

論文の内容の要旨

論文題目 Epidemiological surveillance and virological analyses of highly pathogenic H5N1 avian influenza viruses in Indonesia.

(インドネシアにおける高病原性 H5N1 鳥インフルエンザウイルスの疫学的調査及びウイルス学的解析)

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Highly pathogenic avian influenza (HPAI) virus of the H5N1 subtype has been enzootic among avian species, and they have caused sporadic human cases with mortality rate of more than 50%. Although human HPAI H5N1 cases have been so far limited to those with close contact with infected poultry, there always exists a risk of HPAI H5N1 viruses causing human endemics and global pandemics, in case they acquire efficient replication and transmission capability among humans.

Highly pathogenic avian influenza H5N1 viruses have been circulating in Indonesia since 2003, and sporadic human H5N1 cases have been reported until 2017. However, there is no report on epidemiology and virological characteristics of currently circulating HPAI H5N1 viruses, and their potential of human endemic or pandemic is unknown. With the aim to elucidate the virological characteristics of currently circulating HPAI H5N1 viruses in Indonesia, we have conducted epidemiological surveillance of poultry and swine in Indonesia between 2010 and 2016. Two distinct sub-clades of H5N1 viruses, clade 2.1.3 and clade 2.3.2.1d, were identified, and it was suspected that clade

2.3.2.1d strains had recently become dominant among poultry in Indonesia. Clade 2.3.2.1d strains revealed mammalian adaptive traits including higher viral polymerase activity and moderate replication capability in human lung epithelial cells, and high virulence in BALB/c mice. Our findings warranted further continuation of surveillance for HPAI H5N1 in Indonesia, in order to detect emergence of viruses possessing endemic or pandemic capability among humans.

Among analyzed Indonesian HPAI H5N1 viruses, we identified two genetically-close viruses with different characteristics; A/chicken/South Kalimantan/UT521/2010 (UT521) possessing higher replication efficiency in human lung epithelial cells and higher pathogenicity in BALB/c mice, while A/chicken/South Sulawesi/UT541/2010 possessing low replication efficiency and low pathogenicity. Further analysis of UT521 and UT541 strains revealed two amino acid mutations of viral polymerase binding protein 2 (PB2) which enhanced viral replication efficiency in human lung epithelial cells and pathogenicity in BALB/c mice. The mechanism of which these two PB2 amino acid mutations enhance virulence in mammalian hosts has not yet been elucidated, but our findings are beneficial for assessing the risk of avian-to-human transmission of highly pathogenic H5N1 avian influenza field isolates.