



# Emerging Diseases

Biosciences in the 21<sup>st</sup> Century

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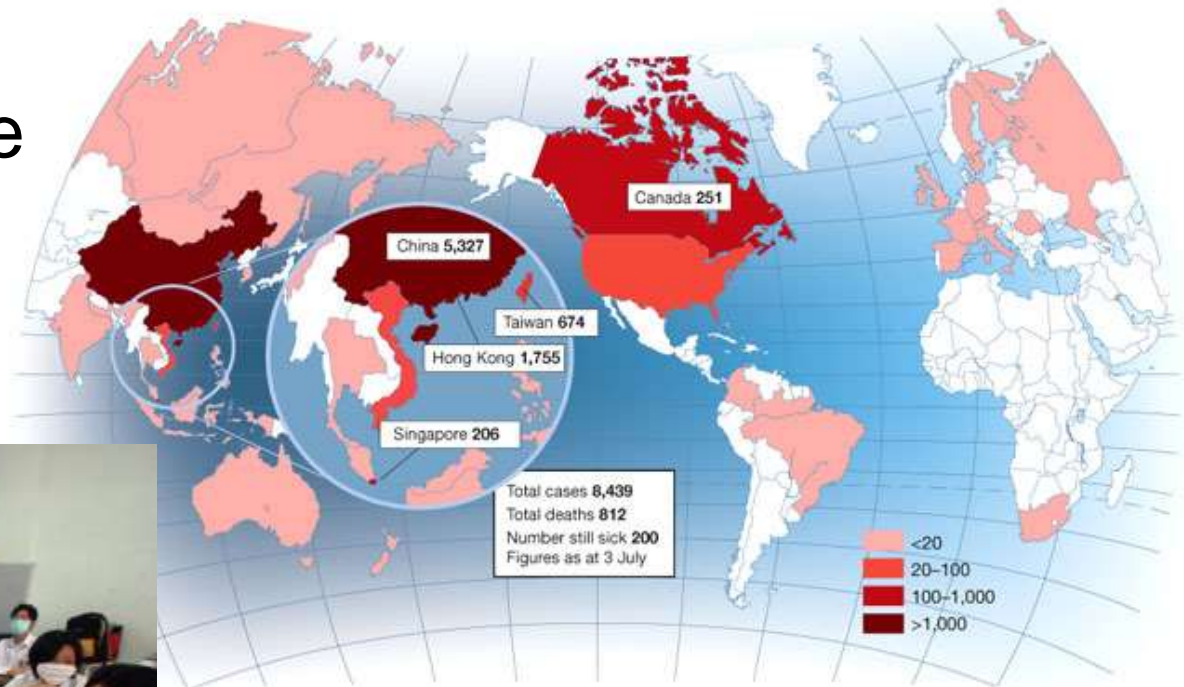
# Outline

- 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



# Disease emergence: a case study

## What was it? Where did SARS come from?

nature

International weekly journal of science

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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#### News

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

News

Nature 422, 247 (

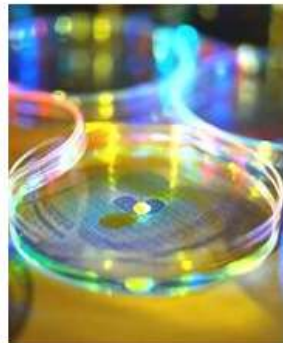
### Deadly virus effortlessly hops species

#### Health lab

Genetic engineering helps reveal origin of deadly 'flu

David Cyranos [Helen Pearson](#)

The World Health Organization is investigating the origin of the virus in the southern



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<sup>1</sup>.

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



have been the pathogen to of JS.

© 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.

