

# **PA45 ADS-J1, an entry inhibitor targeting gp41, prevents HIV-1 transmission in the in vitro and ex vivo models**

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## **ABSTRACT TEXT**

### **Background:**

We have previously demonstrated that ADS-J1 is a potent HIV fusion inhibitor by targeting gp41. Due to its large molecular size, it is unlikely to be used as an orally applicable anti-HIV drug, but it may be developed as a microbicide for preventing sexual transmission of HIV.

### **Methodology:**

We used a dye transfer assay to detect HIV-1 mediated cell fusion and an ELISA to test p24 antigen. The inhibitory activity of ADS-J1 against infection by cell-free and cell-associated HIV-1 in the cervical explants and cell cultures was quantitated by measuring p24 production or reverse transcriptase (RT) activity. The cytotoxicity of ADS-J1 on vaginal epithelial cells was evaluated by a luciferase assay.

### **Results:**

ADS-J1 blocked HIV-1-mediated cell fusion and inhibited infection of MT-2 cells by HIV-1 X4 virus (IIIB) and of dendritic cells (DCs), monocyte-derived macrophages (MDMs) and cervical explants by R5 virus (BaL) at low  $\mu$ M range. Furthermore, ADS-J1 could block transmission of cell-associated primary HIV-1 isolates from DCs to PBMCs, from MDMs to PBMCs and from PBMCs to CEMx174 5.25M7 cells. It has low in vitro cytotoxic effect on vaginal epithelial cells (VK2/E6E7).

### **Conclusion:**

ADS-J1 is an HIV entry inhibitor targeting gp41 with potent inhibitory activity against HIV-1 transmission in both the in vitro and ex vivo models. It may be developed as a tropical microbicide for prevention of sexual transmission of HIV.

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