

each of the 2 serotypes (105 DENV-2 and 68 DENV-3) isolated from children admitted from 1974 to 2001 in Thailand (Bangkok and Kamphaeng Phet) with varying degrees of dengue severity [dengue fever/dengue hemorrhagic fever/dengue shock syndrome (DF/DHF/DSS)]. Our results indicated that there was no obvious molecular correlate between disease severity and the phylogenetic position of their associated E genes. These analyses revealed extensive genetic diversity within a single geographic locality at a single time. The phylogenetic trees of DENV showed a strong temporal structure, ladder-like structure for both serotypes; viral strains isolated at the earliest time-points tended to fall near the root of the trees. These temporal orderings are caused by the continual birth and death of viral lineages; new lineages are regularly produced by mutation, but most go extinct relatively rapidly and few progress to circulate in subsequent years. Consequently, the rapid turnover of DENV lineages observed is, at most, the consequence of high, rates of deleterious mutations in the viral genome coupled with seasonal fluctuations in the size of the vector population.

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MOLECULAR EPIDEMIOLOGY OF DENGUE VIRUS SEROTYPE 3 AND 4 IN BANGKOK, THAILAND

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Dengue represents a major public health problem in Thailand, with all four viral serotypes co-circulating. To determine the evolutionary forces shaping the genetic diversity of dengue virus serotype 3 (DENV-3) and serotype 4 (DENV-4), and in particular to determine whether the changing prevalence of DENV-3 and DENV-4 could be attributed to instances of adaptive evolution in the viral genome, we undertook a large-scale molecular epidemiological analysis of DENV-3 and -4 (60 DENV-3 and 53 DENV-4 isolates from children in Bangkok, Thailand, admitted with varying degrees of dengue severity [dengue fever/dengue hemorrhagic fever/dengue shock syndrome (DF/DHF/DSS)] from 1974 to 2002) using both E gene sequences of sixty DENV-3 and fifty three DENV-4, and six complete viral genomes of DENV-4. These analyses revealed extensive genetic diversity within a single locality at a single time, including the discovery of a new and divergent genotype of DENV-4. However, despite this abundant genetic variation, there was no evidence of adaptive evolution in any gene, codon, or lineage of DENV-4. Consequently, the rapid turnover of DENV-3 and -4 lineages observed is, at most, the consequence of high rates of deleterious mutations in the viral genome coupled with seasonal fluctuations in the size of the vector population. (ACMCIP abstract)

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