Emerging Diseases

Biosciences in the 21st Century

Dr. Amber Rice

October 23, 2013

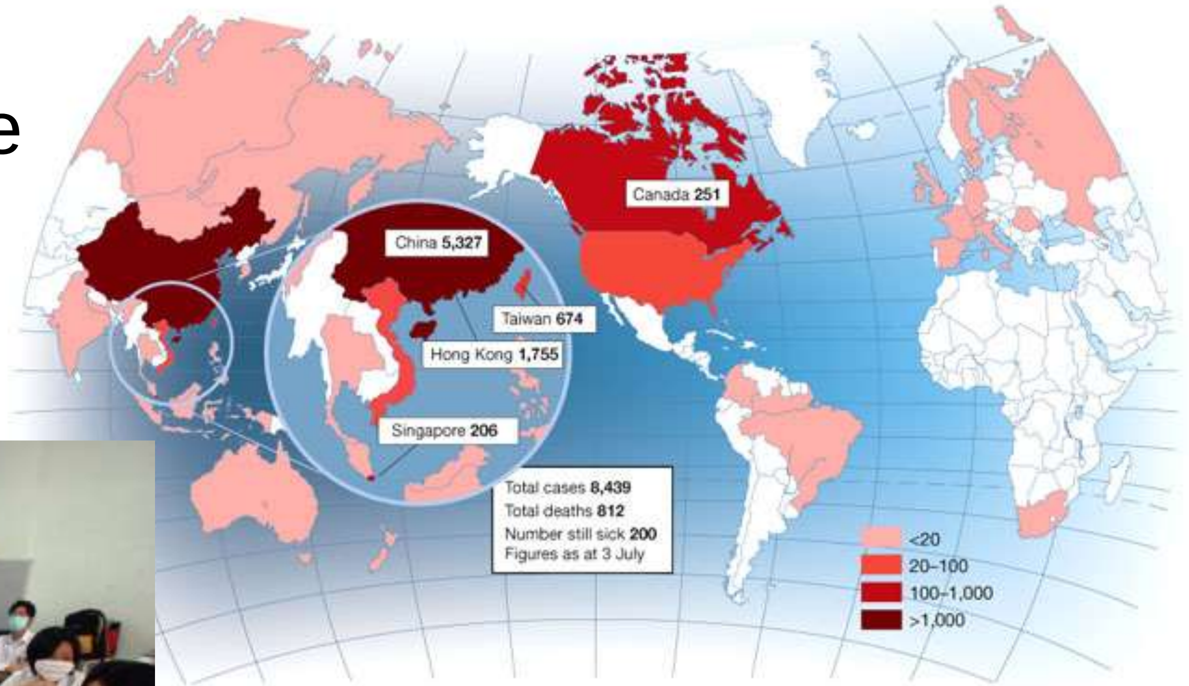
Outline

- 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?

nature International weekly journal of science

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- Nature News
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News

Nature **422**, 247 (

Health lab

David Cyranos

The World Hea
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Published online 2 April 2003 | Nature | doi:10.1038/news030331-4

News

Deadly virus effortlessly hops species

Genetic engineering helps reveal origin of deadly 'flu

Helen Pearson

SARS coronavirus might have arisen when an animal and human virus met and swapped genes.

© GettyImages

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[1].

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

Published online 20 March 2003 | Nature | doi:10.1038/news030317-8

News

Identity of mystery pneumonia bug sharpens

Questions raised over readiness for lethal SARS epidemic.

Helen Pearson

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of
us.

© Corbis

As laboratories worldwide home in on the virus responsible for the mysterious global outbreak of pneumonia, critics say that researchers could have been better prepared to anticipate the epidemic.

So far, 264 people worldwide are known to have been infected and 9 have been killed by Severe Acute Respiratory Syndrome (SARS). This flu-like condition is characterized by high fever and breathing problems. Fears began escalating after the World Health Organization put out an exceptional alert last week.

Laboratories in Hong Kong, Germany and Singapore have now found signs that the culprit may be a new type of