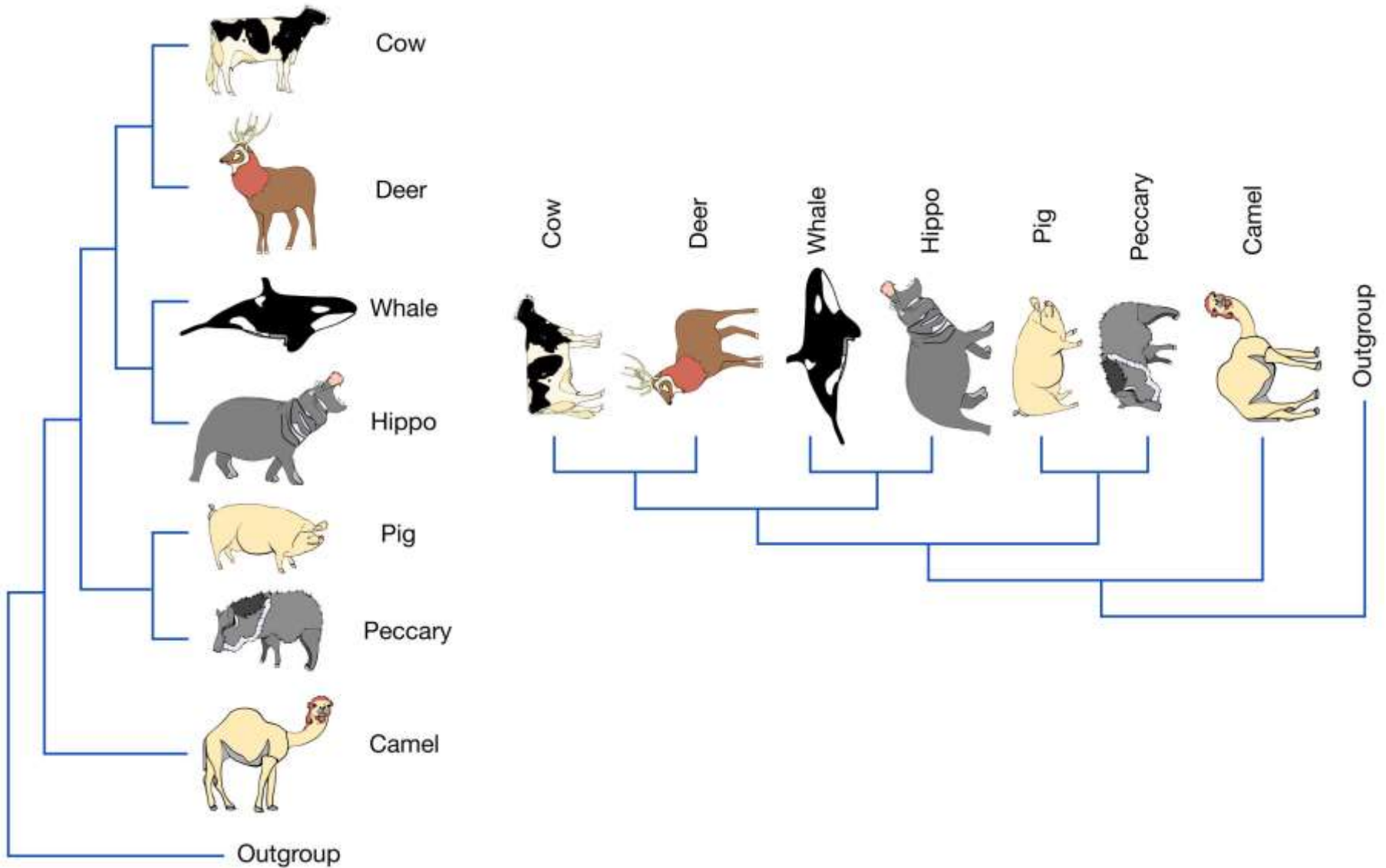
Laboratories in Hong Kong, Germany and Singapore have now found signs that the culprit may be a new type of

