HIV-1 transmission and phylogenetics

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This issue of Current Opinion in HIV and AIDS focuses on the contribution of HIV-1 phylogenetics to our understanding of the HIV-1 epidemic and, more specifically, of HIV-1 transmission. HIV-1 epitomizes viral diversity with extensive variability across circulating strains and continuous diversification, sometimes augmented by superinfection, in infected individuals. Phylogenetic analyses have shown that nine subtypes exist for the main group of HIV-1 viruses as well as almost a hundred circulating recombinant forms and unique recombinants.

The first part of this issue describes the central role HIV-1 phylogenetics plays in monitoring HIV-1 infections globally. Bbosa et al. (pp. 153–160) provide a comprehensive overview of HIV-1 worldwide diversity. HIV-1 shows particular geographic distribution patterns with founder effects that led to the predominant presence of a given subtype in specific areas, such as HIV-1 subtype B in the Americas and Western Europe or HIV-1 subtype C in sub-Saharan Africa. Importantly, because of the significant burden of infections in sub-Saharan Africa, about half of all HIV-1 infections correspond to HIV-1 subtype C. They stress that recombinant strains represent a continuously growing proportion of HIV-1 infections, a fact that is becoming better appreciated thanks to increasing numbers of sequences corresponding to full-length HIV-1 genomes. To overcome the relatively small numbers of full-length data from sub-Saharan Africa, Abeler-Dörner et al. (pp. 173–180) describe the PANGEA consortium. The authors report that more than 18 000 HIV-1 genomes have already been sequenced from five countries in East and Southern Africa. This level of sampling is fundamental for characterizing the evolution of the HIV-1 epidemic through novel molecular epidemiology techniques.

Molecular epidemiology is a very active area of research in HIV-1 phylogenetics and constitutes the second part of this issue with five articles providing details on key aspects for the study of HIV-1 transmission. Maleitch Junqueira et al. (pp. 161–172) highlight features that are critical for defining the structure and dynamics of HIV-1 transmission networks, describing that there is currently no unani-

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mous methodology for these analyses and highlighting that the gene chosen and length of the sequence fragment under study can affect the results. Ragonnet-Cronin et al. (pp. 205–212) show the advantages of using phylodynamics approaches over clustering methods. They describe how densely sampled epidemics can provide a novel understanding of HIV-1 transmission risk by bringing to the forefront critical risk groups that correspond to undisclosed or missing links in phylogenetic networks. This review also clearly illustrates the difficulty of assessing age disparity in HIV-1 transmission networks. Next, Leitner (pp. 181–187) describes how to further resolve viral transmission patterns by integrating HIV-1 within-host diversity into the analyses. New methods explicitly use measures of HIV-1 diversity within a sample to more precisely infer transmission patterns, a crucial advance as retrospective studies have shown that phylogenies based on sequences from linked hosts were not necessarily congruent with the transmission history. Wertheim et al. (pp. 213–220) consider the potential benefits of transforming the aforementioned molecular epidemiology methodologies into more prospective tools to address public health goals. Although it is evident that real-time applications of molecular epidemiology could foster HIV-1 prevention public health goals, questions remain on the feasibility of such approaches given our incomplete knowledge of actionable processes between individual and cluster levels. Finally, on the molecular epidemiology topic, Mehta et al. (pp. 221–226) address the fundamental ethical issues behind molecular epidemiology analyses. As methodological advances permit a greater understanding of HIV-1 transmissions structures and patterns, the risk of disclosure and privacy loss is also greatly augmented; risks of harm that are also more important in certain social and legal contexts. Efforts are needed to raise the awareness of the risks and benefits of molecular epidemiology approaches.
for researchers, community, and public health stakeholders.

The third part of this issue emphasizes how HIV-1 phylogenetics can help gain a better understanding of clinically relevant aspects of the epidemic. Bale et al. (pp. 188–193) describe how phylogenetics have helped understand the impact of antiretroviral therapy (ART) on HIV-1 populations, highlighting the lack of replication during ART and providing ways to evaluate the contribution of different cell subsets or organs as well as the impact of therapeutic interventions. Avila-Rios et al. (pp. 194–204) provide a sweeping overview of the impact of cytotoxic T lymphocyte (CTL) escape mutations as a driver of HIV-1 evolution. They emphasize the immunological and clinical importance of CTL escape mutations and the differential patterns across localized epidemics and ethnic groups while concluding that CTL-driven adaptation of HIV-1 would most likely not offset the impact of preventive interventions. In the last review, I argue that phylogenetics have been integrated to HIV-1 vaccine research in a more limited way than could be expected given how HIV-1 diversity has been considered a major obstacle for HIV-1 vaccine development.

Together, the 10 articles in this issue show how recent advances in phylogenetics offer a more detailed understanding of the dynamics of HIV-1 transmissions. By combining epidemiology, phylogenetic, and phylodynamic approaches, we can now obtain an unprecedented level of understanding of HIV-1 epidemics. These methods provide knowledge on epidemic drivers and give new opportunities to uncover risk groups and HIV-1 transmission patterns not identified with traditional epidemiology methods. Implementing these methods should yield more accurate surveillance data that can be harnessed to design better prevention campaigns. However, methodological progress in phylogenetics and the opportunities it offers should not overshadow important limitations. The link between a phylogenetic cluster and its public health benefit remains contentious, and the risk of privacy loss must not be dismissed. It is only by working together with community advocates and public health officials that researchers can find ways to maximize the potential of novel phylogenetic approaches to prevent HIV-1 transmission in communities.

Acknowledgements

None.

Financial support and sponsorship

The work was supported by a cooperative agreement between The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., and the U.S. Department of the Army [W81XWH-18-2-0040].

Conflicts of interest

There are no conflicts of interest.