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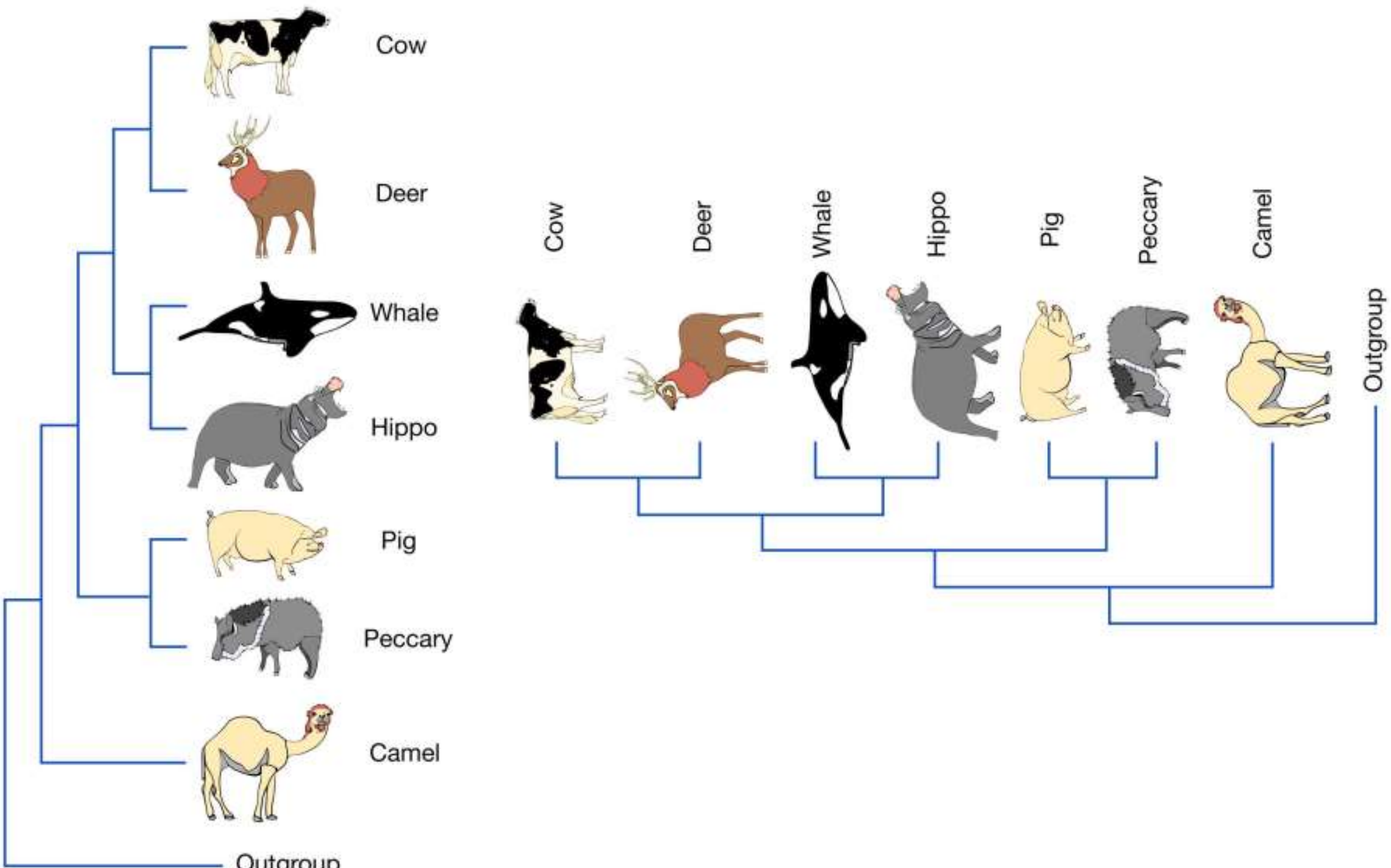
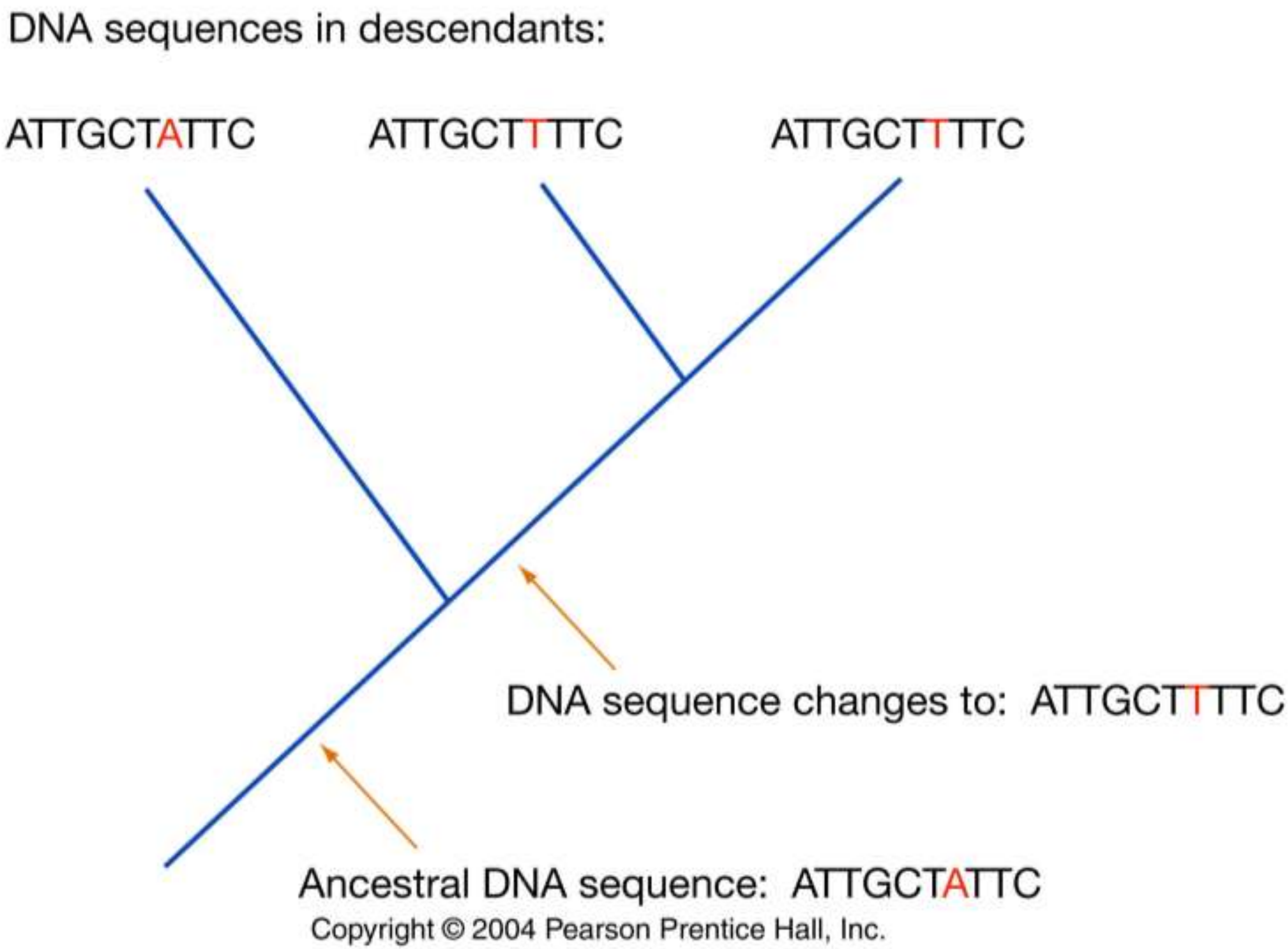
