Immune Modulation With Rapamycin as a Potential Strategy for HIV-1 Eradication

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RESULTS: Rapamycin does not inhibit expression of HIV-1 by αCD3/αCD28 stimulation

To determine whether the immunosuppressant rapamycin would affect transcription of HIV-1 elicited by global T cell activation, we purified CD4+ cells from HIV-1 infected individuals on suppressive ART and treated 5 million cells each with vehicle alone, αCD3/αCD28 alone, or αCD3/αCD28 plus rapamycin (5 ug/ml) or cyclosporin (500 nM) for 24 hours. Following treatment RNA was isolated from lysed cells and intracellular HIV-1 mRNA was measured using previously described primers and probes specific to HIV-1 polyadenylated transcripts (2).

METHODS & RESULTS

RESULTS: Effects of immunosuppressant treatment on in vitro predictors of clinical toxicity

In order to be clinically relevant, rapamycin must not only allow for HIV-1 expression, but also inhibit toxicity associated with T cell activation. A primary mediator of unacceptable clinical toxicity is pro-inflammatory cytokine release. Therefore, we measured supernatant concentration of IL-2, TNF, and IFNγ.

CONCLUSIONS

Rapamycin downregulates toxic effects of T cell activation without affecting expression of HIV-1. These findings suggest that latency reversing agents that induce some level of T cell activation may be safely and effectively used in the presence of immunomodulators such as rapamycin.

REFERENCES

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