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Circulating cellular and extracellular microRNAs as biomarkers of lentiviral infection and disease progression

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Antiretroviral therapy (ART) has fundamentally changed the HIV/AIDS pandemic, reducing mortality and morbidity, and recent research supports early treatment with the constituent medications. However, as patients live longer with HIV, some disorders, such as the HIV-associated neurocognitive disorders, continue to pose problems. Biomarkers are needed to classify at-risk individuals and to identify those who do not require early treatment. For example, there are currently no biomarkers of elite suppressors (ES): individuals who control HIV-1 replication without ART. Whether isolated from circulating blood cells or from plasma, where they are remarkably stable, microRNAs have been largely unexploited in the HIV disease biomarker search. We have profiled miRNAs in circulating cells and in plasma of ES, viremic patients, and controls using complementary profiling and validation techniques. PBMC miRNA profiles distinguished ES and controls, which generally cluster together, from viremic HIV-1-infected individuals. miRNAs that are downregulated in cells of viremic patients support reported mechanistic roles in HIV-1 latency (e.g., miRs-125b and -150), while others have previously uncharacterized connections with HIV-1. The utility of small RNAs as biomarkers of lentiviral infection and disease progression is also supported by results from an animal model of HIV infection. More than 40 miRNAs are differentially expressed during acute simian immunodeficiency virus (SIV) infection. At least six of these miRNAs, when used together in a prognostic test, predict development of central nervous system disease. These results suggest that both circulating and cellular miRNAs should be investigated further as biomarkers of specific lentivirus-associated conditions.

Biography

Kenneth W. Witwer earned his doctorate in the Biochemistry, Cellular and Molecular Biology Program at Johns Hopkins University, supported by a National Science Foundation Graduate Research Fellowship. He performed postdoctoral fellowship in the Department of Molecular and Comparative Pathobiology, also at Johns Hopkins, and joined the faculty in 2011. Witwer has been recognized with several young investigator awards for his work on innate and intrinsic immune responses to retroviral infection.

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