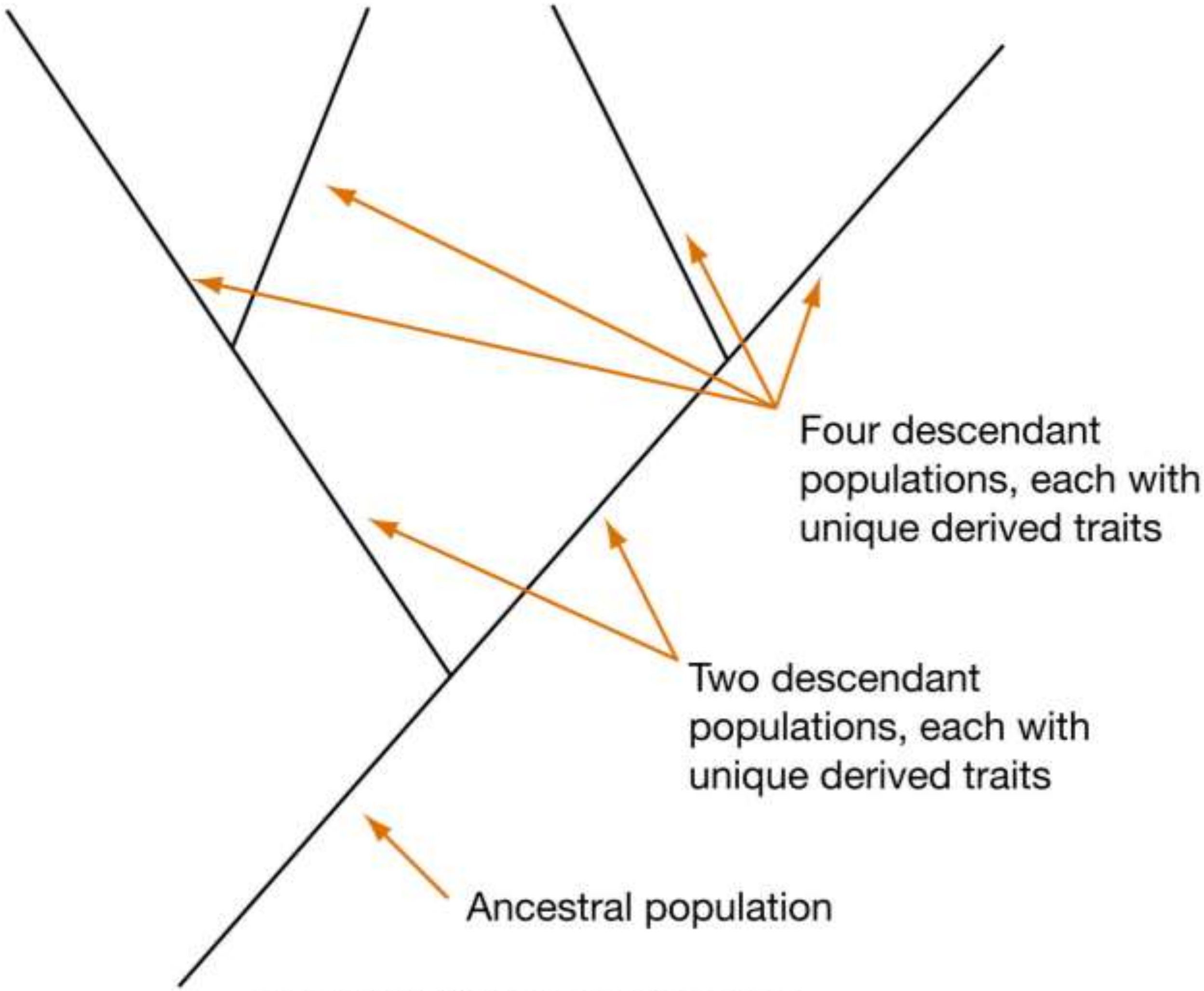
Phylogenetic tree: A visual representation of the evolutionary history of populations, genes, or species



