

Partial inhibition of HIV cell-to-cell spread results in more HIV infected lymph node cells

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Short Abstract — HIV is known to cause cell death. In infections with multiple HIV transmissions per cell, partial inhibition may lead to increased numbers of live infected cells as eliminating surplus viral copies reduces cell death. Using a cell line and lymph node cells, we observed increased numbers of live infected cells when infection was partially inhibited with the antiretroviral efavirenz or antibody. We observed more live infected cells, but fewer HIV DNA copies per cell, relative to no drug. Hence, reduction in HIV transmissions per cell may increase live infected cell numbers in environments where the force of infection is high.

Keywords — HIV, cell-to-cell spread, multiple infections per cell, cell death.

I. BACKGROUND

HIV infection is known to result in extensive cell depletion in lymph node environments [1], where infection is most robust [2]. Cell death occurs by several mechanisms. For example, double strand breaks in the host DNA caused by integration of the reverse transcribed virus results in cell death by the DNA-PK mediated activation of the p53 response [3].

Multiple infections per cell have been reported in cell-to-cell spread of HIV. In this mode of HIV transmission, an interaction between the infected donor cell and the uninfected target results in directed transmission of large numbers of virions [4-7]. Here we examined the effect of reducing the number of HIV transmissions per cell on the number of live infected cells in cell-to-cell spread.

II. RESULTS AND CONCLUSION

We introduce a model of infection where each donor to target transmission leads to an infection probability r and

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death probability q per infection attempt, and a number of infection attempts per cell n . In our experimental system, one infection attempt is measured as one HIV DNA copy. The probability of a cell to be infected and not die after it has been exposed to n infection attempts is:

$$P_n = (1 - (1 - r)^n)(1 - q)^n. \quad (1)$$

We experimentally measured parameter values for this relation. n was measured by PCR to detect the number of reverse transcribed copies of viral DNA in the cell by splitting each individual infected cell over multiple wells. $n=15$ in RevCEM cell line infection and 20 in primary human lymph node cells. We also experimentally measured r and q , which were observed to be 0.28 and 0.15 respectively.

We observed that Equation (1) resulted in a peak in live infected cells when the value of n was decreased from that measured in the absence of inhibitor. We therefore dialed down the number of HIV DNA copies per cell using the reverse transcriptase inhibitor efavirenz or a neutralizing antibody and obtained an increase in live infected cells with partial inhibition, followed by a decrease in infection once inhibition was further increased.

Partial inhibition of HIV infection may therefore provide a surprising advantage to the virus as it may reduce infection mediated cell death and hence increase the number of live infected cells.

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