ID-09

TRANSGENIC AND KNOCKOUT ANIMAL-BASED STUDY ON DENGUE VIRUS INFECTION: INVESTIGATION OF PROTECTIVE ROLE OF NON-STRUCTURE PROTEIN NS1 IN DNA VACCINE

C-K Tseng[1], S-F Wu[2], T-L Hsieh[1], H-K Sytwu[2]

Department of [1]Internal Medicine, Sungshan Air Force General Hospital, Taipei, Taiwan

Division of [2] Microbiology and Immunology, National Defense Medical Center, Taipei, Taiwan

BACKGROUND/AIMS: Accumulating data indicate that dengue nonstructural protein 1 (NS1) can serve as a vaccine protecting mice against dengue infection. Moreover, by using MHC class I and II knockout mice as vaccination/challenge models, we found $CD8^+$ T cells are essential for pD2NS1 vaccination-induced protection. To further investigate the virus-induced immune responses and protective mechanisms involved in pD2NS1 immunization, we established similar vaccination/challenge models by using Th1 and Th2 double transgenic and B-cell deficient mice in this study.

METHODS: We characterized the protective efficacy and immune responses of BALB/c Th1/Th2 transgene and B-cell deficient mice intramuscularly injected with plasmid encoding DEN-2-non-structural protein 1 (pD2NS1). Intravenously challenged by lethal DEN-2 mice vaccination with NS1-DNA. Splenic cells from immunized mice were cultured for T cell proliferation assay and flow cytometry analysis respectively.

RESULTS: In Th1 and Th2 double transgenic mice immunized with pD2NS1, there is a significant increase of $CD4^+$ subpopulation and enhancement of Th2-type response. Similar results of increasing $CD4^+$ cells and Th2 immunity were found in these pD2NS1-immunized mice following viral challenge. Mice deficient in B cells immunized with pD2NS1 were still protected from subsequent viral challenge, indicating that NS1-specific antibody can be dispensable in DEN-2 NS1 DNA-mediated protection. However, compared with wild type littermates, unimmunized B-cell deficient mice showed much higher mortality after lethal viral challenge, suggesting that humoral immune response still plays a certain role in host against DEN infection.

DISCUSSION/CONCLUSIONS: These results may help us to understand host immunity against DEN infection and provide further insight into vaccine development.

Key words: Dengue 2 virus, Non-structure protein