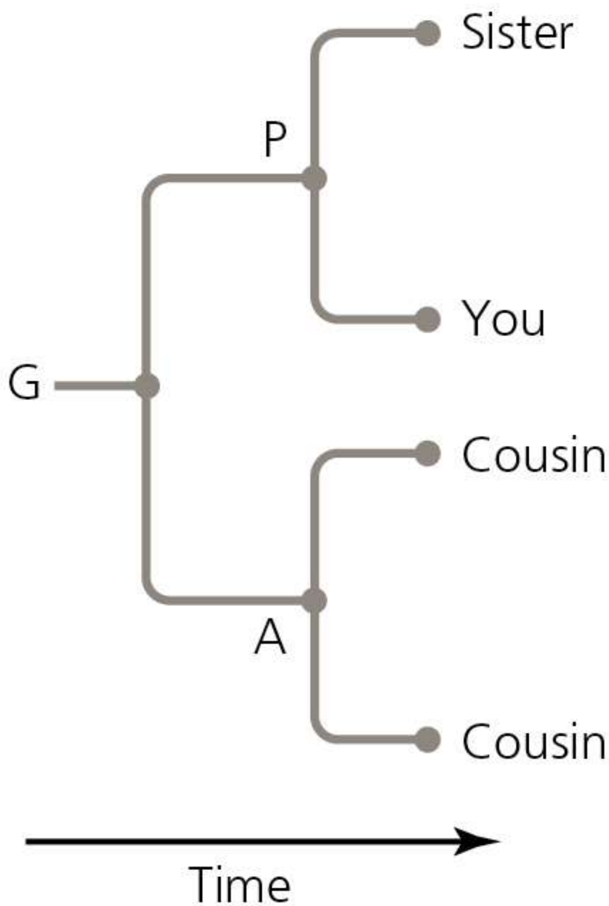
Constructing phylogenies with sequence data



