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Development of IFN-Deficient System to Manufacture IFN-Sensitive Influenza Vaccine Virus

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Interferon (IFN)-sensitive influenza viruses are likely to be the alternatives to inactivated and attenuated virus vaccines. Some IFN-sensitive influenza vaccine candidates with modified non-structural protein 1 (NS1) are highly attenuated in IFN-competent hosts but induce robust antiviral immune responses. However, little research has been done on the manufacturability of these IFN-sensitive vaccine viruses.

In this study, RIG-I-knockout 293T cells were used to package the IFN-sensitive influenza A virus expressing the mutant NS1 R38A/K41A. We found that the packaging efficiency of the NS1 R38A/K41A virus in RIG-I-knockout 293T cells was much higher than that in 293T cells. Moreover, the NS1 R38A/K41A virus could no longer replicate in A549, MDCK, and Vero cells after 3-6 passages, indicating that the replication of NS1 R38A/K41A virus is limited in conventional cells. Therefore, we further established a stable Vero cell line expressing the wild-type (WT) NS1based on the Tet-On 3G system. The NS1 R38A/K41A virus was able to steadily propagate in the NS1-overexpressing Vero cell line with high titers for at least 20 passages. Additionally, the replication of NS1 R38A/K41A virus was limited in mice but triggered strong antiviral immune responses.

In conclusion, we presented a promising IFN-deficient system, involving a RIG-I-knockout 293T cell line to package the IFN-sensitive vaccine virus and a stable NS1-overexpressing Vero cell line to propagate the IFN-sensitive vaccine virus. The IFN-deficient system is applicable for the manufacture of IFN-sensitive and replication-limited vaccine virus.

Biography:

Lei Sun obtained her doctoral degree from the Yangzhou University. Dr. Sun is an associate professor working at CAS Key Laboratory of Pathogenic Microbiology of Immunology, Institute of Microbiology, Chinese Academy of Science. Her research focuses on the replication and pathogenesis of influenza virus, the post-translational modification of viral protein, and the antiviral immunity. The research works are designed to increase fundamental knowledge as well as to facilitate the development of new approaches to control of viral infection.