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VIRUS LIKE PARTICLES EXPRESSED IN INSECT CELLS AND MAMMALIAN CELLS AS A PLATAFORM FOR THE DEVELOPMENT OF A ZIKA VACCINE

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The Zika virus (ZIKV) is an emergent mosquito-borne virus of the flaviviridae family that has caused severe challenges to global health since 2015. It causes Guillain-Barré syndrome and congenital malformations. Although case numbers have decreased, it is important to develop a vaccine for outbreaks. One alternative is the use of virus like particles (VLP) as vaccines. ZIKV is enveloped and is composed of three main structural proteins: enveloped (E), pre-membrane (M), and capsid. The main target of neutralizing antibodies is the E glycoprotein, which is glycosylated in some strains. The N-glycosylation profile is determined by the producer host cell. ZIKV has both insect and human hosts, and the N-glycosylation profile of the E protein produced by each host is expected to be different. It can be expected that glycosylation pattern has an impact on immune response against the E protein, but its effect on the immunogenicity against VLP of ZIKV has not been determined. For this reason, the present work seeks in the first instance, to design and produce VLP of ZIKV (ZIK VLP) in insect and human cells.

To produce ZIK VLP, a chimeric gene was designed containing the M and E ZIKV genes fused to the transmembrane (TM) domain of Japanese encephalitis virus (JEV), ss- M-E (minus) ZIKV, TM JEV. After that, a recombinant baculovirus that contains the chimeric sequence was generated for VLP expression in insect cells. Production kinetics were followed, and the best conditions for VLP production were determined. For expression in human cells, the chimera was introduced into lentiviral vectors and was produced in HEK-293T/17 cells and used for the stable transfection of HEK-293 cells producing ZIKV VLP. High producing clones were selected by flow citometry. ZIK VLP were purified and characterized. In this work, strategies were developed for the efficient production of PPV in both systems, which can be used for further research. Ongoing studies are focused on determining the glycosylation profile of VLP expressed in both systems and on investigating the impact of glycosylation pattern of ZIK VLP immunogenicity in an animal model.