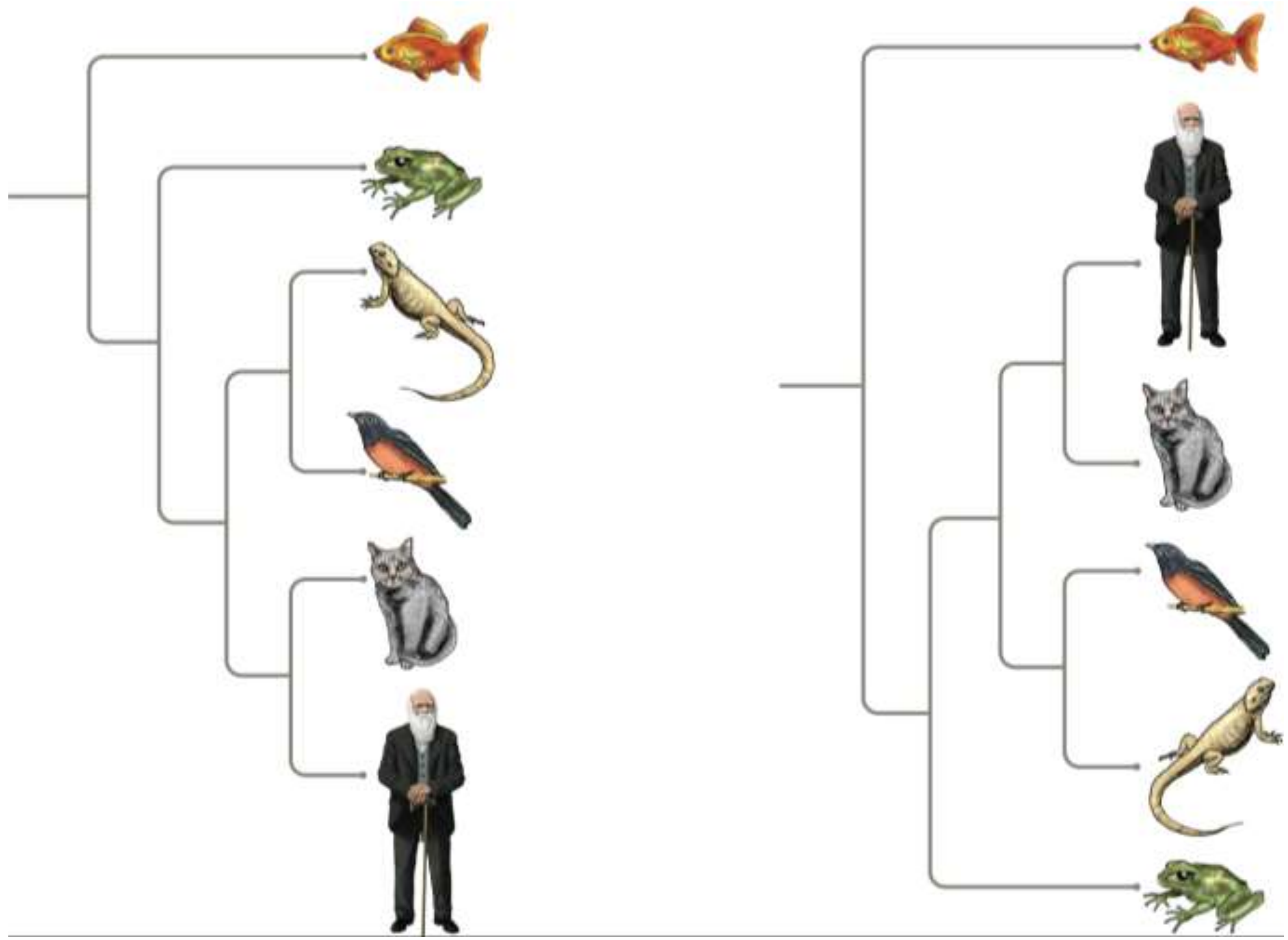
Reading a phylogenetic tree



No currently existing species is ancestral to any other

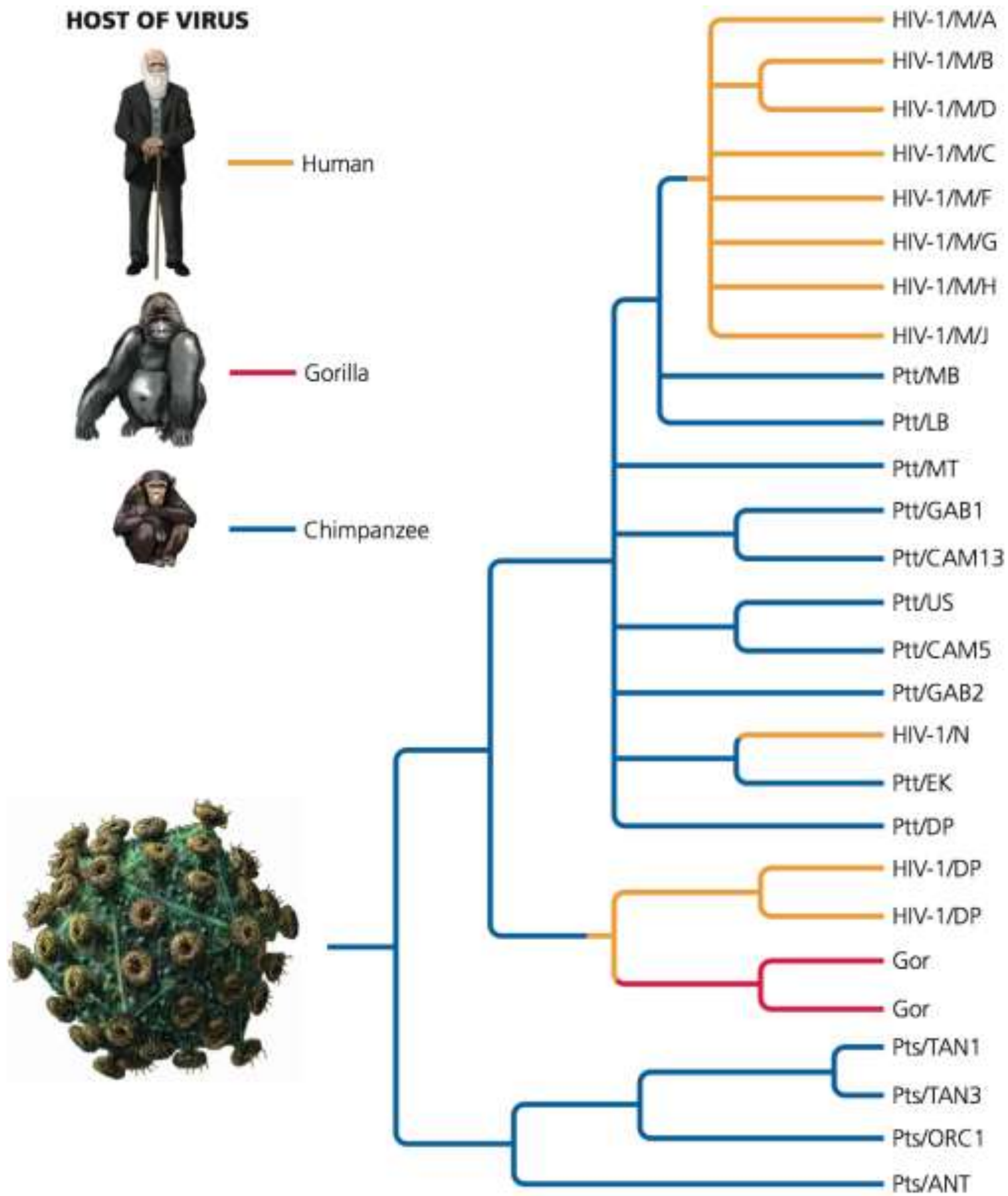


Different arrangements show the same relationships



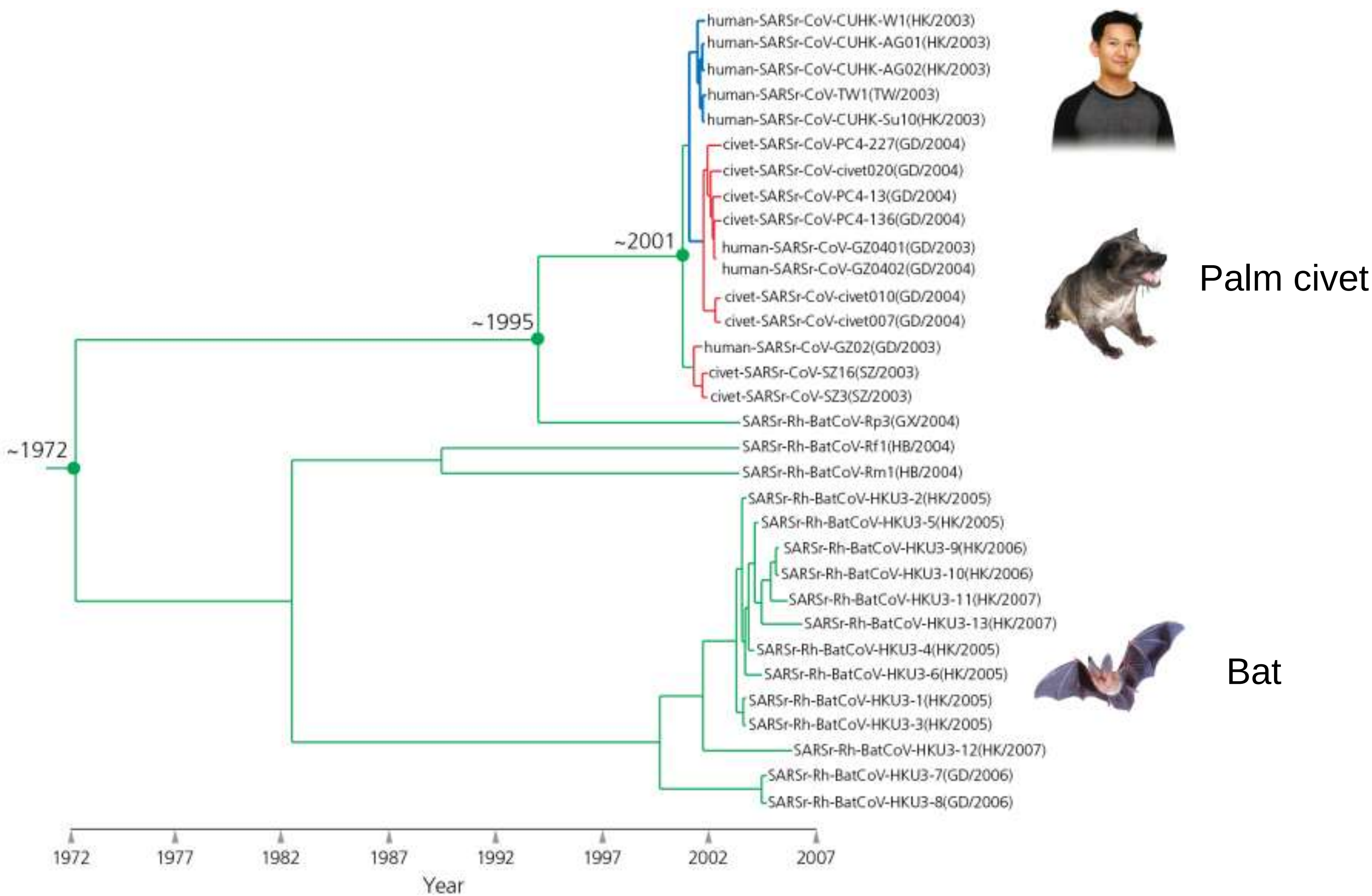
There is no linear ancestor-descendent relationship! Humans did not evolve from cats or fish!

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

AA

aa

AA

Aa

70% A
30% a

time

Generation t+1

Aa

Aa

AA

Aa

aa

AA

AA

aa

AA

Aa

60% A
40% a

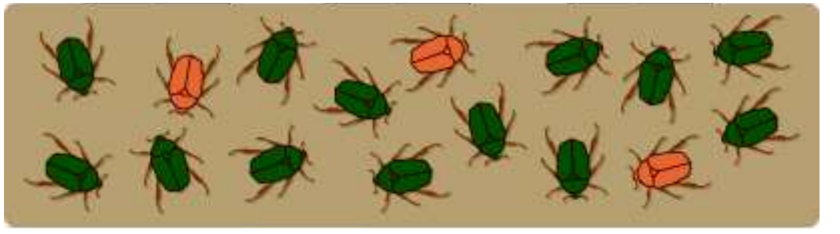
Natural selection is one mechanism of evolution

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.

