Inhibition of Influenza A Virus Replication by a Mammalian Specific Small RNA

Sheng-Yu Huang[1*]

[1.] Chang Gung University

Background/Objective
Wild aquatic birds are the primary natural reservoir for all subtypes of influenza A viruses (except several subtypes observed in bats), and most influenza A viruses cause asymptomatic or mild infections in birds. However, avian influenza viruses can traverse the species barrier and infect humans.

Method
To analyze the specific regulators associated with the virulence of influenza A virus in humans, we compared the miRNA expression profile of influenza-A-virus-infected human cells with that of influenza-A-virus-infected avian cells and identified hsa-miR-1290 as a human-specific regulator.

Result
Hsa-miR-1290 is up-regulated 2-fold in human (A549) cells after influenza A/WSN/33(H1N1) virus infection. The inhibition of hsa-miR-1290 by LNA-1290 (inhibitor of hsa-miR-1290) significantly decreased the viral yields by 10-fold in human cells. We determined that human vimentin is a target of hsa-miR-1290 because both its mRNA and protein levels was down-regulated to at least 50% by hsa-miR-1290 overexpression. Down-regulated vimentin was restored by LNA-1290 in virus-infected cells. Moreover, the inhibition of vimentin significantly enhanced the viral yields by 10-fold in human cells. Conducting a sequence analysis did not detect hsa- miR-1290 in avian species as expected. Although avian species posses vimentin, they lack the hsa-miR- 1290 targeting site; when hsa-miR-1290 was overexpressed in avian cells, no changes in the viral titers were observed.

Conclusion
Therefore, hsa-miR-1290 is a human-specific factor positive for influenza virus replication, which can be replicated through the inhibition of human vimentin (a negative regulator for influenza virus replication). This finding can be useful for treating of influenza A virus infections in humans.