LWNVIVAT: Limiting West Nile Virus impact by novel vaccines and therapeutics approaches

Description

West Nile virus (WNV) is considered one of the most widespread mosquito-borne viral disease in the world. While most of WNVinfected individuals are asymptomatic, 1% of WNV-infected individuals develop a severe illness that affects the central nervous system, causing encephalitis or meningitis and eventually the death. The case-fatality rate notoriously increases inimmunosuppressed individuals and in population over 60 years old (up to 30%) and, to date, there is no prophylaxis or treatment forthis disease.

Here, we aim to develop a safety prophylactic WNV vaccine that cover WNV diversity and protect elderly individuals bypromoting the generation of potent and long-lasting neutralizing humoral and T cell responses, with limited or no cross-reactiveactivity against other flaviviruses. If success, the present proposal may guide the development of effective vaccines against otherviruses, particularly flaviviruses. We will use outstanding computational tools to design novel Envelope-based immunogens that cover the global WNVgenetic variability. Immunogens will be designed for eliciting highly-specific neutralizing humoral responses, with limited potential tomediate antibody-dependent enhancement (ADE) of infection or disease. In addition, we will also seek for T cell responses that work synergistically with antibodies to generate a long-lasting and polyfunctional protective anti-WNV immune response. Besides a classical and highly effective recombinant protein-based vaccine approach, we will explore novel and innovative strategies based on Virus Like Particles, and the use of antibodies as adjuvants, that may improve vaccine immunogenicity and efficacy. For immunogenicity analysis we have designed a complete set of assays that encompasses from in vitro testing, using human immunecells (tonsil and PBMCs) to in vivo evaluation using both young and old mice, and a complementary swine model.

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