



## Letter to the Editor

**A Dengue virus serotype 4-dominated outbreak in central Vietnam, 2013**

Dear Editor

Dengue diseases are transmitted by *Aedes* mosquitoes. Dengue virus (DENV) belongs to the family *Flaviviridae*, genus *Flavivirus* [1], and has 4 serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. Over the past 50 years dengue has spread extraordinarily; only 9 countries were reported to have dengue transmission prior to 1970, whereas over 100 countries have been reported in 2014 (WHO, 2014). Vietnam is a dengue endemic country, especially southern Vietnam a hyper-endemic area [2]. The in-house report of the National Institute of Hygiene and Epidemiology (NIHE) showed that there were about ten-fold more dengue cases in southern Vietnam than in central Vietnam annually (Table S1). Yearly, about 10,000 dengue cases have been reported from central Vietnam. DENV-4 has been found in each area of Vietnam, but DENV-4-dominated outbreak has not been known in this country since 2001. Over 50 DENV-4 strains isolated in Vietnam (northern, central, southern) were available in GenBank, and all of them belonged to genotype I (Fig. 1).

In 2013, a large DENV outbreak occurred with 204,661 clinical cases in central Vietnam. During the dengue season, September–December 2013, a total of 1532 collected blood samples were screened by dengue NS1 Ag ELISA in Hue central hospital. Out of the 702 samples positive by NS1 Ag ELISA, 501 samples were positive by serotype specific realtime – reverse transcription (RT)-PCR method [3] (Table S2). As a result, DENV-4 was the dominant serotype (245 cases, 48.9%), followed by DENV-1 (141 cases, 28.1%), DENV-3 (63 cases, 12.6%) and the last DENV-2 (52 cases, 10.4%). None of dengue negative specimens showed Chikungunya positive by RT-PCR (data not shown) [4]. The DENV-4 positive samples were subjected to virus isolation, and 21 DENV-4 strains were isolated. Infected culture fluid-derived RNA was used for the sequence (Table S3.) The complete nucleotide sequences of the envelope (E)-protein coding region for those isolates were determined and deposited in GenBank (accession no. KP292911–KP292931).

In 2013, DENV-3 outbreaks were reported in Solomon islands [5] and in China [6], whereas DENV-4-dominated outbreak has

not been reported in the neighboring countries around Vietnam. In central Vietnam, nearly 20-fold more DENV-4 cases were found in 2013 than in 2012, and the percentage of DENV-4 cases also increased from 22.6% (2012) to 48.9% (2013) (Table S4). The number of severe cases were not dramatically increased, and there have been no recorded climate changes, such as heavy rainfall, higher temperature in central Vietnam in 2013 (data not shown). In 2012, many dengue cases were reported from southern Vietnam, and the dominant serotype was DENV-1, which was also dominant in central Vietnam (Table S4). It is possible that the epidemic serotype of DENV may be similar between central and southern Vietnam.

There are several possible considerations for the sudden increase of DENV-4, such as, introduction of other genotype, or virus genome acquired mutations for adaptation in hosts, or the change of immunity in human population. Interestingly, the other genotype of DENV-4 was not found from this outbreak according to the phylogenetic analysis (Fig. 1). Currently, we consider research on the in vitro and in vivo properties of virus isolates, adaption to mosquitoes or humans, and immunity in human population.

