Long-term SHIV Suppression Using AAV Delivery of Monoclonal Antibodies

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Background
Long-term delivery of anti-HIV monoclonal antibodies using adeno-associated virus (AAV) holds promise for the treatment of HIV infection. We have previously reported monkey rh2438 in which a single administration of AAVs encoding a combination of potent and broadly neutralizing antibodies during the chronic phase of infection resulted in an abrupt decline in plasma viremia which remained below the limit of detection for 38 successive measurements over a 3-year period (Martinez-Navio & Fuchs et al. Immunity 2019). The field has nicknamed this monkey “the Miami monkey” analogous to “the Berlin patient”, a person that was cured of his HIV infection. This monkey never received antiviral drugs at any time and therefore appeared functionally cured.

Methods
Indian-origin rhesus macaques (*Macaca mulatta*) housed at the Wisconsin National Primate Research Center were used for our studies. Monkeys received recombinant AAV vectors expressing full length authentic IgG1 versions of the monoclonal antibodies. Rhesus monkeys were infected with SHIV-AD8 months before receiving AAV expressing constant-region *rhesusized* versions of select anti-HIV monoclonal antibodies. Antibody and anti-antibody levels were measured by ELISA.

Results
Here we report that monkey rh2438 continues to be suppressed (5 years and counting) and expressing high levels of antibodies 10-1074 and 3BNC117 in serum. Monkey rh2438 generated little or no anti-drug antibodies to these antibodies. Additionally, we have two other macaques, r14121 and r14097, which also received AAVs coding for a cocktail of neutralizing anti-HIV antibodies during the chronic phase of infection and have shown suppressed viral loads for the last 2 years. Monkey r14121 showed sustained delivery of reasonable levels of antibody PGT128 and a late rise of antibody N6. Monkey r14097 showed sustained delivery of antibodies PGT128 and N6 at reasonable levels and a late rise of antibodies 35O22 and PGT145.

Conclusions
Our data show that durable, continuous antibody expression can be achieved after one administration of AAV and support the potential for lifelong suppression of viral loads with the AAV-antibody approach.