

Scientists Find Two Gene Variants Linked To Dengue Fever Susceptibility

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<http://www.asianscientist.com/in-the-lab/wellcome-trust-astar-dengue-fever-susceptibility-genes-102011/>

AsianScientist (Oct. 20, 2011) - Researchers in Southeast Asia have identified two genetic variants associated with increased susceptibility to severe dengue.

Dengue is globally the most common mosquito-borne infection after malaria, with an estimated 100 million infections occurring annually. Epidemiological studies have suggested that certain populations are more susceptible to severe dengue, implying that some people's genetic make-up makes them more susceptible to the disease.

To test this hypothesis, researchers at the Wellcome Trust Vietnam Research Program and Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam, together with researchers from the Genome Institute of Singapore, conducted the first ever genome-wide association study to compare the genomes of children with severe dengue against population controls.

The researchers identified changes in the DNA code located within two genes – MICB on chromosome 6 and PLCE1 on chromosome 10 – that appeared to increase a child's susceptibility to dengue shock syndrome. These findings are published in the journal *Nature Genetics* this week.

MICB is known to play a role the body's immune system and the researchers believe that a variant of this gene may affect the activation of natural killer cells or CD8 T-cells, two types of cells that play a key role in combating viral infection. If these cells are not properly functioning, their ability to rid the body of the dengue virus becomes impaired. This hypothesis is consistent with evidence that increased viral loads occur in the tissues of patients with severe dengue.

Mutations in PLCE1 have previously been linked to nephrotic syndrome, a childhood disease characterised by impairment of the normal barrier and blood filtering functions of cells in the kidney. The researchers believe that PLCE1 may also contribute to the normal functioning of the vascular endothelium, the thin layer of cells that lines the interior surface of blood vessels, with some variants of PLCE1 predisposing an individual to leakage from the blood vessels.

"This study implicates genetic variation in a molecule that activates natural killer cells as a culprit for increased susceptibility to severe dengue," said Dr. Khor Chiea Chuen, first author of the study.

"This is surprising as prior to this it was thought that defects in other components of the immune response, such as T-cells, B-cells or dendritic cells, were responsible. However, they did not show up in our large, well-powered genome scan," Khor added.

Professor Danny Altmann, Head of Pathogens, Immunology and Population Health at the Wellcome

Trust expressed optimism that this study - the first of its kind for dengue - is a step along the road towards developing treatments and vaccines for the disease.

The article can be found at: [Khor CC et al. \(2011\) Genome-wide association study identifies susceptibility loci for dengue shock syndrome at MICB and PLCE1.](#)

Source: [Wellcome Trust](#).

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