

Evolutionary analysis of pandemic influenza A(H1N1) viruses

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URL	http://hdl.handle.net/10097/58363

(書式12)

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学位の種類	博士 (医学)
学位授与年月日	平成 25 年 9 月 25 日
学位授与の条件	学位規則第 4 条第 1 項
研究科専攻	東北大学大学院医学系研究科 (博士課程) 医科学専攻
学位論文題目	Evolutionary analysis of pandemic influenza A(H1N1) viruses (パンデミックインフルエンザ A (H1N1) の進化系統解析)
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論文内容要旨

(Abstract)

Influenza virus is one of the major etiological agents for acute respiratory infections causing a total about three to five million yearly case of severe illness and about 250,000 to 500,000 yearly deaths. Among the three genera of the influenza viruses, major epidemics and pandemics are caused by influenza A virus. Influenza viruses can evolve in two different ways: antigenic drift and antigenic shift. Influenza viruses are changing by antigenic drift continuously, but antigenic shift occurs rarely. The first pandemic of the 21st century was caused by a novel H1N1 influenza virus in 2009 which was derived through antigenic shift and spread globally.

It is important to elucidate the genetic variability and molecular evolution of influenza A(H1N1)pdm09, which caused the pandemic in 2009 in different regions to understand its diversification. To examine this, I did the sequence analysis of hemagglutinin (HA1) and neuraminidase (NA) genes during two consecutive seasons, 2009–2010 and 2010–2011 in Sendai, Japan. I have found that the substitution rate of nucleotides for HA1 in 2010–2011 has an increasing trend. Sendai isolates were also clustered with global clade 7 characterized by S203T mutation in HA1 gene, and two distinct cluster for HA1 and NA gene were revealed

in both phylogenetic as well as Bayesian Markov Chain Monte Carlo (MCMC) phylogenetic tree. A slightly increasing trend of genetic diversity was also observed in 2010-2011 season in Bayesian skyline plot model analysis. Selection analysis showed that position 197 was positively selected site in HA1 which is closed to receptor binding sites and also near to the sites important for viral transmission. In case of NA gene, position 46 which was positively selected, is a potential glycosylation site located in the T-cell antigenic regions and associated with host adaptation after the virus was introduced from birds to humans. Evolutionary analysis is therefore needed for influenza A(H1N1)pdm09 virus for its effective control including vaccine strain selection.

The current study render the insight that genetic surveillance and genome sequencing of influenza viruses have an immense significance in understanding the evolutionary mechanisms of influenza viruses particularly in the field of pandemic influenza. Moreover, molecular evolutionary and phylogenetic analysis can provide a new dimension to explore the underlying driving mechanisms of emerging viral epidemics and pandemics.