

9th International Virology Congress and Expo

March 13-14, 2017 London, UK

Cofilin is a clinical marker of HIV-mediated CD4 T cell dysfunction

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HIV infection leads to the gradual depletion of blood CD4 T cells. It has long been recognized that the residual peripheral blood CD4 T cells in HIV-infected patients have numerous functional abnormalities such as loss of T helper function, T cell anergy, abnormal T cell homing and migration. Given the low number of infected T cells found in the peripheral blood, these T cell defects largely result from a bystander effect. It is possible that chronic immune activation, persistent exposure to viral proteins, or abortive infections may trigger persistent signals in CD4 T cells, pushing them towards dysfunctioning. Nevertheless, a molecular marker clinically representing HIV-mediated T cell dysfunction is lacking. Cofilin is an actin-depolymerizing factor that regulating actin dynamics for T cell migration and activation. Previously, we demonstrated that during HIV-1 infection of blood resting CD4 T cells, the viral envelope protein triggers CXCR4 signaling to activate cofilin to overcome the static cortical actin restriction in resting CD4 T cells. We have also speculated that in HIV-infected patients, cofilin activity could be abnormally altered by gp120-CXCR4/CCR5 signaling. To test this hypothesis, we conducted a clinical trial to examine the cofilin status in blood resting CD4 T cells of HIV-infected MSM cohort in the AIDS Clinical Center of China Medical University. Cell lysates from un-stimulated blood resting CD4 T cells were prepared and analyzed by a reverse phase phospho-cofilin microarray (performed by Theranostics Health Inc. Rockville, MD). We found that there is a significant difference in cofilin phosphorylation between infected and healthy controls. HIV-infected patients carry significantly higher levels of active cofilin (dephosphorylated). Surprisingly, ART treatment did not restore cofilin phosphorylation to the healthy control level. These results demonstrate that cofilin could serve as a new clinical marker to quantify HIV-mediated T cell dysfunction; complementary therapies additional to ART may also be required to restore cofilin phosphorylation to a healthy level.

Biography

Yuntao Wu has completed his PhD from Queen's University at Kingston, Ontario, Canada, and Post-doctoral studies from the National Institute of Health, Bethesda, Maryland, USA. He is a Professor at the National Center for Biodefense and Infectious Diseases, George Mason University, Virginia, USA. He has published more than 50 papers in reputed journals (*Cell*, *Science*, *PLoS Patho*, *J. Virol*, *Virology*, *J. Bio. Chem*), and has been serving as an Editorial Board Member of a number of virology journals.

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