Abstract of the Thesis

Ephedrine enhances HIV-1 reactivation from latency through elevating Tumor Necrosis Factor Receptor II (TNFRII) expression

Background: HIV latency is serious problem to cure HIV infection. Previous study showed that *Ephedrae Herba,* a component of Japanese herbal medicine Maoto demonstrated activation of HIV-1 replication from latent infected U1 cells. The mechanism to enhance HIV-1 replication is induction of NF-κB nuclear translocation. We aim to explore new latent reversing agent (LRA) and to study the effect and mechanism of ephedrine, the main component of *Ephedrae Herba* on reactivation of HIV from latency.

Method: U1 cells were treated with either ephedrine or TNF-α or combined treatment for 48 hour. Intracellular p24 expression was detected by flow cytometer to determine level of HIV-1 reactivation. The p24 secretion was detected by ELISA. HIV gag and Tat-Rev mRNA were detected by real time PCR. Compusyn program was used to analyze the synergistic effect of TNF-α and ephedrine combined treatment.

Results and Discussion: Combined treatment of ephedrine and TNF-α enhanced HIV-1 reactivation. Ephedrine itself lost ability to activate HIV-1 replication. Interestingly, combination of ephedrine and TNF- α treatment demonstrated synergistic effect of HIV-1 reactivation compared to TNF-α single treatment. At 6h post treatment, HIV Tat-Rev mRNA was detected at the rising level after combined treatment of ephedrine and TNF-α. Whilst, HIV-1 Gag mRNA was clearly raised at 12h post treatment. Catecholamine activates tumor necrosis factor receptor (TNFR) on U1 cells. Ephedrine has similar structure as catecholamine and represented higher expression of TNFR2 at early time point after treatment. However, the mechanism of ephedrine on HIV-1 reactivation is still unclear, the reactivation activity could be related to TNFR2 receptor expression. In conclusion, our results indicated that ephedrine enhances HIV-1 reactivation from latency with combination of TNF-α treatment. This data provides information about new reagent, which could support reactivation effect of other LRAs in clinical.