学位論文内容の要旨

Abstract of the dissertation

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Name

学位論文題名

The title of the doctoral dissertation

Studies on the epidemiology of severe fever with thrombocytopenia syndrome virus infection and the role of glycoproteins in the intracellular transportation of viral structural proteins

（重症熱性血小板減少症候群ウイルス感染の疫学およびウイルス構造タンパク質の細胞内輸送における糖蛋白質の役割に関する研究）

Severe fever with thrombocytopenia syndrome virus (SFTSV); genus *Phlebovirus;* family *Phenuiviridae,* is an important human pathogen in China, Japan and South Korea transmitted by *Haemaphysalis longicornis* and *Amblyomma testidunarium* ticks. Though SFTS is endemic to west Japan the SFTSV genome was detected in ticks in geographic areas outside the disease endemic regions. Thus, it is important to describe the geographic distribution of SFTSV infection in wild animals in Japan.

Chapter 1 of this thesis describes a serological survey conducted in sika deer and rodents in Japan. Sika deer sera from Hokkaido, a non SFTS-endemic area and Miyazaki, an SFTS-endemic area as well as banked rodent serum samples collected between 1997 and 2009, were screened.

Similar to distribution of SFTS patients, SFTSV antibodies were detected in sika deer from Miyazaki (4.9%, 2/41) but not in sika deer from Hokkaido (0%, 0/315). The information obtained in this survey is useful for defining SFTS-endemic areas, necessary for monitoring the spread of SFTSV and assessing the risk of human infection with SFTSV in Hokkaido and Miyazaki. Anti-SFTSV antibodies were not detected in rodent sera that were screened (0%, 0/910). The role of rodents in the transmission of SFTSV is unclear even though sero-positive rodents were reported before in China. Further work is required for monitoring circulation of SFTSV in Japan.

In chapter 2, the role of SFTSV glycoproteins (GP) in targeting L protein and nucleocapsid protein to the secretory pathway was studied. Progeny virions of representative viruses in

the *Bunyavirales* order bud at the Golgi complex. In the *Hantaviridae* family virus budding also takes place at the endoplasmic reticulum Golgi intermediate compartment (ERGIC). Targeting structural proteins to intracellular budding compartments is critical for formation of progeny virions. Localization of SFTSV structural proteins to intracellular compartments has not been described. This study thus aimed at revealing the subcellular localization of SFTSV structural proteins in SFTSV infected cells and in cells expressing recombinant proteins. The role of GP in targeting NP and L protein to the subcellular compartments was also studied.

Localization of GP, NP and L to the ER, ERGIC and Golgi complex was analysed by immunofluorescence assay in cells infected with SFTSV. GP and L localized to the ER, ERGIC and Golgi while NP localized to the ERGIC and Golgi. When the proteins were transfected singly, only GP trafficked through the secretory pathway independent of other SFTSV structural proteins. The effect of co-expressing GP with L or NP was assessed. In the presence of GP, L, but not NP, localized to the ERGIC and Golgi, however when HA-fused NP was expressed in the presence of SFTSV, HA-NP localized to the ERGIC and Golgi, suggesting another viral component is required for localizing NP to the budding sites. Further studies should clarify the role of the ERGIC and Golgi in formation of SFTSV virions and the viral factors required for NP to localize to these compartments.

This study reveals steps in the lifecycle of SFTSV and could provide a basis for development of virus inhibitors.