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### Enhanced immunogenicity of a vero cell-derived inactivated Japanese encephalitis vaccine formulated with advax adjuvant

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We previously developed an inactivated Japanese encephalitis virus (JEV) vaccine (ccJE) using serum-free cultured Vero cells. The immunogenicity of this ccJE vaccine was enhanced by formulation with Advax<sup>TM</sup>, a novel polysaccharide adjuvant based on delta inulin thereby enabling JEV protection after just a single immunisation. Advax adjuvant potently stimulated humoral and cellular immunity but avoided the reactogenicity of other adjuvants. Immunisation of mice with the ccJE-Advax vaccine combination induced cross-neutralising antibodies against other Flaviviruses belonging to the JEV serocomplex, including Murray Valley encephalitis virus (MVEV) and West Nile virus (WNV). We thereby sought to identify the immune mechanism underlying this cross protection. The ccJE-Advax combination changed the balance of T cell immunity as reflected by changes in the IgG antibody isotypes. Splenocytes from mice immunized with ccJE-Advax when compared to mice immunized with ccJE antigen alone exhibited increased IFN- $\gamma$  and IL-17 production when stimulated with ccJE antigen, consistent with Advax adjuvant increasing Th1 and Th17 immunity. Increased antigen-specific T-cell IL-17 production and protection against JEV challenge was also seen in an IFN- $\gamma$  knockout mouse model, indicating that IFN- $\gamma$  was not critical to ccJE-Advax mediated protection. Thus the combination of ccJE-Advax induces broad humoral and cellular immunity against JEV, translating into single-dose protection. This broader immunity obtained through use of Advax adjuvant in the vaccine enables enhanced cross-neutralising antibody and T-cell responses against not just JEV but also other JEV serocomplex flaviviruses including WNV and MVEV, with enhanced antigen-specific Th1 and Th17 immune responses.

#### Biography

Hiroko Toriniwa received her PhD from Faculty of Environmental Earth Science, Hokkaido University. She is Senior Researcher of Vaccine Research Laboratories, R&D Division, The Kitasato Daiichi Sankyo Vaccine Co., Ltd. She has researched development of Japanese encephalitis virus vaccine. She is coauthor of the patent: Method of producing Japanese encephalitis vaccine stably storable over long time and use of the vaccine with reference PCT/JP2008/073732.

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