



“Identification of Host Factors that Affect the Ebola Virus RNA Polymerase Protein”

Monday, September 7, 2015 10:00 – 11:00

@Conference Room C756, Lab3

Abstract:

Ebola virus (EBOV) is a member of the negative-sense single-strand RNA viruses and causes a severe hemorrhagic fever in humans and nonhuman primates with extremely high mortality rate. During the infection of host cells, EBOV proteins must interact with various host proteins for virus replication. Up to now, the host proteins involved in the invading process and budding process of EBOV and their molecular mechanisms have been revealed, however, the host proteins that participate in the transcription and replication of the EBOV genome remains largely unknown. In this study, to identify the host proteins that interact with EBOV RNA-dependent RNA polymerase protein L (EBOL) and contribute to the transcription and replication of the viral genome, cellular proteins interacting with EBOL were immunoprecipitated with EBOL and identified the precipitants by mass spectrometry analysis and investigated their biological significance in EBOV replication by using EBOV minigenome system and biologically contained EBOV. Of the candidate proteins identified, a nuclear protein named DNA topoisomerase 1 (TOP1) which is known to localize in the nucleus and unwind helical structure of DNA and RNA was identified as a novel host protein that affects the EBOV RNA polymerase activity. Knockdown of TOP1 caused an approximately 80% of reduction of EBOV polymerase activity and significantly reduced the growth of biologically contained Ebola virus by approximately 1 log unit. Surprisingly, it was found that the nuclear protein TOP1 interacted with EBOL in the cytoplasm, where the transcription and replication of the viral genome occur. Furthermore, it was elucidated that the endogenous functions of TOP1, the phosphodiester bridge-cleaving function and the recombination function, are required for the viral RNA polymerase activity. These results demonstrate that the TOP1 is an important cellular factor for the transcription and replication of the EBOV genome and, as such, plays a key role in EBOV life cycle.

