Abstract

Progression of HIV infection in HIV-positive patients can now be successfully controlled by the combined antiretroviral therapy. However, due to persistence of the latent reservoir, HIV infection cannot be cured. The immune system nor current therapeutic approaches can target the pool of latently infected cells, thus strategies aiming at reactivation and subsequent elimination of the reservoir cells are recognized as possibly curative.

This thesis has examined previously demonstrated latency-reversing capacity of heme arginate (HA), another redox modulator, and their synergism with Protein Kinase C inducer phorbol myristate acetate (PMA) to reactivate HIV-1 in the context of heme metabolism. HIV-1 reactivation was assessed by the intensity of green fluorescence in the model Jurkat cell line clone (A2), containing HIV-1 *"mini-virus"* (LTR-Tat-IRES-EFGP-LTR), as well as in the A2 cells stably transfected with plasmid vectors encoding cDNA for specific factors of heme metabolism and for control luciferase. While the administration of redox modulator alone did not stimulate expression from the HIV-1 LTR and HA reactivated the *"mini-virus"* only slightly, both compounds revealed a synergy with PMA in all cell lines studied. Basal and induced expression of EGFP was found variable in cells transfected with plasmids encoding cDNA for the individual factors examined. The results provided in this work suggest that studied genes are potentially significant for HIV-1 reactivation and that heme metabolism might play an important role in HIV-1 latency reversal and maintenance.

Keywords: HIV-1 latency, heme metabolism, heme arginate, redox modulator, latency-reversing agents