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Effect of Antioxidants in Cathepsin B Release by HIV Infected Macrophages

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Effect of Antioxidants in Cathepsin B Release by HIV Infected Macrophages*

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Abstract

During HIV infection of macrophages, the lysosomal protein cathepsin B is released and induces neurotoxicity. Also, the levels of cathepsin B are increased in plasma and post-mortem brain tissue of patients with HIV-associated dementia. Oxidative damage is increased in HIV-infected patients, while antioxidants are decreased in HIV-associated dementia. Dimethyl fumarate (DMF), an antioxidant, has been reported to decrease HIV replication and neurotoxicity caused by HIV-infected macrophages. Since HIV also increases cathepsin B, we hypothesize that DMF will also reduce cathepsin B release from HIV-infected macrophages. Monocyte-derived macrophages (MDM) were isolated from healthy donors and inoculated with HIV-1_{ADA}. After removal of infection, MDM were treated with DMF at different concentrations (15, 30, and 60 μ M) until day 12 post-infection, changing and collecting media every three days. HIV-1p24 and cathepsin B levels were assessed from HIV-infected MDM supernatants at the end of cultures using ELISA. Results indicate that DMF reduced HIV-1 replication and cathepsin B secretion from HIV-infected macrophages, in a concentration-dependent manner, in comparison with vehicle (DMSO)-treated controls. However, cathepsin B secretion was not affected by HIV infection in vehicle-treated controls. In conclusion, DMSO may have had an unexpected effect in cathepsin B secretion in our experiments, and this could explain why cathepsin B secretion was not affected by HIV infection. Future experiments will include an untreated control group to determine if DMSO vehicle is having an effect in cathepsin B secretion. This will lead us to determine the role of DMF in cathepsin B secretion from HIV-infected macrophages.

KEYWORDS: Cathepsin B; HIV; DMF; MDM

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During HIV infection of macrophages, the lysosomal protein cathepsin B is released and induces neurotoxicity. Also, the levels of cathepsin B are increased in plasma and post-mortem brain tissue of patients with HIV-associated dementia. Oxidative damage is increased in HIV-infected patients, while antioxidants are decreased in HIV-associated dementia. Dimethyl fumarate (DMF), an antioxidant, has been reported to decrease HIV replication and neurotoxicity caused by HIV-infected macrophages. Since HIV also increases cathepsin B, we hypothesize that DMF will also reduce cathepsin B release from HIV-infected macrophages. Monocyte-derived macrophages (MDM) were isolated from healthy donors and inoculated with HIV-1_{ADA}. After removal of infection, MDM were treated with DMF at different concentrations (15, 30, and 60 μ M) until day 12 post-infection, changing and collecting media every three days. HIV-1 p24 and cathepsin B levels were assessed from HIV-infected MDM supernatants at the end of cultures using ELISA. Results indicate that DMF reduced HIV-1 replication and cathepsin B secretion from HIV-infected macrophages, in a concentration-dependent manner, in comparison with vehicle (DMSO)-treated controls. However, cathepsin B secretion was not affected by HIV infection in vehicle-treated controls. In conclusion, DMSO may have had an unexpected effect in cathepsin B secretion in our experiments, and this could explain why cathepsin B secretion was not affected by HIV infection. Future experiments will include an untreated control group to determine if DMSO vehicle is having an effect in cathepsin B secretion. This will lead us to determine the role of DMF in cathepsin B secretion from HIV-infected macrophages.

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