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

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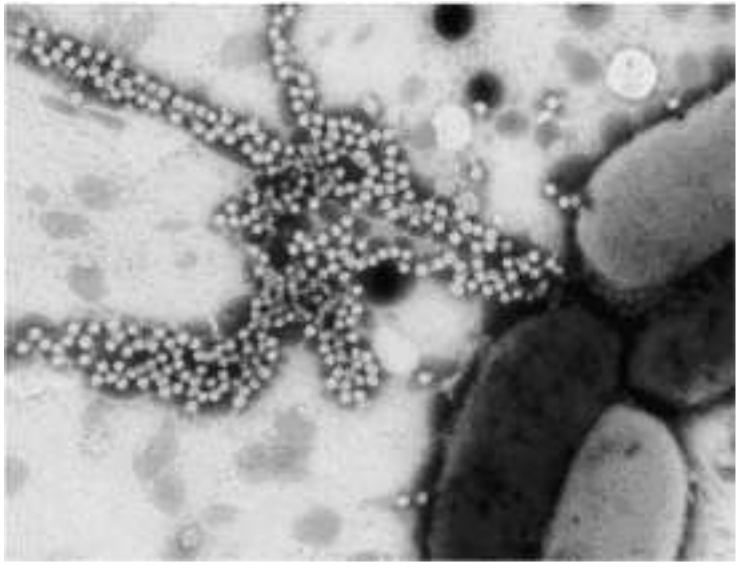
Shifting to another host species

- 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

Duffy et al. 2007

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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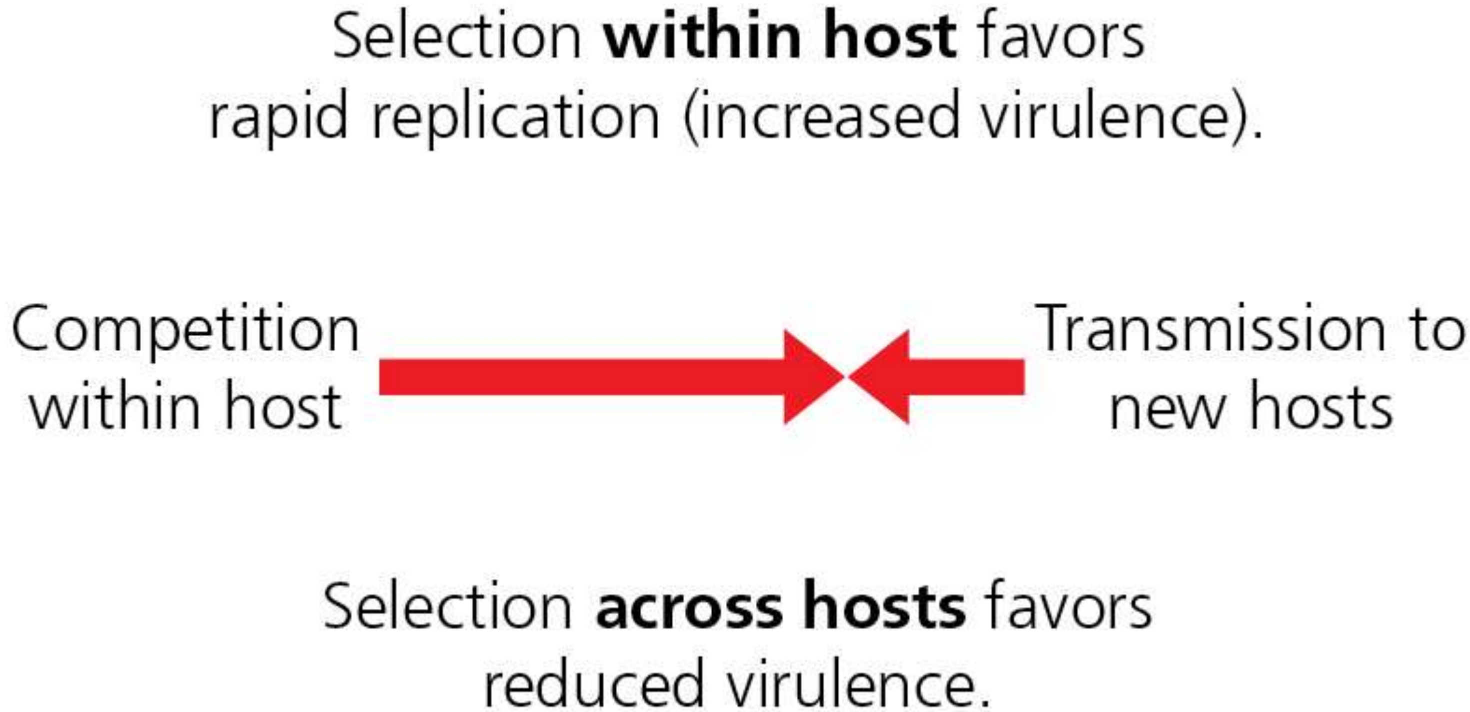
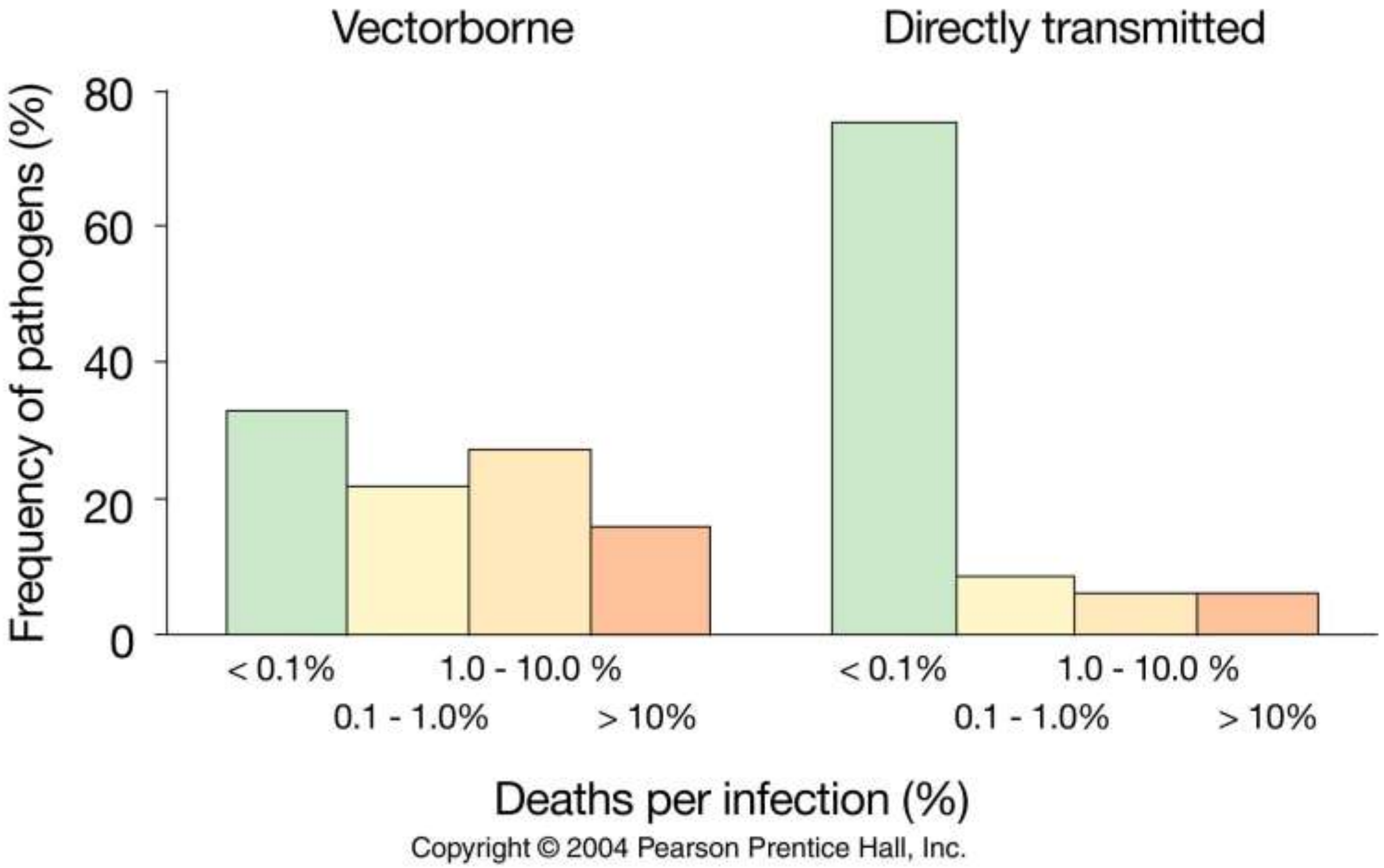
Evolution of virulence: a trade-off



