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“Do HIV-1 strains matter in the context of cure research?”

HIV is a blood-borne pathogen that infects human CD4+ cells. Upon infection, the virus integrates into the human chromosome, resulting in the life-long infection the host. Without daily doses of antiretroviral treatment to suppress viral replication, an infected individual would develop acquired immunodeficiency syndrome (AIDS), which often results in death. Antiretroviral treatment has successfully prolonged lifespans of infected individuals, but it comes at the cost of lifelong dependence, requires strict adherence, and requires a strong health care system to monitor treatment efficacies. HIV cure is a major research priority outlined by the USA National Institute of Health. A cure to HIV is defined as the elimination of integrated HIV DNA reservoirs (sterilizing cure) or the permanent silencing of viral transcription of genome-intact proviruses to prevent virologic rebound (functional cure) in the absence of antiretroviral therapy. To-date, there are only three known cases of sterilizing cure through bone-marrow transplantation in individuals with cancer, a procedure that is considered too risky for the general public. Other strategies to cure HIV includes: “Shock and kill,” which aims to eliminate or reduce viral reservoir sizes by using latency reversal agents (LRAs) to activate viral transcription, thereby exposing HIV-infected cells to viral cytopathic effect, and/or natural and/or interventional immune clearance; “block and lock,” which aims to force proviruses into a transcriptionally dormant state; and “genome editing” through zinc finger nucleases or CRISPR/Cas9 approaches, which aims to excise and decapacitate integrated proviral genomes and/or a host protein CCR5 which function as one of HIV entry co-receptors. Except bone-marrow transplantation and host CCR5 knock out, all other aforementioned approaches are potentially susceptible to viral genetic and integration site diversity. However, current reservoir and persistent studies focus heavily on a specific strain of HIV: subtype B HIV-1. Whether viral strain-specific genotypic differences drive differences in reservoir profiles is poorly understood. Achieving a broad understanding of reservoir composition diversity across HIV subtypes is a prerequisite to evaluating whether a given cure strategy is broadly applicable.



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