World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:13, No:01, 2019

Dual-functional Peptide With Defective Interfering Genes Protecting Mice From Avian and Seasonal Influenza Virus Infection

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Abstract : Limited efficacy of current antivirals and antiviral-resistant mutations impair anti-influenza treatment. Here, we evaluated the in vitro and in vivo antiviral effect of three defective interfering genes (DIG-3) of influenza virus. Virus replication was significantly reduced in 293T and A549 cells transfected with DIG-3. Mice transfected with DIG-3 encoded by jetPEI-vector, as prophylaxis and therapeutics against A(H7N7) virus respectively, had significantly better survivals (80% and 50%) than control mice (0%). We further developed a dual-functional peptide TAT-P1, which delivers DIG-3 with high transfection efficiency and concomitantly exerts antiviral activity by preventing endosomal acidification. TAT-P1/DIG-3 was more effective than jetPEI/DIG-3 in treating A(H7N7) or A(H1N1)pdm09-infected mice and showed potent prophylactic protection on A(H7N7) or A(H1N1)pdm09-infected mice. The addition of P1 peptide, preventing endosomal acidification, could enhance the protection of TAT-P1/DIG-3 on A(H1N1)pdm09-infected mice. Dual-functional TAT-P1 with DIG-3 can effectively protect or treat mice infected by avian and seasonal influenza virus infection.

Keywords : antiviral peptide, dual-functional peptide, defective interfering genes, influenza virus
Conference Title : ICIDM 2019 : International Conference on Infectious Diseases and Diagnostic Microbiology
Conference Location : Sydney, Australia
Conference Dates : January 30-31, 2019