A Battle of Host vs Virus:
HIV-1 Vif adaptation to host immune pressure mediated by diverse cytidine deaminases

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APOBEC3 proteins: an intrinsic block to HIV

**Producer Cell**

- Replication can occur
- HIV-1 Vif
- APOBEC3G

**Target Cell**

- Reverse Transcription
  - mutations
- Viral replication disabled

**HIV-1 RNA**
N-terminal region of Vif binds to APOBEC3 proteins

Vif residues responsible for binding to different APOBEC proteins
Goal and Hypothesis

**Goal:** To understand which APOBEC3 protein mediates immune pressure on the virus *in vivo*.

**Hypothesis:** HIV-1 Vif will adapt to the APOBEC3 protein that exerts immune pressure on the virus *in vivo*.
Vif variants were tested at acute infection (2-4 weeks post infection) and at one year post infection.

- HPP Acute Infection Cohort
- FRESH Cohort

Peak Viremia

Acute infections Identified
- Antibody negative
- RNA positive

Time Post Infection

2-4 weeks post infection (Baseline)

Acute Phase

Chronic Phase

One year post infection

n = 31
Vif variants were subtype C, limited intrapatient diversity

Baseline

One year post infection

n = 80 clones from 25 patients

Patients sequenced at baseline and one year post infection = 17
Minimal amino acid changes from baseline to one year post infection

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<th>Amino Acid position</th>
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<th>Baseline or Transmitter/Founder clone</th>
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A3G binding sites in HIV-1 Vif are highly conserved
A3H binding sites in HIV-1 Vif are highly conserved
A3F binding sites in HIV-1 Vif are highly conserved
Transmitted/founder virus Vif degrades APOBEC3 proteins and rescues infectivity
Transmitted/founder virus Vif preferentially degrades APOBEC3G
Evidence that HIV1-Vif acquires ability to degrade A3F as disease progresses

- Overall there are no significant changes in patient derived Vifs to degrade different A3 proteins.
- However after one year post infection there is trend for increased A3F degradation.
Conclusions

• A3 binding sites on Vif were highly conserved with some variability observed

• Vif shows significant heterogeneity in its ability to degrade different A3 proteins

• Transmitter/founder virus Vif preferentially degrades A3G

• However, the ability of HIV-1 Vif to degrade A3F increases at one year post infection compared to T/F Vif
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