NEW CHEMICAL METHOD OF VIRAL INACTIVATION FOR VACCINE DEVELOPMENT BASED ON MEMBRANE FUSION INHIBITION

Stauffer, F[1], Ávila, FLQ[1], Oliveira, NS[1], Miranda, JM[1], Carneiro, FA[1], Alves, AMB[2] and Da Poian, AT[1]

[1]Instituto de Bioquímica Médica, UFRJ;
[2]Departamento de Bioquímica e Biologia Molecular, IOC Fiocruz

Vesicular Stomatitis Virus (VSV) infection is mediated by virus spike glycoprotein G, which binds to the cell surface and induces the fusion between viral envelope and endosomal membrane at the acidic environment of the endosomal compartment. In a previous work, we showed that His modification with diethypyrocarbonate (DEPC) inhibited VSV membrane fusion and impaired virus replication in vitro. In the present study, we evaluated the potential use of His modification with DEPC to the development of a new process of inactivated virus vaccine. Mice mortality profile and inflammatory response in the central nervous system indicated that DEPC treatment eliminates the ability of the virus to cause disease. In addition, the conformational integrity of surface proteins of VSV inactivated with DEPC was preserved. Furthermore, BALB/c mice were also immunized intranasally or intraperitoneally with VSV or VSV inactivated with DEPC alone or with adjuvants. The titer of antibodies measured by ELISA after intraperitoneal inoculation of virus modified with 0.5 mM DEPC with adjuvant was very similar to that of untreated virus. Finally, immunized mice were completely protected against intracranial challenge with a lethal dose of VSV. These results together suggest that His modification of viral proteins with DEPC might be used as a new approach to generating inactivated vaccines.