Deadly evolution: HIV
What is HIV?
• Virulence: Why is it so deadly?
• Therapies: How to treat infections?
• Vaccine: How to design a prevention?

Chapter 1, Box 1
Course Info

Lecture Notes
• Available on website after class
• Take notes in class
• Use web notes to rewrite your notes

What is Organic Evolution?
Darwin's Insight
Darwin's Theory of Evolution
The Insight
Alfred Russell Wallace
1823-1913
• Similar ideas
• Less evidence
Descent with Modification
Organic Evolution --> tree-like branching
• splitting, extinction of lineages

1. Species are Ancestral & Derived
2. Common ancestors

Phylogeny
Descent with Modification
Natural selection
Before Darwin
Course Info

LAB Reminders

Lab Manuals are in Bookie

Go to lab sections this week
(Eastlick 170)

Read the lab before lab

Bring Lab Manual to lab section
World's deadliest organisms?

Disease Vectors!
World’s deadliest organisms?

Disease organisms!

Short generations, evolve quickly

Viruses (flus, HIV)

Bacteria (bubonic plague)

Plasmodium (malaria)
HIV and AIDS

- Over 60 million people infected with HIV-1
- 17% of men in major US cities
- Causes 5% of all deaths (8,000 per day)
- AIDS: 90 million deaths by 2020
The HIV-AIDS Epidemic

- North America: 950,000
- Caribbean: 420,000
- Western Europe: 550,000
- North Africa & Middle East: 500,000
- South and Southeast Asia: 5.6 million
- Sub-Saharan Africa: 28.5 million
- Latin America: 1.5 million
- Australia and New Zealand: 15,000

Adult prevalence rate:
- 15.0%–39.0%
- 5.0%–15.0%
- 1.0%–5.0%
- 0.5%–1.0%
- 0.1%–0.5%
- 0.0%–0.1%
- Not available

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Outcome of disease: affected by Adaptation, creation of biodiversity

1. Virulence: Why is it so virulent?
2. Therapies: How to treat infected people?
3. Vaccine: How to design a vaccine to prevent infection?
HIV: a retrovirus

Host Cell: T cell, macrophage

Figure 1.3
HIV Life Cycle

HIV virion attaches to host cell

RNA and reverse transcriptase move from virion into host cell

Figure 1.3
HIV Life Cycle

Reverse transcriptase creates DNA from HIV RNA

DNA copy inserts itself into host DNA

Figure 1.3
HIV Life Cycle

Host genetic system transcribes HIV DNA to mRNA

mRNA moves out of nucleus and into cytoplasm

Figure 1.3
HIV Life Cycle

Host machinery makes reverse transcriptase & protein coat

Reassembly creates more virions

Figure 1.3
How does evolution affect HIV-AIDS

1. Virulence: Why is it so deadly?
2. Therapies: How to treat infections?
3. Vaccine: How to design a prevention?
Virulence: Why is it so deadly?

- Evolution within a human!
- Mutation of gp120 gene: variation in peptides (epitopes)
• T cell attack selects for gp120 diversity within a human (aka genetic distance)

• Rare variants escape recognition by T cells, attack T cells

• Relaxed selection on gp 120 after 8 years
How does evolution affect HIV-AIDS

1. Virulence: Why is it so deadly?
2. Therapies: How to treat infections?
3. Vaccine: How to design a prevention?
Therapy

AZT breaks down reverse transcriptase step

Figure 1.3
AZT Therapy

Fig. 1.5
Resistance to AZT: Selection for Reverse Transcriptase

Fig. 1.9

- Virion susceptible to AZT
- Virion partly resistant to AZT
- Virion highly resistant to AZT

Time
Resistance to AZT

(a) Resistance of HIV in two patients, followed over time

Patient 1

Patient 2

Months of therapy

Years

Concentration of AZT ($\mu$M)

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Multi-Drug Therapies:
See box 1.1 in textbook (p. 14)

• Probability of resistance mutant to each of three drugs, A, B, and C
  \[ P (A) = 0.001, \quad P (B) = 0.001, \quad P (C) = 0.001 \]

• Probability of resistance to all three drugs?
  \[ P (A, B, C) = (0.001)^3 = 0.000000001 \]
How does evolution affect HIV-AIDS

1. Virulence: Why is it so deadly?
2. Therapies: How to treat infections?
3. Vaccine: How to design a prevention?

- Vaccine “primes” T cells to recognize epitopes (coded by gp 120)
- T cells eliminate real infection
- But: extreme epitope diversity
- Which epitopes to include?
gp 120 Phylogeny

Fig. 1.12b

Most AIDS cases

M group

N group

O group

Human HIV-1

Chimp SIV
Vaccine design solutions?

- **M-group epitopes**
  - diversity within M group!
- **Vaccines with mixed epitopes?**
- **Reconstruct ancestral gp 120 sequence?**
  - generalized epitope & T cell recognition?
- **Regional epitope types?**
HIV: Lessons from Evolutionary Biology

- Virulence: Rapid evolution of epitopes that evade immune system
- Therapies: Rapid evolution of resistance
- Vaccines: Rapid evolutionary diversification makes successful vaccines unlikely