St John AL (2019). Immune synapses between mast cells and γδ T cells limit viral infection. *Journal of Clinical Investigation*. DOI: 10.1172/JCI122530

Provided by Duke-NUS Medical School