

# Indicator proteins could help identify patients at risk of complications during dengue fever infection

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Dengue virus (DENV) infection threatens over half of the world's population, and with millions of cases each year, scientists are working hard to fully understand the disease and bring it under control. Now, A\*STAR researchers have uncovered several molecular markers whose levels are elevated during DENV and provide a measure of the severity of the disease.

While the majority of DENV infections result in a mild, self-limiting fever, some cases develop into the more severe, life-threatening dengue shock syndrome. The key process that determines [disease severity](#) is plasma leakage—the amount of blood leaking from capillaries. During the first week of infection, scientists believe that the cell dysfunction inside blood vessels, coupled with increasing levels of small proteins called cytokines, combine to increase the permeability of the vascular system, resulting in varying degrees of plasma leakage.

"Dengue fever has been a problem in Singapore for more than three decades, but in recent years more severe forms have been on the rise, such as plasma leakage and hemorrhagic shock," explains Lisa Ng from the Singapore Immunology Network. Ng co-led the project together with Yee-Sin Leo and clinicians at the Institute of Infectious Diseases and Epidemiology. "We sought to identify the immune mediators of plasma leakage in dengue [patients](#), classified according to disease severity and phase of infection," says Ng.

The team collected samples from 90 DENV patients who attended Tan Tock Seng hospital in Singapore between 2010 and 2012. They grouped the patients according to disease phase, whether they had a primary or secondary DENV infection (infection during or after treatment for another illness), and levels of plasma leakage. For each patient the researchers monitored various clinical parameters of [disease](#) progression and tracked the levels of 46 different immune mediators.

"We discovered that patients suffering from secondary DENV infection were far more likely to have significant plasma leakage," says Ng.

"Those patients also displayed very high levels of particular cytokines, including hepatocyte growth factor (HGF). We also uncovered associations between enzymes called matrix metalloproteinases and the onset of plasma leakage." Future investigations could trial the use of chemicals that inhibit these enzymes to control severe DENV [infection](#).

The [molecular markers](#) revealed in this study could help doctors differentiate between primary and secondary DENV infections and prompt early medical intervention. The elevated level of HGF appears to be a phenomenon unique to DENV, and may provide a way for doctors to distinguish between DENV and similar tropical diseases circulating in Singapore.

**More information:** Zhisheng Her et al. Severity of Plasma Leakage Is Associated With High Levels of Interferon  $\gamma$ -Inducible Protein 10, Hepatocyte Growth Factor, Matrix Metalloproteinase 2 (MMP-2), and MMP-9 During Dengue Virus Infection, *Journal of Infectious Diseases* (2017). [DOI: 10.1093/infdis/jiw494](https://doi.org/10.1093/infdis/jiw494)

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