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Heterologous prime-boost tetravalent dengue vaccine strategy elicits complete protection against DENV-2 in non-human primates

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Dengue is a growing public health problem. Although the first dengue vaccine, the Sanofi CYD-TDV live attenuated vaccine (LAV), was recently licensed, an overall protective efficacy is around 60%. This study provides the proof-of-concept that a new heterologous prime-boost strategy can protect against dengue virus (DENV) challenge in Cynomolgus macaques. By priming with a dengue tetravalent live attenuated vaccine (TLAV) then boosted 2 months later with three times (2-week interval) tetravalent DNA vaccine (TDNA), all vaccinated animals developed neutralizing antibodies against all four dengue serotypes following the first TDNA boost and maintained the constant titers after the second and final boost. As expected, no neutralizing antibody was detected in the negative control animals that received saline and empty plasmid. Both groups of animals were challenged with DENV-2 at one month after the final boost and determined the viremia by real-time PCR. All vaccinated animals exhibited undetectable viral RNA, while negative animals had detectable viral RNA from day 1-9 post-challenge. The presence of viremia post-challenge correlated with >32-fold boost in DENV-2 neutralizing titer at 1 month post-challenge, whereas no >4-fold titer boost was observed in the completely protected animals. Based on these results, we demonstrated the sterilizing protection against the DENV-2 challenge in the heterologous TLAV prime and TDNA boost macaques. Regarding the protective efficacy of a new heterologous TLAV prime-TDNA boost approach, an enlarged experiment to prove the hypothesis by challenging with all dengue serotypes is being conducted.

Biography

Chutitorn Ketloy has her expertise in DNA vaccine development and evaluation in both mice and non-human primates. She aims to improve DNA vaccine platform technology and develop immunogens (such as viral like particle) able to prevent dengue virus infection. This is succeeded by optimizing DNA vaccine expression, delivery (needle free injection, in vivo electroporation, and liposome) as well as synergy with other vaccine platform as a prime-boost vaccination.

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