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



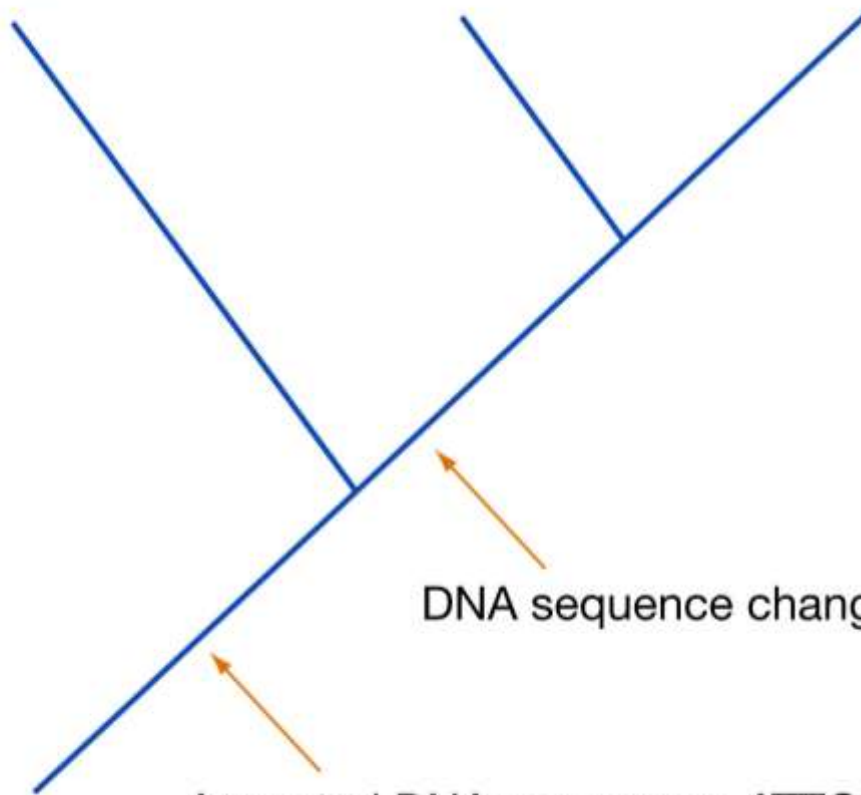
# Constructing phylogenies with sequence data

DNA sequences in descendants:

