## Development of Flavivirus vaccines based on the novel VLP design concept.

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Dengue virus (DENV) is a viral pathogen transmitted by mosquitoes and classified within the Flaviviridae family. It encompasses four distinct serotypes, denoted as types 1 to 4. Nevertheless, the antibodies generated as a result of DENV infection exhibit limited ability to provide immunity against other serotypes, thereby facilitating the occurrence of multiple DENV infections. This, in turn, elevates the likelihood of severe disease manifestation during subsequent infections with serotypes distinct from the initial infection. Antibody Dependent Enhancement (ADE) is a phenomenon that is believed to contribute to the heightened severity of infection, wherein antibodies targeting distinct serotypes are implicated. Hence, there is a need to establish a tetravalent vaccine targeting DENV infection that possesses the capability to elicit potent neutralizing antibodies against all serotypes. To date, a clinical application has been made of Denvaxia, a recombinant attenuated live vaccine that utilizes YF-17D, an attenuated strain of the yellow fever virus from the Flaviviridae family, as its vector. The efficacy of this vaccine in preventing infection is reported to be 60.3%. It received approval in Mexico in 2015; however, its usage has been limited since then. This is primarily due to concerns that the vaccine may lead to severe dengue virus (DENV) infection in naive individuals who lack antibodies against DENV at the time of first immunization. Furthermore, the final stage of development is underway for a recombinant attenuated live vaccine known as "DENVax," which utilizes a DENV2 attenuated strain as a vector. Additionally, researchers are actively working on the creation of other vaccine designs, including inactivated vaccines and subunit vaccines. Nevertheless, the development of a vaccine specifically aimed at mitigating the occurrence of adverse drug events (ADEs) has not yet been achieved. The objective of this study is to develop a technique for the efficient generation of chimeric virus-like particles (VLPs) representing serotypes 1-4 of Dengue virus (DENV). This will be achieved by substituting the epitopes of DENV with sequences derived from other flaviviruses that exhibit distinct antigenic properties compared to DENV and carry a reduced likelihood of triggering antibody-dependent enhancement (ADE) responses.