**Competing interests**

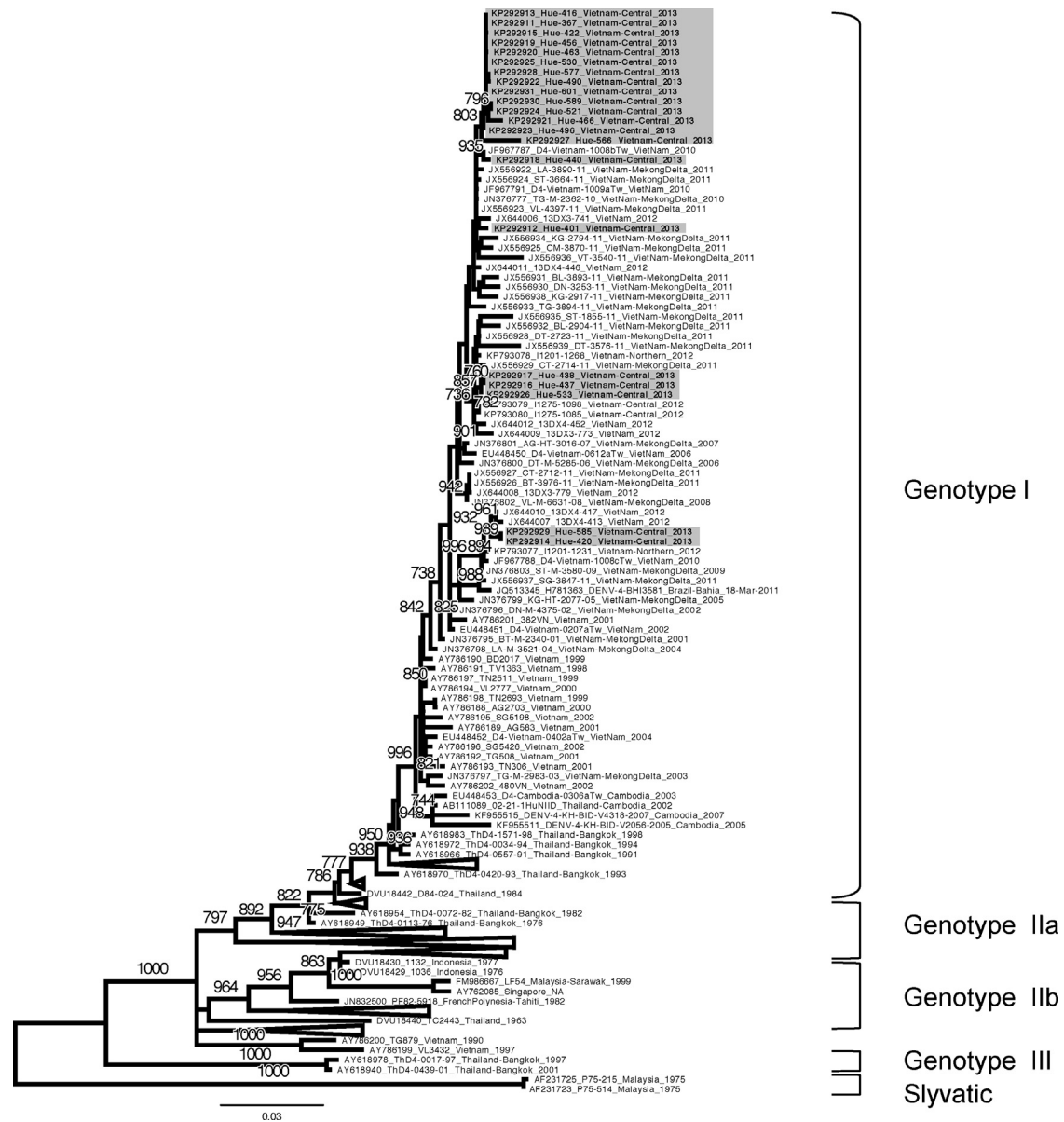
The authors have declared that no competing interests exist.

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**Ethical approval**

This study was approved by the Institutional Review Board of NIHE, Vietnam (No.15-HDD, January 18, 2011).



**Fig. 1.** ML-phylogenetic tree. Bootstrap values over 700 are shown at the nodes. Labels of strains conform to the following format: (GenBank accession nos) - (Strain name) - (Country-region) - (Year of isolation). The shaded strains are isolates from central Vietnam in 2013.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jcv.2015.02.016>.

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