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学位論文内容の要旨

博士の専攻分野の名称：博士（獣医学）

氏名：金平克史

学位論文題名

Molecular epidemiology and pathogenicity of animal influenza viruses isolated in Japan
(日本で分離された動物インフルエンザウイルスの分子疫学と病原性に関する研究)

Animal influenza viruses affect livestock and poultry industry. Three swine influenza viruses (SIVs) and one highly pathogenic avian influenza virus (HPAIV) isolated in Japanese farms were analyzed phylogenetically and virologically.

In 2013, three reassortant SIVs—two H1N2 and one H3N2 subtypes—were isolated from symptomatic pigs in Japan; each contained genes from the pandemic A(H1N1)2009 virus and endemic SIVs.

Phylogenetic analysis revealed that the two H1N2 viruses, A/swine/Gunma/1/2013 and A/swine/Ibaraki/1/2013, were reassortants that contain genes from three distinct lineages: 1) H1 and NP genes derived from a classical swine H1 HA lineage uniquely circulating among SIVs in Japan; 2) NA genes from human-like H1N2 swine viruses; and 3) other genes from pandemic A(H1N1)2009 viruses. The H3N2 virus, A/swine/Miyazaki/2/2013, comprised genes from two sources: 1) HA and NA genes derived from human and human-like H3N2 swine viruses; and 2) other genes from pandemic A(H1N1)2009 viruses. Phylogenetic analysis also indicated that each of the reassortants may have arisen independently in Japanese pigs. The antigenic reactivities of A/swine/Miyazaki/2/2013 with antisera generated for some seasonal human-lineage viruses isolated during or before 2003 were high, but A/swine/Miyazaki/2/2013 reactivities with antisera against viruses isolated after 2004 were clearly lower. In addition, antisera against some strains of seasonal human-lineage H1 viruses did not react with either A/swine/Gunma/1/2013 or A/swine/Ibaraki/1/2013. These findings indicated that emergence and spread of these reassortant swine influenza viruses is a potential public health risk.

An H5N8 subtype of HPAIV, A/chicken/Kumamoto/1-7/2014, was isolated from a Japanese chicken farm during an outbreak in April 2014. Phylogenetic analysis of the virus revealed that it belonged to HA clade 2.3.4.4. All eight genomic segments shared high sequence homologies with H5N8 subtype HPAIVs, A/broiler duck/Korea/Buan2/2014 and A/baikal teal/Korea/Donglim3/2014, which were isolated in Korea in January 2014. Intranasal experimental infection of chickens and ducks with A/chicken/Kumamoto/1-7/2014 was performed to assess the pathogenicity of the virus in chickens and the potential for waterfowl to act as a virus reservoir and carrier. A high titer virus challenge (10^6 EID₅₀/animal) was lethal in chickens but they were unaffected by lower virus doses (10^2 EID₅₀ or 10^4

EID₅₀/animal). Virus challenge in all doses examined was found to asymptotically infect ducks. Hemagglutination inhibition assay revealed that A/chicken/Kumamoto/1-7/2014 possessed relatively low cross-reactivity with H5 viruses belonging to clades other than clade 2.3.4.4. These results suggest that migratory waterfowl acted as the carrier of A/chicken/Kumamoto/1-7/2014 into Japan, and specific and effective serological diagnostics for the HPAIVs belonging to clades 2.3.4.4 need to be prepared for controlling prospective outbreaks.