THE MOLECULAR EPIDEMIOLOGY OF DENGUE VIRUS SEROTYPE 4 IN BANGKOK, THAILAND

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Dengue represents a major public health problem in Thailand, with all four viral serotypes co-circulating. Dengue virus serotype 4 (DENV-4) is the least frequently sampled serotype, although one that is often associated with hemorrhagic fever during secondary infection. To determine the evolutionary forces shaping the genetic diversity of DENV-4, and particularly whether its changing prevalence could be attributed to instances of adaptive evolution in the viral genome, we undertook a large-scale molecular epidemiological analysis of DENV-4 in Bangkok using both E gene sequences and complete viral genomes. This analysis revealed extensive genetic diversity within a single locality at a single time, including the discovery of a new and divergent genotype of DENV-4, as well as a pattern of continual lineage turnover. However, despite this abundant genetic variation, there was no evidence for adaptive evolution in any gene, codon, or lineage of DENV-4. Consequently, the rapid turnover of DENV-4 lineages through time is most likely the consequence of a high rate of deleterious mutation in the viral genome coupled to seasonal fluctuations in the size of the vector population.

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Dengue represents a major public health problem in Thailand, with all four viral serotypes co-circulating. Dengue virus serotype 4 (DENV-4)is the least frequently sampled serotype, although one that is often associated with hemorrhagic fever during secondary infection. To determine the evolutionary forces shaping the genetic diversity of DENV-4, and particularly whether its changing prevalence could be attributed to instances of adaptive evolution in the viral genome, we undertook a large-scale molecular epidemiological analysis of DENV-4 in Bangkok, Thailand, using both E gene and complete coding region sequences. This analysis revealed extensive genetic diversity within a single locality at a single time, including the discovery of a new and divergent genotype of DENV-4, as well as a pattern of continual lineage turnover. We also recorded the highest average rate of evolutionary change for this serotype, at 1.072×10^{-3} nucleotide substitutions per site, per year. However, despite this abundant genetic variation, there was no evidence for adaptive evolution in any gene, codon, or lineage of DENV-4, with the highest rate of nonsynonymous substitution observed in NS2A. Consequently, the rapid turnover of DENV-4 lineages through time is most likely the consequence of a high rate of deleterious mutation in the viral genome coupled to seasonal fluctuations in the size of the vector population.

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