

APOPTOSIS OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN CHILDREN WITH ACUTE DENGUE INFECTION

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Apoptosis is an important modulator of immune responses during systemic viral infections, but little is known about the role of apoptosis in dengue virus (DV) infections. Peripheral blood mononuclear cell (PBMC) apoptosis and plasma soluble levels of CD95 (sCD95), a mediator of apoptosis, were determined in coded samples from hospitalized children from 1995-1997. Apoptosis was examined in 58 children with dengue fever (DF), 59 children with dengue hemorrhagic fever (DHF) and 68 children with other febrile illnesses (OFI) by the TUNEL assay. Plasma sCD95 levels were determined by sandwich ELISA from 116 children. Around defervescence, PBMC apoptosis was higher in children with DHF, compared to DF ($p=0.001$) and OFI ($p<0.001$). $CD8^+$ T-lymphocytes comprised at least half of the peak apoptotic PBMC in children with dengue as evidenced by dual color staining. Maximum plasma levels of sCD95 were also higher in DHF compared to DF ($p\leq 0.03$). Apoptosis in PBMC is likely to be involved in modulation of the innate and adaptive immune responses to DV infection, and the degree of PBMC apoptosis correlates with dengue disease severity.

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CLADE EXTINCTION AND REPLACEMENT IN DENV-1 PHYLOGENIES IN THAILAND IS ASSOCIATED WITH CHANGING SEROTYPE PREVALENCE

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Virus envelop gene of 98 DEN-1 viruses and complete genome of 10 DEN-1 strains isolated from pediatric patients with varying degrees of clinical dengue severity in Queen Sirikit National Institutes of Child Health (QSNICH), Bangkok and Kamphaeng Phet Provincial Hospital (KPP) were sequenced to determine intra-serotype variations of DEN-1 viruses circulating in Thailand for the past 3 decades and the structure of viral genetic diversity in the locality and the evolutionary processes responsible for this structure; and investigate whether the E gene of DENV contains genetic information that correlates with disease severity. Our results showed that the DENV-1 strains sampled from Thailand fall into two of the three genotypes, vast majority of Thai DEN-1 strains fall into genotype I except five strains collected in 1980 and 1983 fell into genotype III. Within genotype I, the Thai strains fell into three distinct clades, two of are associated with different sampling times. Clear Phylogenetic groups associated with time of sampling are present in genotype I. Our data also showed that the branches separating the two clades of DENV-1 were defined by 13 amino acid changes. Of the 13, it was striking that four were located in the E gene, and most of these positions were invariant in the other serotypes suggesting that amino acid change at these positions will have major consequences for fitness. We propose that there is a