Nullbasic Inhibits HIV Replication Through A Latency-like Suppression of HIV-1 Gene Expression In Jurkat Cells

Dr Hongping Jin

Introduction

Nullbasic (NB) is a mutant of the basic domain of Tat.

Nullbasic: FITKALGISYGRKSSGQAGGDPGQGTHQVSLSKOPT
Tat: FITKALGISYGRKQQRRPQGGQGTHQVSLSKOPT

Basic domain

Nullbasic inhibits HIV production and viral spread in human T cells by 3 independent mechanisms:

- inhibition of the transcriptional activation function of Tat
- disruption of HIV mRNA trafficking by interfering with the viral Rev regulatory protein
- inhibition of HIV reverse transcription

Hypothesis

Stable expression of Nullbasic will result in better protection of T cells from productive HIV replication.

Results

NB was delivered to Jurkat cells with a third generation lentiviral vector pSicoR-EF1a (SR).
No HIV was detected in infected Jurkat.NB.ZsG cells in 6 independent experiments for up to 64 days.

HIV DNA was detected in infected Jur.NB.ZsG cells.

Jurkat cells chronically and productively infected with HIV-1 were treated with NB.ZsG VLPs to achieve >95% expression of NB.ZsG.
NB significantly inhibits HIV gene expression by preventing RNA polymerase II from binding to LTR promoter

Conclusions

- Jur.NB.ZsG cells suppress viral production and spreading following HIV-1 infection.
- NB induces a latency-like effect, which could not be fully reactivated by PMA.
- NB can strongly inhibit HIV-1 gene expression by preventing RNA polymerase II from binding to LTR promoter.

Nullbasic is a potential candidate anti-HIV-1 gene therapy agent.

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