Development Of A Novel Live-Attenuated Tick-Borne Encephalitis Vaccine Using The Langat Virus Platform

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Background: Tick-borne encephalitis (TBE) is a growing public health concern in Europe and Asia, driven by the increasing spread of the TBE virus (TBEV) and its tick vectors. Although current vaccines provide protection, their multi-dose schedule and reduced efficacy in the elderly contribute to occasional vaccine failures. This study aims to develop a novel TBE vaccine offering enhanced protection with fewer doses, focusing on mucosal immunization.

Methods: Infectious clone of Langat virus (LGTV IC) was designed and rescued- in our laboratory. We assessed the safety and immunogenicity of the LGTV IC as a live-attenuated TBE vaccine platform in a murine model. Mice were vaccinated with LGTV IC via intranasal or intramuscular routes at low or high doses. We evaluated viremia, viral presence in cerebrospinal fluid, general health, and immune responses.

Results: Intranasal immunization with LGTV IC induced strong immune responses. It elicited robust anti-TBEV IgG responses and strong TBEV NS3-specific IFN-γ and IL-2 production. Notably, low-dose intranasal immunization outperformed higher doses of both routes, inducing a more balanced and effective immune response. Low-dose intranasal administration was well tolerated, with no clinical signs, weight loss, or viral presence in the central nervous system. In contrast, intranasal immunization caused potential adverse effects at elevated doses.

Conclusion: These findings support LGTV IC as a promising vaccine platform for TBE, with intranasal administration emerging as a putative safe, well-tolerated, and effective needle-free alternative to intramuscular injection when given at a low dose. Ongoing efforts are focused on further attenuating LGTV IC to enhance its safety profile for future applications.