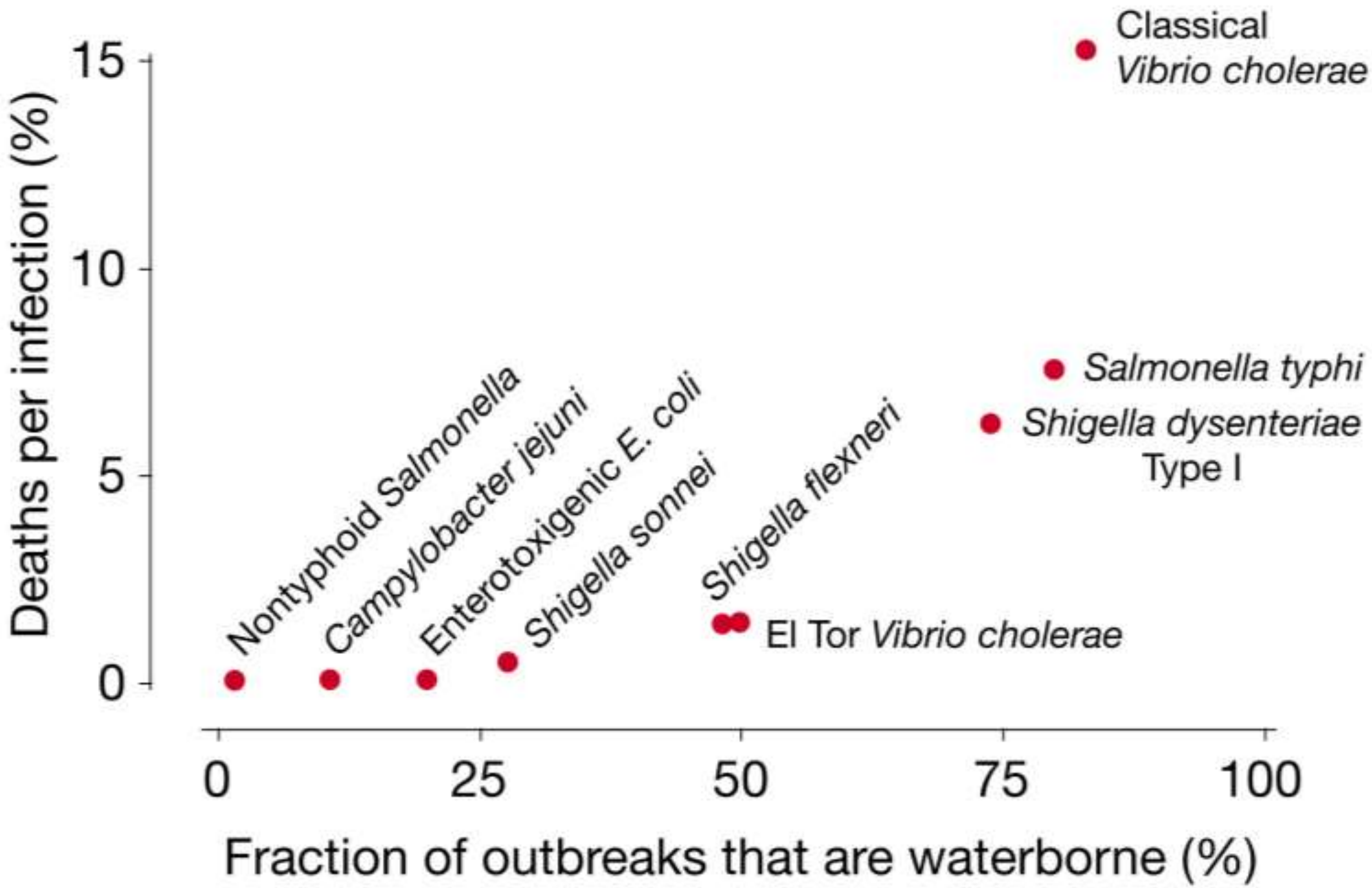
Mode of transmission affects virulence

Direct transmission, vectorborne, waterborne

Mode of transmission affects virulence



Mode of transmission affects virulence

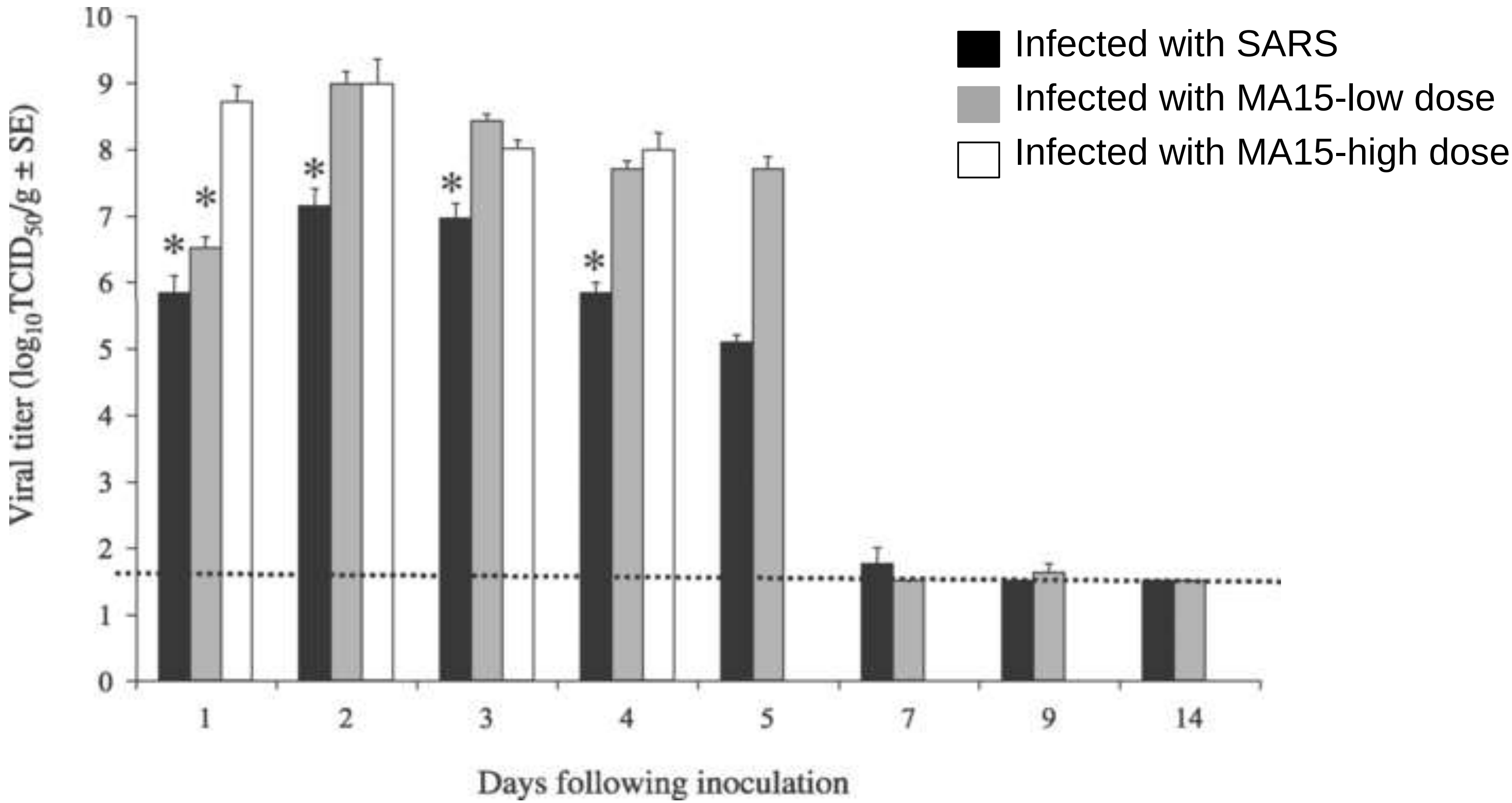


Back to our case study: virulence in SARS

- 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

Roberts A, Deming D, Paddock CD, Cheng A, et al. (2007)

Back to our case study: virulence in SARS

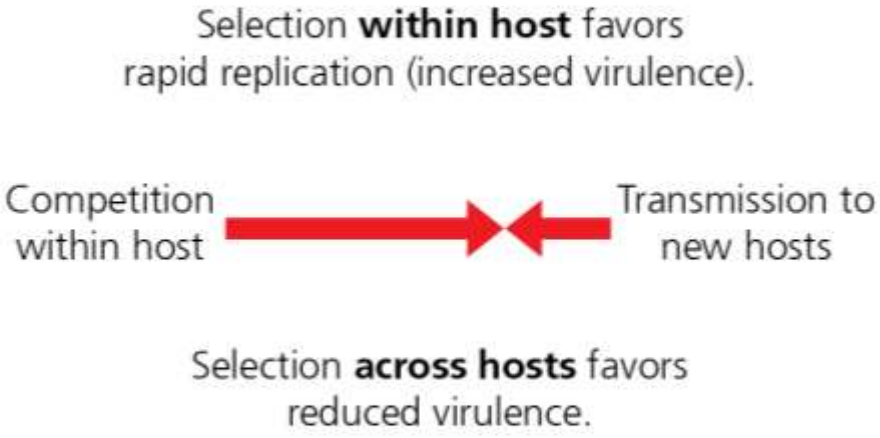


Roberts A, Deming D, Paddock CD, Cheng A, et al. (2007)

Evolution of virulence: implications for public health

Select for <u>lower</u> virulence by interfering with transmission

- Improve hygiene
- Wear masks
- Provide clean water
- Widespread vaccination

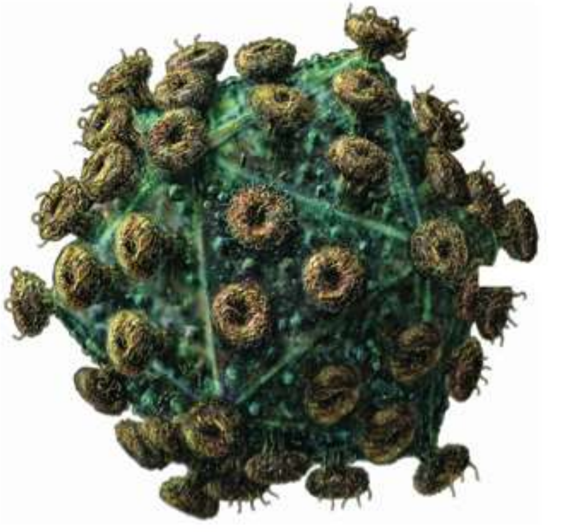


Current research aims

- 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