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Selective elimination of latently HIV-1 infected cells via anticancer drugs-induced p53 pathway

Cheol-Hee Yoon, Young Hyun Shin, Byeong-Sun Choi, Kyung-Chang Kim, Yong Kwang Park and **Chun Kang**
Korea National Institute of Health, South Korea

Despite the successful inhibition of human immunodeficiency virus type 1 (HIV-1) replication by combination antiretroviral therapy, cells latently infected with HIV-1 remaining in patients are a major obstacle for eradication of HIV-1 infection. The tumor suppressor factor p53 is activated by HIV-1 infection and inhibits HIV-1 replication. However, a therapeutic strategy based on p53 activity has not been considered for elimination of latently infected cells. Herein, p53-linked apoptosis of cells latently infected with HIV-1 and uninfected cells were compared. Upon treatment with 5-fluorouracil (5-FU), apoptosis was increased in latently infected ACH2 cells encoding competent p53 compared with uninfected parent A3.01 cells, while the apoptosis of latently infected p53 null J1.1 cells was less than that of uninfected cells in analysis with flow cytometry and Western blotting using antibodies for cleaved caspase-3 and PARP. The levels of expression and activation of p53 were higher in both latently infected ACH2 and NCHA2 cells than in uninfected cells. Furthermore, the levels of p53 in both cells were further increased upon 5-FU treatment. Consistent with p53 status, apoptosis of ACH2 and NCHA2 cells were markedly increased compared with uninfected and J1.1 cells upon treatment with other anticancer drugs such as doxorubicin and etoposide. Knockdown of p53 in cells with latent HIV-1 infection diminished apoptosis upon 5-FU treatment. Our results indicate that when treated with anticancer drugs, apoptosis of cells with latent HIV-1 infection was increased via the p53 activation pathway and may provide information for application of anticancer drugs to selectively eliminate HIV-1 reservoirs.

Biography

Cheol-Hee Yoon has completed his PhD from Sungkyunkwan University in 2008 and studied from Sothern California University School of Medicine as Postdoctoral Fellow. He is studying in a field of chronic viral disease as Scientific Researcher of Division of AIDS, Korea National Institute of Health. He has published more than 25 papers in peer reviewed journals.

kmc755@korea.kr

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