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Editorial: HIV/SIV basic research update

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Editorial on the Research Topic
HIV/SIV basic research update

Since its identification as an etiological agent for acquired immunodeficiency syndrome (AIDS) and AIDS-related disease complex (ARC) in 1983, the extent of studies on human immunodeficiency virus type 1 (HIV-1) has been unprecedented (1). Because of the severity of the disease, its pandemic nature, and also the inherent intellectual curiosity of scientists for the novel virus, we virologists have made every effort to explore HIV-1 and related viruses in detail. From these far-reaching systemic studies performed by numerous virologists and their colleagues in different expert fields, we have gained a remarkably wide variety of basic and medical virological knowledge and insights on a range of HIV/AIDS issues (2–7). It should be noted here that the achievements in HIV-1 research in the four decades since its discovery (i.e., those of actual virological findings, virological concepts, strategic approaches, practical experimental tools/systems, scientific findings/concepts/research systems not confined to the virology research field, etc.) are applicable not only to HIV-1 and its related viruses but also to viruses of other families. In this regard, we would like to underscore the importance of the basic and applied HIV-1 research conducted so far for human virology as a whole.

In this Research Topic on HIV/SIV-related subjects (i.e., in our Research Topic designated "HIV/SIV basic research update"), there are nine full articles, six original research and three review articles, contributed by actively working researchers in the HIV/SIV-related fields in Canada, Japan, Rwanda, Uganda, and the USA. Each work presented addresses a currently crucial theme concordant with or closely relevant to the major aim of our Research Topic, as clearly expressed by its title and keywords. Meissner et al. comprehensively summarize the virology of representative primate retroviruses (HIV-1, HIV-2, and human T-cell leukemia virus type1 (HTLV-1)) in the first review article of this Research Topic. They provide a sophisticated overview of the viral replication cycle, genomic and biological diversity, and also of host cellular proteins that most notably affect viral replication. McAllister et al. investigate the Sp family proteins in cells of the monocyte-macrophage lineage and find that the binding of Sp1 to viral LTR increased relative to that of Sp3 following monocytic differentiation. It is also shown that the activity of Sp proteins is additionally regulated at the post-translational level. Miyakawa et al. identify a cellular transmembrane protein MAL that substantially inhibits HIV-1 virion production by the bioluminescence resonance energy transfer (NanoBRET) assay. Of note,

the antiviral activity of MAL was partially antagonized by that viral Nef protein. Umviligihozo et al. examine the sequence and function of viral Nef and Vpu proteins in a cohort of Rwandan long-term survivors with HIV-1 subtype A. It is suggested that the attenuated function of Nef, but not Vpu, is responsible for slowing disease progression. Kaku et al. produce five anti-idiotypic antibodies from mice immunized with 1C10, a ladle-type anti-HIV-1 subtype B V3 antibody, in order to analyze the epitope-paratope interactions between 1C10 and HIV-1 V3 loop. They demonstrate that the anti-idiotypic antibodies raised against the potent cross-neutralizing human antibody 1C10 recognize a key amino acid formation essential for steric interactions between the 1C10 and V3 loop. Curlin et al. evaluate virus replication kinetics, CD4+ T cell dynamics, and genetic adaptive changes in humanized BLT mice using three simian immunodeficiency viruses (SIVs) designated SIVmac239, SIV_{B670}, and SIV_{hu}. All three biologically distinct SIVs originating from SIVsm are shown to infect and replicate in these model animals and are found to be genetically adaptable in the hosts. The small model animals, susceptible to both SIV and HIV, may open a novel avenue for future comparative studies. Whitehurst et al. examine the effect of HIV co-infection on Epstein-Barr virus (EBV) replication and EBV-induced tumorigenesis using humanized NSG mice. They demonstrate that HIV co-infection enhances systemic EBV replication, host immune activation, and EBV-induced tumorigenesis. The results showing a direct effect of HIV co-infection on EBV pathogenesis and disease progression may facilitate detailed studies in the future. In their review article, Sukegawa and Takeuchi describe how cells of the monocyte/macrophage lineage influence HIV-1 infection. They focus on the monocyte/macrophage impact on HIV-1 replication and virus-reservoirs establishment. They also refer to recent approaches toward HIV-1 eradication by specific targeting of cells of a monocyte/macrophage lineage. Vargas and Sluis-Cremer outline the so-called "block and lock" therapeutic approach to a functional cure for HIV-1 infection in their review article. They focus on the small molecules, nucleic acids, and recombinant proteins reported to block and/or lock HIV-1 in the latent state, providing a clear overall picture of the "block and lock" approach against HIV-1.

Lastly, we briefly describe the HIV/AIDS issues that remain to be solved. From our perspective, major issues can be organized and summarized as follows: (i) detailed molecular biological understanding of viral replication and viral structural proteins (8–14); (ii) elucidation of viral adaptation and evolution in various circumstances and proactive prediction of viral adaptive mutations (15–17); (iii) clear determination of the biological significance of viral accessory proteins (18–21); (iv) establishment of animal models suitable for each research project (22, 23); (v) identification of viral reservoirs and a functional cure for HIV-1 infection (24–28). While we have accomplished many of the themes listed above in the past four decades, much still remains elusive. Anti-HIV-1 drugs have been successfully developed, and thus AIDS is no longer an incurable disease. However, a complete or functional cure is not yet achieved. Importantly, in addition, scientifically interesting and crucial but unsolved matters await clarification. In collaboration with experts in other research fields, we virologists have to seriously tackle the issues described above and move toward valid anti-HIV-1 strategies with a solid background in biological and molecular biological virology (29, 30).

Author contributions

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

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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Publisher's note

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