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Pre-Clinical Development of a Novel Tick-Borne Encephalitis Vaccine for Mucosal Immunization

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Background. Tick-borne encephalitis (TBE) is a significant disease in Europe and Asia, with a rising incidence due to the spread of the TBE virus (TBEV) and its vectors. Current vaccines, although essential, have a complex immunization schedule and lower effectiveness in the elderly, leading to occasional vaccine failures. We aim to create a new TBE vaccine that provides better protection with fewer doses.

Aim. We aim to develop an effective vaccine that can be delivered via the mucosal route. The current study covers a pilot study that evaluates live-attenuated vaccine using LGTV IC as candidate for TBE vaccine.

Methods. We developed a genetically modified Langkat virus (LGTV) so-called LGTV infectious clone (LGTV IC). In-vivo evaluation was done on mice model to assess tolerability and immunogenicity of LGTV IC. LGTV IC was delivered to mice via two different routes, mucosal and intramuscular, in two different doses. The study assessed the peak and kinetics of viremia, as well as the elicited humoral, cellular, and mucosal immune responses.

Results. The mucosal administration of LGTV IC intranasally, at 1×10^3 PFU, was well tolerated in mice, as evidenced by the absence of clinical signs post-administration and no observed body weight loss. This immunization regimen consistently elicited anti-TBEV IgG antibodies in serum, irrespective of the dosage. Furthermore, a robust cellular immune response targeting TBEV non-structural protein 3 antigens (NS3), as well as capsid (C) and envelope (E) antigens, was observed. Intriguingly, lower dosage mucosal immunization proved more effective in eliciting both humoral and cellular immune responses compared to higher dosage mucosal administration and intramuscular immunization. Evidence of mucosal immunity was detected in select mucosal samples from the low dosage mucosal immunization group.

Conclusion and perspective. Administration of LGTV IC via mucosal route seems promising suggesting that LGTV IC can be considered as a candidate for a live TBE vaccine. Ongoing efforts involve further attenuation of LGTV IC, with successful attenuated variants undergoing in-vitro evaluation. Subsequently, these variants will be assessed in vivo as potential live-attenuated vaccine candidates.

Key words: TBE, vaccine, mucosal immunization, LGTV