

## **EVOLUTION OF DENGUE VIRUS POPULATIONS**

**Craig S, Thu HM, Wittke V, Robb TE, Lowry K, Nisalak A, Nimmannitya S, Kalayanrooj S, Vaughn DW, Endy T, Holmes EC and Aaskov JG**

The nature and rate of change in dengue virus populations may have a profound effect on the epidemiology of dengue disease and the symptoms associated with it. These factors also may influence the efficacy of any vaccine. Being RNA viruses, it has been assumed that individual populations of dengue virus are diverse. However, there are almost no reports of this diversity having been quantitated. A further obstacle to the study of dengue virus evolution has been gaps in the virological record. A longitudinal study of dengue 3 virus in Thailand from the epidemic in 1987 to the epidemic in 1997 revealed extinction of the virus lineage in 1992 and the emergence of two new lineages - possibly due to a genetic bottleneck. No similar changes have been reported for other dengue serotypes in this area in this interval. Similar extinctions of dengue 3 lineages appear to have occurred in the past. We have quantitated the diversity within dengue 2 virus populations from individual patients and mosquitoes in Myanmar by cloning and sequencing the E protein gene from individual hosts. Variation from the consensus nucleotide sequence rarely exceeded 0.5% and many changes were silent. Nucleotide insertions and deletions which would have produced defective virions also were detected. A recombinant virus and both its parental viruses were detected in a single mosquito. One of the parental viruses was circulating in the human population at the same location at the same time and virus similar to the second parent had been isolated in a neighbouring country. Viruses with the recombinant genotype have not been isolated from other mosquitoes or humans. It is of note that the most significant changes in genotype that we have detected were due to recombination, a genetic bottleneck during a period of low virus transmission (possibly) and not to selective pressure.

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