30 Years with AIDS:
Where it Came From and Why It’s Still With Us

Part I: The Origins of HIV and the AIDS Epidemic
Kevin McCarthy

Part II: HIV: The Retrovirus
Ben Morris

Part III: An HIV Vaccine: What's the hold up?
Jamie Schafer
Roadmap

• How is HIV different from a cell?
• How does HIV infect a cell?
• Why can’t we kill it?
How is HIV different from a cell?

- Cells are small, viruses are tiny
- Viruses cannot live without a host cell
- HIV stores genetic information in an unusual way

The Central Dogma of Molecular Biology

DNA ➔ RNA ➔ Protein

Cyclic process
PDB ID: 3BSE
Protein

PDB ID: 1HHO
Wikimedia Commons
PDB ID: 1HHO

Wikimedia Commons
The Central Dogma of Molecular Biology

DNA

RNA

Protein

ATTGCAACATTG TAGT
Retrovirus: Biology goes Backwards

DNA

RNA

Protein

Reverse Transcription

Transcription
The HIV Life Cycle
IT’S ALIVE!
(or is it?)
The HIV Life Cycle

1. Entry
2. Reverse Transcription
3. Integration
4. Exit
Timothy Brown: The Berlin Patient

- Developed Leukemia
- Received a bone marrow transplant in 2007
- Donor was resistant to HIV
- The only person to ever be cured of HIV
The HIV Life Cycle

1. Entry
2. Reverse Transcription
3. Integration
4. Exit
Integration

• Viral DNA stably inserted into host DNA
• Can lie dormant for years
• Current therapies would take 70 years to cure a patient
Antiretroviral Therapy

1. Entry
2. Reverse Transcription
3. Integration
4. Exit

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Why can’t we kill it?

- Infects the immune system
- Integration leads to dormant population
- Mutation rate and generation time
Mutation

- ~10,000 bases in HIV genes
- ~1 mistake every replication cycle
- ~10,000,000,000 new viruses per day
- Constantly moving target!
- How did HIV evolve this way?

- Resistance to cancer drugs and antibiotics
Highly Active Antiretroviral Therapy

• Combination therapy: cocktail of 3 or more different therapies

• Challenges:
  – Access
  – Cost
  – Adherence

To cure or not to cure?