Understanding the initial immune response after dengue virus infection

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A study led by scientists at the Walter Reed Army Institute of Research sheds new light on the body's initial response to dengue virus (DENV) infection, describing the molecular diversity and specificity of the

antibody response. These results, published in *EBioMedicine*, a journal published by *The Lancet*, identify a heretofore unappreciated role for DENV-reactive IgA antibodies.

DENV is a member of the clinically-relevant Flavivirus genus alongside Zika virus, yellow fever virus and others. With four distinct serotypes, DENV is thought to infect between 280 and 550 million people worldwide every year.

While the majority of individuals suffering from dengue fever recover without showing severe symptoms or requiring extensive medical intervention, approximately 500,000 individuals per year develop severe dengue which has a mortality rate of up to 20%. Dengue is of particular concern for deploying Service Members, and the development of effective countermeasures to prevent dengue infection is a priority for the Department of Defense.

Subclinical exposure is a significantly complicating factor for public health and vaccine development, as those individuals previously exposed to one DENV serotype are at greater risk for severe symptoms than those with no previous exposure. Therefore, determining the previous exposure history of a patient experiencing symptoms of DENV infection can provide insight to the patient's risk of developing severe disease.

In this study, researchers used single cell RNA sequencing technology to measure the products of B cell plasmablasts, the antibody-producing cells found in greatest numbers immediately after DENV exposure. They also used a range of analyses to describe the ability of these antibodies to neutralize DENV and characterize their structure.

They discovered that IgA represented a significant fraction of antibodies expressed by B cell plasmablasts circulating after DENV infection, most dramatically in individuals experiencing their first DENV infection.

"The fact that we observed such a profound IgA signature in individuals experiencing their first DENV infection may improve our ability to rapidly determine a patient's DENV exposure history and risk of developing severe disease" says Dr. Adam Waickman, the lead author on the study.

Though these data were generated from a small group of children, this is the first study to measure and characterize the entire output of plasmablasts without limitations to specific types of antibodies. These insights set the stage for future work to fully characterize the body's immune response to DENV, understand risk factors to severe dengue and ultimately could be critical to the development of new diagnostic tools as well as a safe, efficacious dengue vaccine.

More information: Adam T. Waickman et al, Transcriptional and clonal characterization of B cell plasmablast diversity following primary and secondary natural DENV infection, *EBioMedicine* (2020). DOI: 10.1016/j.ebiom.2020.102733

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