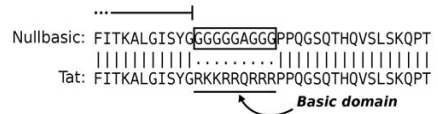


**Nullbasic Inhibits HIV Replication Through A Latency-like Suppression of HIV-1 Gene Expression In Jurkat Cells**

Dr Hongping Jin

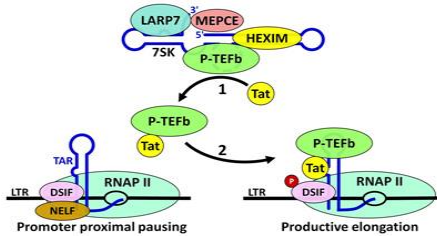
**Introduction**

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



Meredith, et al. Plos one, 2013

**Tat is a transcriptional activator of HIV**



**Role of Tat in HIV transcription**

<http://www.medicine.uiowa.edu/biochem/labs/price/projects/>

**A Mutant Tat Protein Provides Strong Protection from HIV-1 Infection in Human CD4<sup>+</sup> T Cells**

Ann Apoloni,<sup>1</sup> Min-Husan Lin<sup>1,2</sup>, Haran Sivakumaran<sup>1</sup>, Dongsheng Li,<sup>1</sup> Michael H.R. Kershaw<sup>3</sup> and David Harrich<sup>1</sup>

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

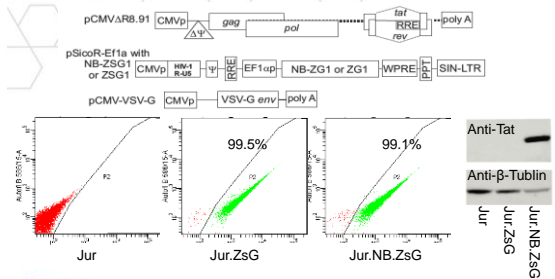
- inhibition of the transcriptional activation function of Tat
- disruption of HIV mRNA trafficking by interfering with the viral Rev regulatory protein
- inhibition of HIV reverse transcription

**Hypothesis**

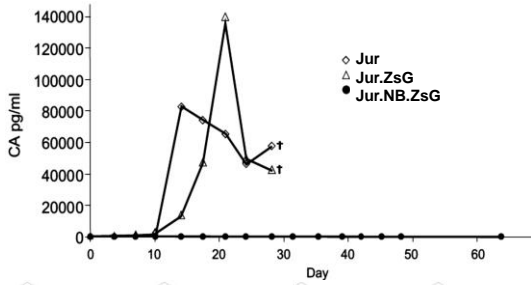
Stable expression of Nullbasic will result in better protection of T cells from productive HIV replication.

**Results**

**NB was delivered to Jurkat cells with a third generation lentiviral vector pSicoR-EF1α (SR).**

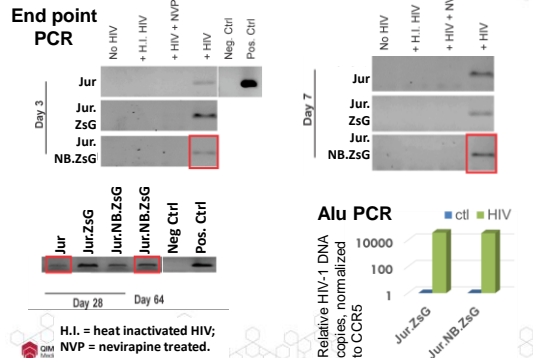


**No HIV was detected in infected Jurkat.NB.ZsG cells in 6 independent experiments for up to 64 days.**



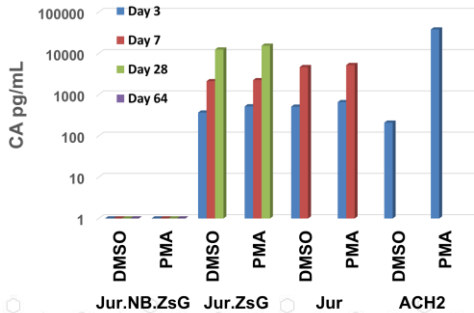
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**HIV DNA was detected in infected Jur.NB.ZsG cells**



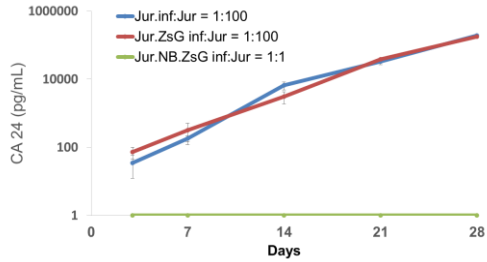
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**PMA cannot stimulate the proviral DNA in Jur.NB.ZsG cells**



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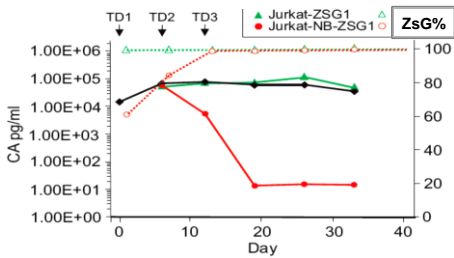
**HIV infected Jur.NB.ZsG could not spread HIV to fresh Jurkat cells**



HIV-infected Jur.NB.ZsG cells were mixed with Jurkat cells at a 1:1 ratio while the infected Jur.ZsG cells and Jurkat cells were mixed with fresh Jurkat cells at a 1:100 ratio.

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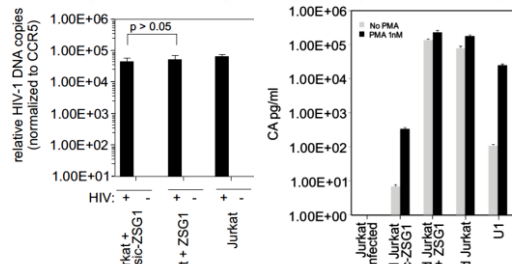
**NB suppressed HIV production in chronically infected Jurkat cells**



Jurkat cells chronically and productively infected with HIV-1 were treated with NB.ZsG VLPs to achieve >95% expression of NB.ZsG.

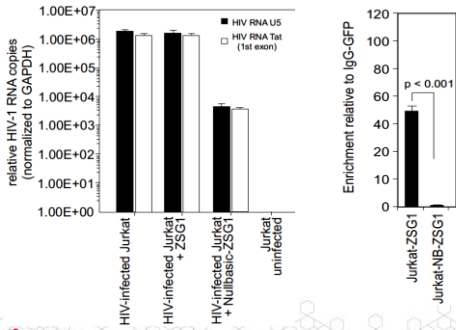
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**PMA can not fully rescue HIV production**



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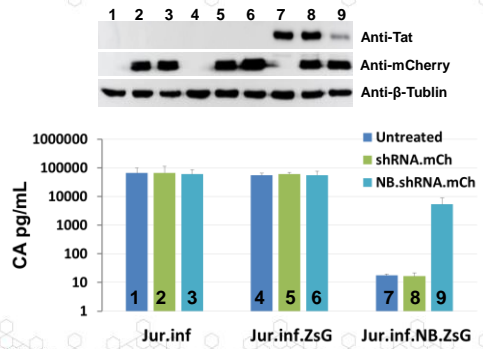
**NB significantly inhibits HIV gene expression by preventing RNA polymerase II from binding to LTR promoter**



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**Knock-down NB increased HIV production**



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**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 in 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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Thank you

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