Xinying Tang et al., J Antivir Antiretrovir 2015, 7:4
http://dx.doi.org/10.4172/1948-5964.C1.025

OMICS International
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5th World Congress on
Virology

December 07-09, 2015 Atlanta, USA

Chimpanzee adenovirus expressing HA-targeting artificial microRNA protects mice against avian influenza virus, H5N1

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Influenza virus (IV) is a continuously evolving virus that widely spreads in humans and contributes to substantial morbidity and mortality. Re-emergence of human infection with avian influenza virus poses extra challenge in IV control. Artificial microRNA (amiRNA) mediated RNA interference has become a powerful antiviral approach due to its high specificity and rapid effect. Here we designed several amiRNAs targeting conserved regions among different clades of H5N1 hemagglutinin. Expression and delivery efficiency were enhanced by presenting functional amiRNA with chimpanzee adenoviruses serotype 68 (AdC68). One amiRNA, HA-1405, significantly limited H5N1 replication *in vitro* and the inhibition efficiency was up to 95% against clade2.3.2 H5N1. Treatment with AdC68 conjugated HA-1405, termed as AdC68 (HA-1405), almost abolished viral structural protein expression as well as virus growth in A549 cell line. Moreover, prophylactic administration with AdC68 (HA-1405) markedly alleviated clinical symptoms and reduced five to ten fold of lung viral titers against four clades of H5N1 in ICR mice. Our results further showed that AdC68 (HA-1405) conferred 70% and 40% immediate protection against lethal clade2.3.2 and clade2.3.4 H5N1 challenge respectively. Taken together, these data provided information that HA-targeting amiRNA delivered by AdC68 could be pursued as a potential agent for highly pathogenic avian influenza viruses prevention and treatment.

Biography

Xinying Tang has completed her Bachelor's degree from Nanjing Normal University in 2012. She is currently a PhD Student at Institut Pasteur of Shanghai. She has published three papers in reputed journals including *Gene therapy, Journal of Virology* and *Emerging Microbes and infections*.

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