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Novel approaches for inactivation of viruses for the development of second generation vaccine

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Alphaviruses are highly infectious enveloped viruses that have been identified as emerging infectious pathogens that have credible bioweapon and bioterror capacity. Currently, there is no FDA approved vaccine for any of the alphaviruses. Therefore, development of safe and efficacious vaccine against alphaviruses is urgently required. Traditional methods of virus inactivation for vaccine preparation have inherent drawbacks like poor immunogenicity due to loss or damage of surface epitopes and in some cases incomplete inactivation. Here we describe novel approaches of virus inactivation which result in better immunogenicity and complete inactivation of viruses.

A photoactive aryl azide, 1, 5 iodonapthyl azide (INA), was used to inactivate Venezuelan equine encephalitis virus (VEEV) and chikungunya virus (CHIKV). INA has been shown to partition into the hydrophobic domain of the bio-membrane and upon short irradiation with UV light covalently binds to the transmembrane domain of the membrane proteins without affecting their ectodomains. In another approach, we used a radio-protective Mn2+-peptide-phosphate complex, which was originally identified in highly radio-resistant bacteria, Deinococcus radiodurans. VEEV was inactivated by exposing it to supralethal doses of gamma irradiation (up to 50,000 kGy) in the presence of Mn2+-peptide-phosphate complexes.

Both the inactivation strategies resulted in completely inactivated and highly immunogenic virus particles. INA treatment resulted in inactivation of the infectious viral genome whereas gamma irradiation resulted in denaturation of the viral genome. INA-inactivated VEEV also protected mice from aerosol challenge with the virulent virus. Our findings show that INA acts by two different mechanism of virus inactivation, one by targeting the viral envelope proteins and second by targeting the infectious RNA genome. These findings present novel approaches towards developing highly immunogenic, safe and completely inactivated second generation viral vaccine(s).

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