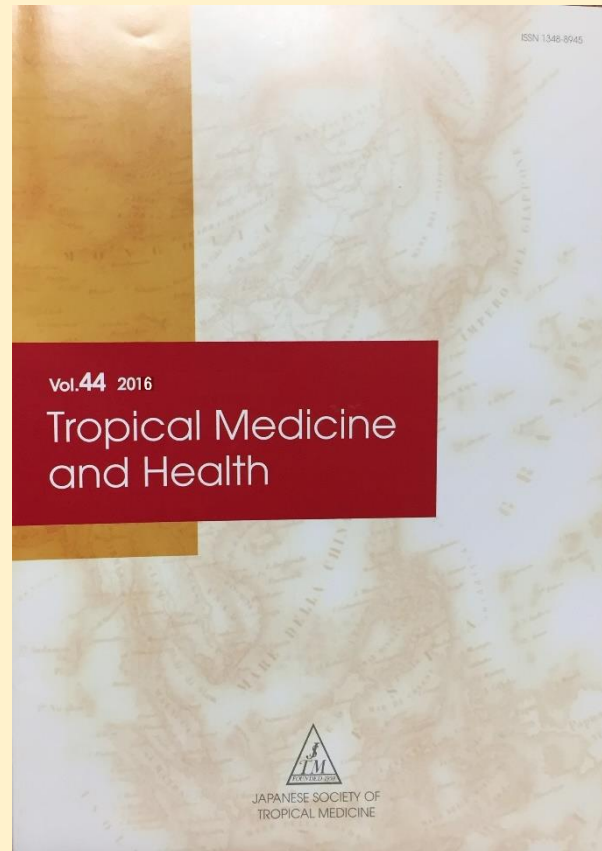


# Tropical Medicine and Health Vol.44 見本

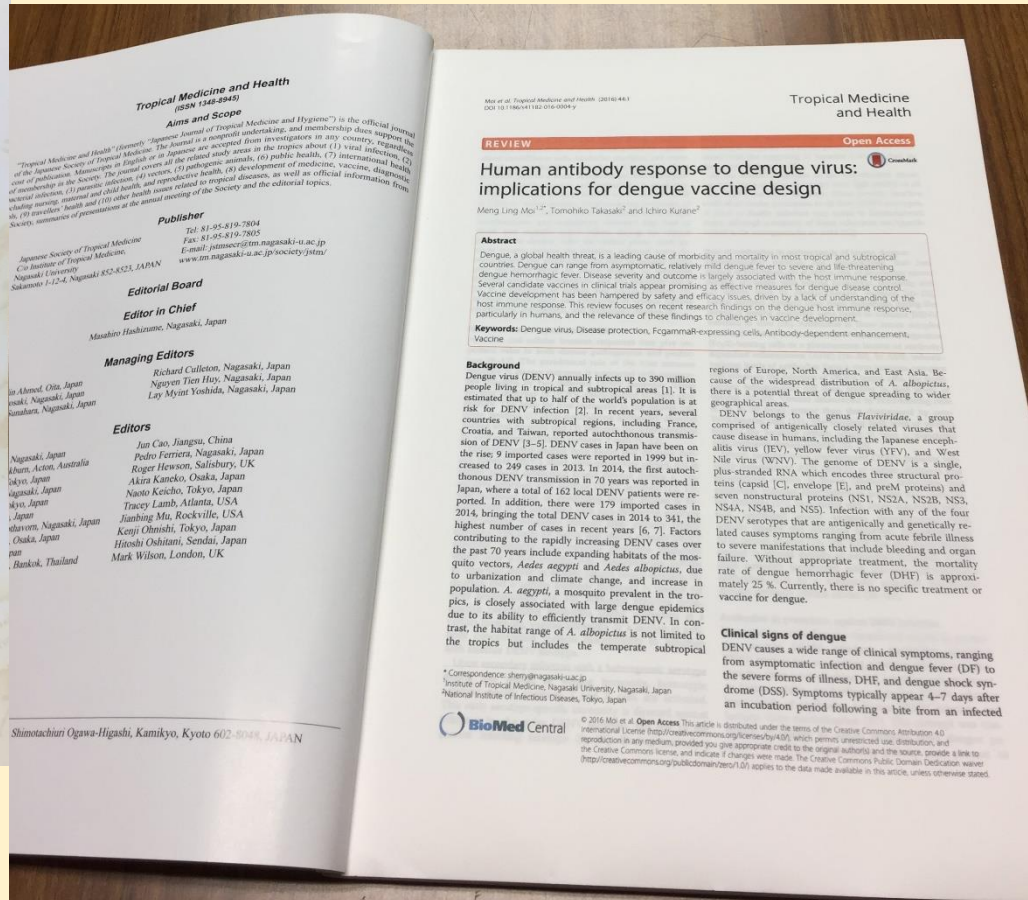


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### Aims and Scope

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Tropical Medicine  
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### REVIEW

### Open Access

## Human antibody response to dengue virus: implications for dengue vaccine design

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### Abstract

Dengue, a global health threat, is a leading cause of morbidity and mortality in most tropical and subtropical countries. Dengue can range from asymptomatic, relatively mild dengue fever to severe and life-threatening dengue hemorrhagic fever. Disease severity and outcome is largely associated with the host immune response. Several candidate vaccines in clinical trials appear promising as effective measures for dengue disease control. Vaccine development has been hampered by safety and efficacy issues, driven by a lack of understanding of the host immune response. This review focuses on recent research findings on the dengue host immune response, particularly in humans, and the relevance of these findings to challenges in vaccine development.

**Keywords:** Dengue virus, Disease protection, Fcγm1aR-expressing cells, Antibody-dependent enhancement, Vaccine

### Background

Dengue virus (DENV) annually infects up to 390 million people living in tropical and subtropical areas [1]. It is estimated that up to half of the world's population is at risk for DENV infection [2]. In recent years, several countries with subtropical regions, including France, Croatia, and Taiwan, reported autochthonous transmission of DENV [3–5]. DENV cases in Japan have been on the rise. 9 imported cases were reported in 1999 but increased to 249 cases in 2013. In 2014, the first autochthonous DENV transmission in 70 years was reported in Japan, where a total of 162 local DENV patients were reported. In