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# The 3rd anniversary of Frontiers in Virology: aiming to consolidate the virus research

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Department of Microbiology, Graduate School of Medicine, Tokushima University, Tokushima, Japan KEYWORDS

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Three years have passed since the launch of our journal "Frontiers in Virology". It was founded to biologically and molecularly clarify the multifaceted nature of viruses by multidisciplinary approaches. Understanding and gaining ascendancy over the complex viruses is tremendously challenging. We virologists have to comprehend them in terms of virus-virus, virus-host, and virus-environment relationships, as well as their fundamental properties. Of note, some viruses are highly or moderately pathogenic for humans and also for animals and plants that are important and/or useful to humans. Furthermore, we need to work with the readily mutable and transmittable viruses. Thus, we must have numerous integral specialty sections in the journal designated "Antivirals and Vaccines", "Bioinformatic and Predictive Virology", "Emerging and Reemerging Viruses", "Fundamental Virology", "Modeling of Viral Replication and Pathogenesis", "Systems Virology", "Translational Virology", "Viral Disease Investigation", "Viral Diversification and Evolution", and "Virus and Host Immunity". For better grasping each section, we are currently revamping and standardizing the scopes of all sections in the journal. All the sections are supposed to coordinate organically. "Frontiers in Virology" is also considerate to authors/researchers by offering numbers of article types such as Original Research, Methods, Review, Hypothesis and Theory, Clinical Trial, Brief Research Report, Perspective, Opinion, and Case Report to increase the optionality and possibility for publication (https://www.frontiersin.org/journals/virology/for-authors/article-types). As stated in the previous Grand Challenge articles (1, 2), we have provided here in "Frontiers in Virology" an innovative platform for integrative research on the most abundant species in nature, i.e., the virus. After the journal initiation, more than 1300 researchers have joined us as editor (specialty chief editor, associate editor, guest associate editor, or review editor) and approximately 250 articles have been published.

Needless to mention, one of the most important issues for modern virology is to cope with the human diseases caused by a wide variety of viruses. Especially, viruses that spread widely/globally and seriously affect humans have been long concerned about. In light of the current world situation, there may emerge not-yet-identified new viruses with such properties at any time. We have experienced a number of repeated pandemics by the influenza virus (IFV) in the past (3). While some effective drugs and vaccines are available to date, IFV is extremely difficult to suppress due to its high mutability and its wild-bird origin. Experts are really anxious about other terrible influenza-pandemics by new type viruses. About 40 years ago, we also encountered another dreadful and readily mutable virus HIV-1 that causes AIDS. Since the AIDS outbreak began, approximately 100 million people have been infected with HIV-1 and 40 million people have died of AIDS/AIDS-

related diseases. AIDS still stays pandemic and functional cure is not yet achieved (4-7). Thus, the causative virus HIV-1 needs to be studied in more detail to precisely understand viral persistent state in humans. Toward this direction, further medical investigation as well as fundamental basic virus research should be performed (8-18). Since retroviral HIV-1 genome integrates into those of infected humans to establish the inseparable virus-host relationship, firm and solid virological understanding of the intracellular events is particularly required to address and follow the significant numbers of pre-clinical and clinical issues on AIDS. And now, we are witnessing new global pandemics caused by the corona and pox viruses (SARS-CoV-2 and Mpox virus, respectively) (19-28). As a matter of course, on the basis of previous profound knowledge of various viruses, extensive efforts have been paid to understand the biology/molecular biology of the two viruses and to establish valid preventive and therapeutic measures. One problem here is that the high adaptability of the two viruses despite their quite low mutation rates (19, 28). This observation can be explained by some specific mechanisms such as recombinational mutations (the nonprocessive replicase-driven template switching mechanism for SARS-CoV-2) (19, 29) and transient gene duplications (the accordion model for Mpox virus) (28, 30). In any case, we have to deal with the mutant viruses appearing in the course of viral infection.

As described above, IFV, HIV-1, SARS-CoV-2, and Mpox are highly mutable and adaptable to their restrictive hostile environments. These viruses are dexterous in being able to ingeniously modify them significantly in response to variously changing circumstances. Through genomic adaptive mutations and/or by their own viral proteins, viruses are able to circumvent the barriers such as cellular anti-viral factors, host natural/acquired immunity against viruses, antivirals, and vaccines. As an example of the viral escape mechanism other than that by viral genomic mutations, HIV-1 innately encodes for its own accessory proteins that allow it to evade cellular restriction factors (31-34). Collectively, viruses are likely to frequently change in an environment-dependent way. So far, we are able to know the entity of the virus concerned only by nucleotide sequencings. This means that we are running behind viruses, just retrospectively following viruses. Most virologists including our group have adopted this research strategy due to limitations in the laboratory virology, whereas many biologically significant results have been accumulated by exploring viruses this way. Our team has investigated the HIV-1 adaptation process to clarify the virological significance of synonymous nucleotide substitutions and the structure-function relationship of viral proteins by combining experimental virology and the data/computational science, and successfully published the results obtained in a series of articles (35-42). On one hand, quite different from the experimental approaches, a new class of virus studies based on big data of massive scope and scale have attracted attention as an unprecedented research strategy and concept in the past decade (43–52). The studies are characterized by the methods to collect and analyze large data sets, such as NSG, CRISPR-based technologies, machine learning, and various algorithms. The research targets in those studies were: epidemiology of virus and viral disease, plant viruses, virus ecology, virus adaptation and evolution, virus drug-resistance, databases in virus research, various computational tools. The data and computational sciences may aid forecasting the future virus-related issues. Big data and experimental approaches surely synergize to consolidate the predictive role of modern virology.

"Frontiers in Virology" continues to be a platform for cutting edge studies on virology. It covers all virological subjects as indicated in the names of various specialty sections. Furthermore, "Frontiers in Virology" highly appreciates articles on the leadingedge technology to precisely understand virus-related matters. The ideal goal of virology is to be able to prospectively foresee everything about the virus and its effects on hosts/environments, being beforehand with viruses. In conclusion, we "Frontiers in Virology" earnestly hope the submission of your important papers with a high scientific value.

## Author contributions

AA: Conceptualization, Writing – original draft, Writing – review & editing. TK: Writing – review & editing. MN: Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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