Evidence for an Actual Cure of a SHIV-infected Monkey

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Abstract

Four rhesus monkeys were infected with SHIV-AD8 for 86 weeks before receiving adeno-associated virus (AAV) vectors expressing truncated b1g1 antibodies targeting the SHIV Env. After 5 weeks of treatment, SHIV-AD8 RNA copies/mL in plasma remained suppressed to below the limit of detection of 30 RNA copies per ml of plasma. Following the initial decline in viremia after AAV administration, viral loads remained undetectable. The SHIV-AD8 infection was not detectable by standard ELISA, adoptive transfer involved surgical removal of lymph nodes from the monkey during the chronic phase of the infection. These findings highlight the potential of AVV-mediated antibody expression for impacting HIV-1 infections.

Methods

After 56 weeks of SHIV-AD8 infection, four rhesus macaques were inoculated intramuscularly with three different AAVs coding for three different broadly neutralizing anti-HIV antibodies in a therapeutic approach:

- SHIV-AD8 infection
- Intramuscular injection of AAV coding for anti-HIV antibodies

Viral loads were measured by RT-PCR. Antibody and anti-antibody levels were measured by standard ELISA. Adoptive transfer involved surgical removal of lymph nodes from the monkey during the chronic phase of the infection. These findings highlight the potential of AVV-mediated antibody expression for impacting HIV-1 infections.

Results

1. Antibody and host anti-antibody levels were quantified by ELISA in all four AAV recipients:

- Absorbance at 450 nm
- Measured by standard ELISA
- Adoptive transfer involved surgical removal of lymph nodes from the monkey during the chronic phase of the infection.

2. After AAV administration, animal rh2438 achieved profound and sustained virologic control during the chronic phase of the infection:

- SHIV Viral loads
- AAV administration

3. Monkey rh2438 persistently maintained high concentrations of broadly neutralizing anti-HIV antibodies 3BNC117 and 10-1074 in serum following the AAV administration:

- Absorbance at 450 nm
- Weeks post AAV inoculation

4. Analysis of the viral reservoir in PBMCs isolated from rh2438 revealed a drop in both, viral RNA and viral DNA, after the AAV inoculation:

- Absorbance at 450 nm
- Weeks from AAV administration

5. Serum from rh2438 showed a sudden and marked decrease in antibody reactivity to p27/gag and g120/envelope after AAV inoculation:

- Absorbance at 450 nm
- Antibodies to p27

6. Attempts to recover SHIV from the peripheral blood of rh2438 did not yield any virus. Importantly, lymph node cells from this animal were not able to transmit infection when inoculated in two separate naive recipient monkeys:

- Absorbance at 450 nm
- Weeks post AAV inoculation

References

1. Chun, T.W. and A.S. Barouch, Molecular Cell and Developmental Biology, University of Miami Miller School of Medicine, Miami, FL, 33136, USA. 4 Wisconsin National Primate Research Center, University of Wisconsin, Madison, WI, 53711, USA. 5 AIDS and Cancer Virus Program, NIAID, NIH, Bethesda, MD, 20892, USA. 6 Laboratory of Molecular Immunology and 7 Howard Hughes Medical Institute, The Rockefeller University, New York, NY 10017, USA.

Conclusions

1. We have shown evidence for an actual cure of a SHIV-infected monkey during the chronic phase of the infection.

2. Long term delivery of potent and broadly neutralizing antibodies with AAV is a very promising approach against HIV.