Emerging Diseases
Biosciences in the 21st Century
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Outline

• Disease emergence: a case study
• Introduction to phylogenetic trees
• Introduction to evolution by natural selection
• How do pathogens shift hosts?
• The evolution of virulence
Disease emergence: a case study

SARS: Severe Acute Respiratory Syndrome

- First detected in China, November 2002
- Spread quickly
- 10% fatality rate

Nature, 2003
Disease emergence: a case study

What was it? Where did SARS come from?

Deadly virus effortlessly hops species

Genetic engineering helps reveal origin of deadly 'flu

A single genetic change could have created the deadly virus that has killed over 50 people and infected more than 1,600, a new study suggests.

A new type of coronavirus is thought to be behind the pneumonia-like disease dubbed severe acute respiratory syndrome (SARS). Now, in a simple overnight experiment, researchers transformed a coronavirus that is lethal to cats into one that infects mouse cells by replacing a single gene.

The result strengthens the idea that the SARS coronavirus might have arisen when an animal and human virus met and swapped genes, says the study's lead scientist, Peter Rottier of Utrecht University in the Netherlands.
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Phylogenetic tree: A visual representation of the evolutionary history of populations, genes, or species.
Constructing phylogenies with sequence data

DNA sequences in descendants:

ATTGCTATTC  ATTGCTTTTC  ATTGCTTTTC

DNA sequence changes to: ATTGCTTTTC

Ancestral DNA sequence: ATTGCTATTC
Reading a phylogenetic tree

Four descendant populations, each with unique derived traits

Two descendant populations, each with unique derived traits

Ancestral population
No currently existing species is ancestral to any other
Different arrangements show the same relationships

There is no linear ancestor-descendant relationship! Humans did not evolve from cats or fish!
Phylogeny of HIV

Three separate introductions from chimpanzees
Back to our case study: the emergence of SARS
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What is evolution?

**Evolution** is a change in a population’s allele frequencies over time.

- **Generation t**
  - AA
  - AA
  - AA
  - Aa
  - Aa
  - AA
  - 70% A
  - 30% a

- **Generation t+1**
  - AA
  - AA
  - AA
  - Aa
  - Aa
  - AA
  - 60% A
  - 40% a
Natural selection is one mechanism of evolution

Natural selection: differential reproductive success

– Non-random
– Not forward-looking, can only work with existing variation
– Only adaptive mechanism of evolution

Figure: Univ. of Calif. Mus. of Paleontology's Understanding Evolution Site
Evolution by natural selection

Ingredients needed for evolution by natural selection

- Variation in traits
- Inheritance
- Differential reproduction (natural selection)

End result: Traits that increase reproductive success increase in frequency in a population.
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Shifting to another host species

- phi 6: virus that infects bacteria (bacteriophage)
- phi 6 only infects *Pseudomonas syringae*
Shifting to another host species

• Could phi 6 switch hosts?
• Plated on 14 different *Pseudomonas* species
• A few viruses infected and survived
• All had mutation in protein for attaching to host
Shifting to another host species

• Once in a new host, must adapt quickly
• Slow growth can lead to extinction
• Host switching leads to strong selection:
  – Infection
  – Evade immune system and replicate
• What factors allow pathogens to evolve quickly?
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Evolution of virulence: a trade-off

Selection **within host** favors rapid replication (increased virulence).

Selection **across hosts** favors reduced virulence.
Mode of transmission affects virulence

Direct transmission, vectorborne, waterborne
Mode of transmission affects virulence
Mode of transmission affects virulence.
Back to our case study: virulence in SARS

• Wanted: an animal model for SARS
• Problem: SARS slowly replicates in mice, but mice do not get sick
• Solution: create selection for increased virulence of SARS in mice
  1. Infect mouse with SARS
  2. After 2 days, purify virus from lungs and infect new mice
  3. Repeat, 14 times

Back to our case study: virulence in SARS

![Graph showing viral titer (log₁₀ TCID₅₀/g ± SE) over days following inoculation.]

- Infected with SARS
- Infected with MA15-low dose
- Infected with MA15-high dose

Evolution of virulence: implications for public health

Select for lower virulence by interfering with transmission

- Improve hygiene
- Wear masks
- Provide clean water
- Widespread vaccination
Current research aims

• Can we predict which pathogens are more likely to shift to humans?
• What makes some strains so much more deadly than others?
• How can we develop effective new vaccines and drugs?
Key points

- New diseases are constantly arising
- Evolution can help us determine
  1. what they are
  2. where they came from
  3. how they infected humans
  4. how they become more/less virulent
  5. how best to fight them
- No currently existing species is ancestral to any other
- Virulence is a trade-off between fast replication and transmission
- Transmission mode affects virulence