

## 【Grant-in-Aid for Scientific Research(S)】

### Biological Sciences (Agricultural sciences)



**Title of Project : Host cell response network in mononegavirus infection**

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Research Area : Agricultural Sciences

Keyword : Pathogenic microorganism

#### 【Purpose and Background of the Research】

Nonsegmented negative-strand RNA viruses (mononegavirales) often cause systemic pathogenesis in patients with high fatality. Pathogenicity is a result of the battle between virus and host immunoresponse, and its entire picture is, despite the numerous intensive researches, hardly elucidated.

We have been studying three morbilliviruses belonging to mononegavirales and closely related Nipah virus (NiV) to decipher the mechanisms of pathogenicity. We have revealed that gene expression profiles of viral infected cells differ greatly, seemingly depending on the cell types and the viral strains.

In our research, the transcription regulatory network and protein interactions in the host cell response induced by viral infection will be studied for morbilliviruses, mainly rinderpest virus (RPV), and NiV using new whole-transcriptome technologies. Furthermore, effect of host cell response in viral pathogenicity will be assessed by using our established reverse genetics technique by which infectious virus are generated from genes, and analyses in animal models.

#### 【Research Methods】

We will carry out CAGE and ultra-high-throughput sequencing to identify the entire population of transcripts induced after morbillivirus infection of epithelial and lymphoid cells, and decipher the cell type-specific regulatory network by bioinformatics analyses. Key transcription factors will be extracted from the network, and viral factors targeting such key factors will be identified using recombinant viruses generated with reverse genetics.

In addition, the interaction between virus and host proteins after morbillivirus infection will be explored using new transcriptome and

proteomics technologies, and function of the candidate proteins will be analyzed. Similar analyses will be carried out for NiV, aiming to define the whole aspect of the transcription regulatory network.

#### 【Expected Research Achievements and Scientific Significance】

Our research aims to comprehend the host cell response network triggered by mononegavirus infection for the first time. Findings in our research will contribute to the understanding of the unknown viral spreading strategy in infected bodies, mechanisms of pathogenicity in different tissues, immunosuppression, and persistent infection.

Mononegavirales contain number of emerging viruses, and many viruses belonging to the order cause significant diseases in animals and humans with high fatality. In our research, studies on an emerging virus NiV enable us to assess the involvement of host-cell response for the actual severe pathogenicity. Our findings will provide important and new aspects in prevention/treatment and drug development targeting host responsive factors.

#### 【Publications Relevant to the Project】

Sato, H. and Kai, C. et al. Measles virus induced cell-type specific changes in gene expression. *Virology*, 321-330, 2008.

Yoneda, M. and Kai, C. et al. Establishment of a Nipah virus rescue system. *Proc. Natl. Acad. Sci., USA*, 103(44), 16508-16513, 2006.

【Term of Project】 FY2010-2014

【Budget Allocation】 167,400 Thousand Yen

#### 【Homepage Address and Other Contact Information】

<http://www.ims.u-tokyo.ac.jp/jikkendoubutsu/index.htm>