

POSTER 56 **β -ESTRADIOL ATTENUATES THE ANTI-HIV-1 EFFICACY OF STAVUDINE (D4T) IN PRIMARY PBL**

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Background: Female hormones are known to play an important role in predisposition for many infectious diseases. Recent work suggests there are gender effects in HIV/AIDS progression. Here we ask whether the sex steroid hormone β -estradiol affects the replication of HIV-1 or the efficacy of a common anti-retroviral drug, Stavudine (D4T).

Results: Human PBL were infected with HIV-1 in the presence or absence of combinations of sex steroid hormones and the anti-retroviral drug, D4T. After seven days in culture, viral supernatants were assayed for HIV-1 p24 protein. β -estradiol resulted in a modest inhibition of HIV-1 replication of ~ 26%. However, 2nM β -estradiol increased the amount of HIV-1 replication in the presence of 50nM D4T from a baseline of 33% (+/- SE= 5.4) to 74% (+/- SE= 5.4) of control virus levels in the absence of drug. Both results were statistically highly significant ($p < 0.001$). β -estradiol did not increase the replication of a D4T-resistant strain of HIV in the presence of D4T. The effects were unlikely to be due to general cell inhibition or toxicity because these concentrations of drug and hormone cause no cytotoxicity in PBL as measured by trypan blue exclusion.

Conclusions: β -estradiol inhibited both HIV-1 replication in primary human PBL and the antiretroviral efficacy of D4T in PBL cultures. To optimize antiretroviral drug therapy, it may be necessary to monitor patient hormonal status.