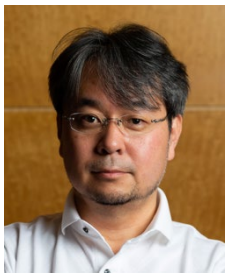
【Grant-in-Aid for Scientific Research (S)】

Broad Section H



Title of Project： Integrated molecular basis for herpesvirus replication and pathogenesis

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Research Project Number: 20H05692 Researcher Number：60292984
Keyword：Virus, proliferation mechanism, pathological expression mechanism

【Purpose and Background of the Research】

Herpes simplex virus (HSV) is a medically important virus that causes various diseases in humans, such as encephalitis, mucosal and skin diseases, and eye diseases. Moreover, HSV infections increase the risk of human immunodeficiency virus infections by 2–4 times and are also involved in the exacerbation of dementia. Although antiviral drugs have been developed for HSV infections, the effects are not sufficient for some infection-related diseases and vaccines have not been developed either. Furthermore, repeated latency and recurrence render the complete cure of HSV infections difficult, and the unmet medical needs are high. Considering that the "overall picture of the proliferation and pathogenic mechanisms of HSV"—a universal question in HSV research—is the "sum of complex infection phenomena," it is not difficult to understand why it would be impossible to elucidate this simply by analyzing "fragmented individual infection phenomena." In this study, we aim to integrate multilayered knowledge into *in-depth* analyses at the biological level by applying basic research knowledge on various HSV infection phenomena that the principal investigator has accumulated over many years. Furthermore, we aim to understand each infection phenomenon unraveled by leading-edge technology in an integrated manner as an "overall picture of the proliferation and pathogenic mechanisms of HSV." Additionally, using the unique knowledge unraveled from HSV research, we will attempt to elucidate new life phenomena that are not bound by conventional virology.

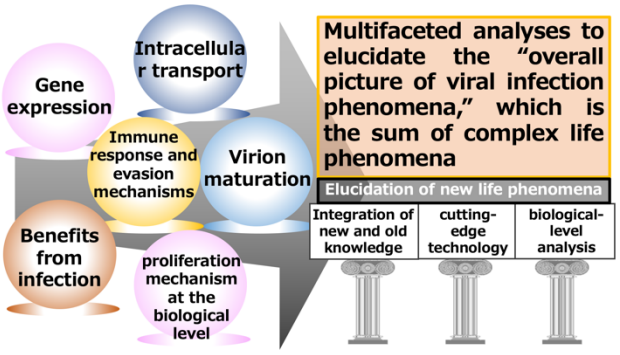

Figure 1 Concept diagram of this research project

【Research Methods】

In addition to conventional virological, molecular biology, cell biology, and experimental zoological methods, this study will be conducted by making full use of advanced technologies, such as single-cell analysis, proximity-dependent labeling for interactome analysis, quantitative phosphoproteomics, microbiome analysis, and gene editing and screening at the cellular and viral levels.

【Expected Research Achievements and Scientific Significance】

Research on HSV has been actively promoted for many years owing to the high unmet medical needs caused by infection-related diseases. Nevertheless, the "overall picture of the proliferation and pathogenic mechanisms of HSV" remains unclear, with the lack of "panoramic forms of research on various infectious phenomena" being suggested as one of the reasons. Following in this research trend, we have performed multifaceted analyses of various infection phenomena. This study, which promotes the elucidation of the "overall picture of viral infection phenomena" (Fig. 1), is not only important internationally but also highly significant in terms of ongoing foundation building in this field. Moreover, by using viruses as biological probes, our approach in elucidating cellular and biological mechanisms that cannot be clarified by conventional research on host cells has the potential to lead to the discovery of new biological phenomena that will have an impact not only on virology but also on general biology.

【Publications Relevant to the Project】

· Maruzuru Y, et al., Herpes simplex virus 1 VP22 inhibits AIM2-dependent inflammasome activation to enable efficient viral replication. ***Cell Host & Microbe*** 23: 254-65, 2018.
· Arii J et al., ESCRT-III mediates budding across the inner nuclear membrane and regulates its integrity. ***Nat. Commun.*** 9: 3379, 2018.

【Term of Project】 FY2020-2024

【Budget Allocation】 152,100 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.ims.u-tokyo.ac.jp/Kawaguchi-lab/KawaguchiLabTop.html