addition, there were 179 imported cases in 2014, bringing the total DENV cases in 2014 to 341, the highest number of cases in recent years [6, 7]. Factors contributing to the rapidly increasing DENV cases over the past 70 years include expanding habitats of the mosquito vectors, *Aedes aegypti* and *Aedes albopictus*, due to urbanization and climate change, and increase in population. *A. aegypti*, a mosquito prevalent in the tropics, is closely associated with large dengue epidemics due to its ability to efficiently transmit DENV. In contrast, the habitat range of *A. albopictus* is not limited to the tropics but includes the temperate subtropical

regions of Europe, North America, and East Asia. Because of the widespread distribution of *A. albopictus*, there is a potential threat of dengue spreading to wider geographical areas.

DENV belongs to the genus *Flavivirus*, a group comprised of antigenically closely related viruses that cause disease in humans, including the Japanese encephalitis virus (JEV), yellow fever virus (YFV), and West Nile virus (WNV). The genome of DENV is a single, plus-stranded RNA which encodes three structural proteins (capsid [C], envelope [E], and preM proteins) and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5). Infection with any of the four DENV serotypes that are antigenically and genetically related causes symptoms ranging from acute febrile illness to severe manifestations that include bleeding and organ failure. Without appropriate treatment, the mortality rate of dengue hemorrhagic fever (DHF) is approximately 25%. Currently, there is no specific treatment or vaccine for dengue.

### Clinical signs of dengue

DENV causes a wide range of clinical symptoms, ranging from asymptomatic infection and dengue fever (DF) to the severe forms of illness, DHF, and dengue shock syndrome (DSS). Symptoms typically appear 4–7 days after an incubation period following a bite from an infected

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