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Potential development of inactivated HIV-1 transmitted/ founder virus (T/F) vaccine

Nearly 80% of sexually transmitted HIV infections are established by one transmitted/founder virus (T/F). Highly mutated bNAbs resulting from chronic infection will not be needed if the initial T/F virus infection is prevented. Our method inactivates HIV by a targeted photo-inactivation of HIV reverse transcriptase (RT). We propose its use to develop a T/F virus polyvalent inactivated whole-virus vaccine with the most frequent subtypes of T/F viruses to prevent initial T/F virus infections. An azido (-N3) group introduced into a diarylpyrimidine (DAPY) creates a photo active DAPY analog (PA-DAPYa). When incubated with HIV-1 particles and exposed to non-microbicidal UV light, there is irreversible cross-link of the PA-DAPYa to the HIV-1 RT. To confirm inactivation, control and test suspensions of SF162 HIV were used to infect PBMCs and incubated up to 21 days. With UV light alone as control HIV virus replicated after 40 minutes. Control-DAPY inhibited replication at 100 nM with variable inactivation effectiveness even at 500 nM. In contrast, at all UV exposure times, 500 nM of PA-DAPYa totally inactivated HIV. HIV p24 was not detected in the supernatant of inactivated HIV cultured in PBMCs. This experiment was repeated with different viral stocks and PBMC donor pools. Incubating a suspension of HIV SF162 with PA-DAPYa followed by UV light exposure completely and irreversibly inactivates HIV-1. We foresee using this inactivation methodology to inactivate T/F viruses to lead to a polyvalent preventive HIV vaccine capable of neutralizing the most common T/F virus strains.

Biography

Adan Rios received the training in Internal Medicine from the Gorgas U.S. Army Hospital in Panama. He completed the training in Medical Oncology at The MD Anderson Cancer Center. In addition to his expertise in General Oncology he has a particular interest in the use of Biological Response Modifiers for the treatment of Cancer and in virally–associated malignancies including HIV-related malignancies. He is a recipient of the MD Anderson Distinguished Alumnus Award and the George Washington University PresidentialMedal.

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