

ABSTRACT

A Molecular and Phylogenetic Investigation of Dengue Viruses

Circulating in the Caribbean basin, 1977-2002

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Over the last 20 – 30 years of the past century the Americas have witnessed the rapid emergence of classic and severe forms of dengue, with the diseases becoming important public health issues. The pattern of dengue emergence has been characterised by a change from hypo- to hyperendemicity. This study presents a molecular epidemiological and phylogenetic history of dengue viruses in the Caribbean throughout that period marked by DHF/ DSS emergence.

Analyses suggest that for each of the four serotypes, at any time, there was only one subtype circulating in the Caribbean basin within the last quarter of the 20th century. The data confirm a high degree of gene flow within the basin, resulting in a pattern of dengue evolution with lineages defined more by time period than geographic origin, with strong evidence for the existence of geographical and socio-economic transmission routes. Evidence points to a common evolutionary pattern of differential rate variation among lineages regionally, with a small degree of variation in the overall evolutionary rates

between serotypes (7.47×10^{-4} subs/site/year for DEN-1, 5.66×10^{-4} subs/site/year for DEN-2, 4.15×10^{-4} subs/site/year for DEN-3, 7.87×10^{-4} subs/site/year for DEN-4). DEN-2 and -4 also exhibited lineage-defining amino acid changes (DEN-2 at E-91 and E-131; DEN-4 at E-163, E-351 and NS1-52), with evidence of lineage extinction and turnover, suggestive of selection. Viral population dynamics indicate that all four serotypes have experienced logistic growth, with effective population sizes constant over the study period within the Caribbean, except for DEN-2 subtype IIIb which showed an increase in effective population size during the early 1980s. The results indicate the importance of large temporal and geographic scale phylogenetic analyses in understanding disease dynamics, and highlight the need for future eradication and disease control efforts to focus on a regional rather than local scale.