ATTGCT**A**TTC

ATTGCT**T**TTTC

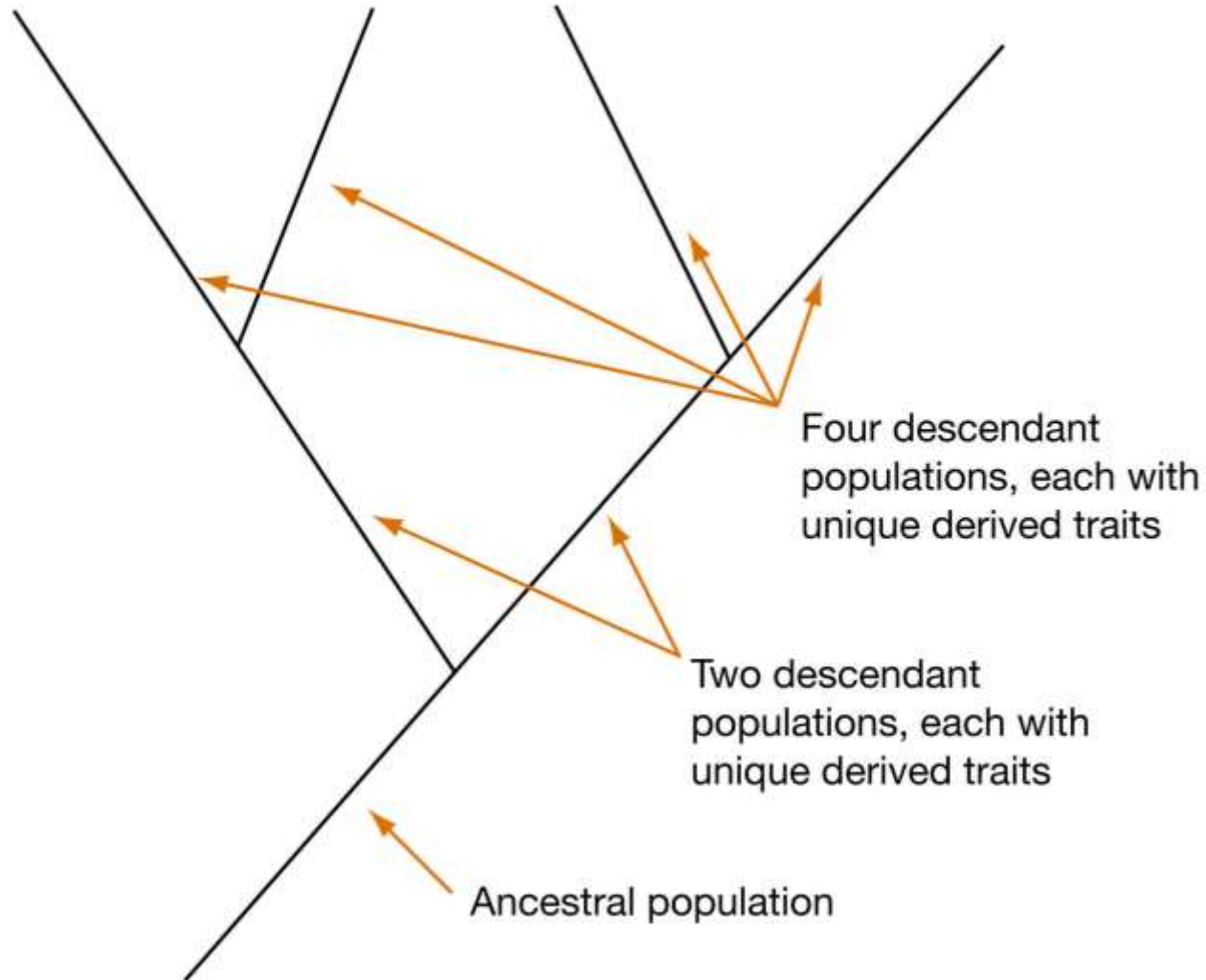
ATTGCT**T**TTTC



DNA sequence changes to: ATTGCT**T**TTTC

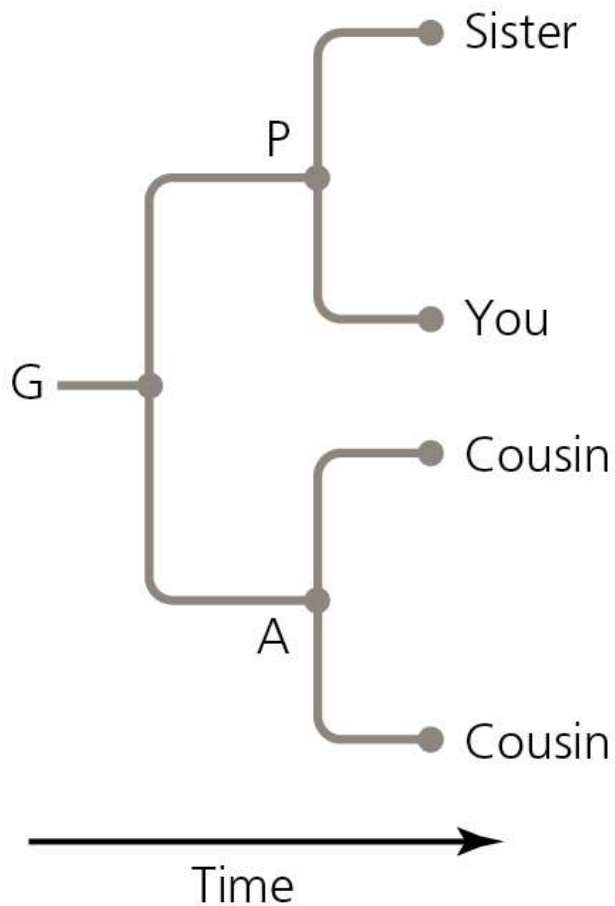
Ancestral DNA sequence: ATTGCT**A**TTC

# Reading a phylogenetic tree

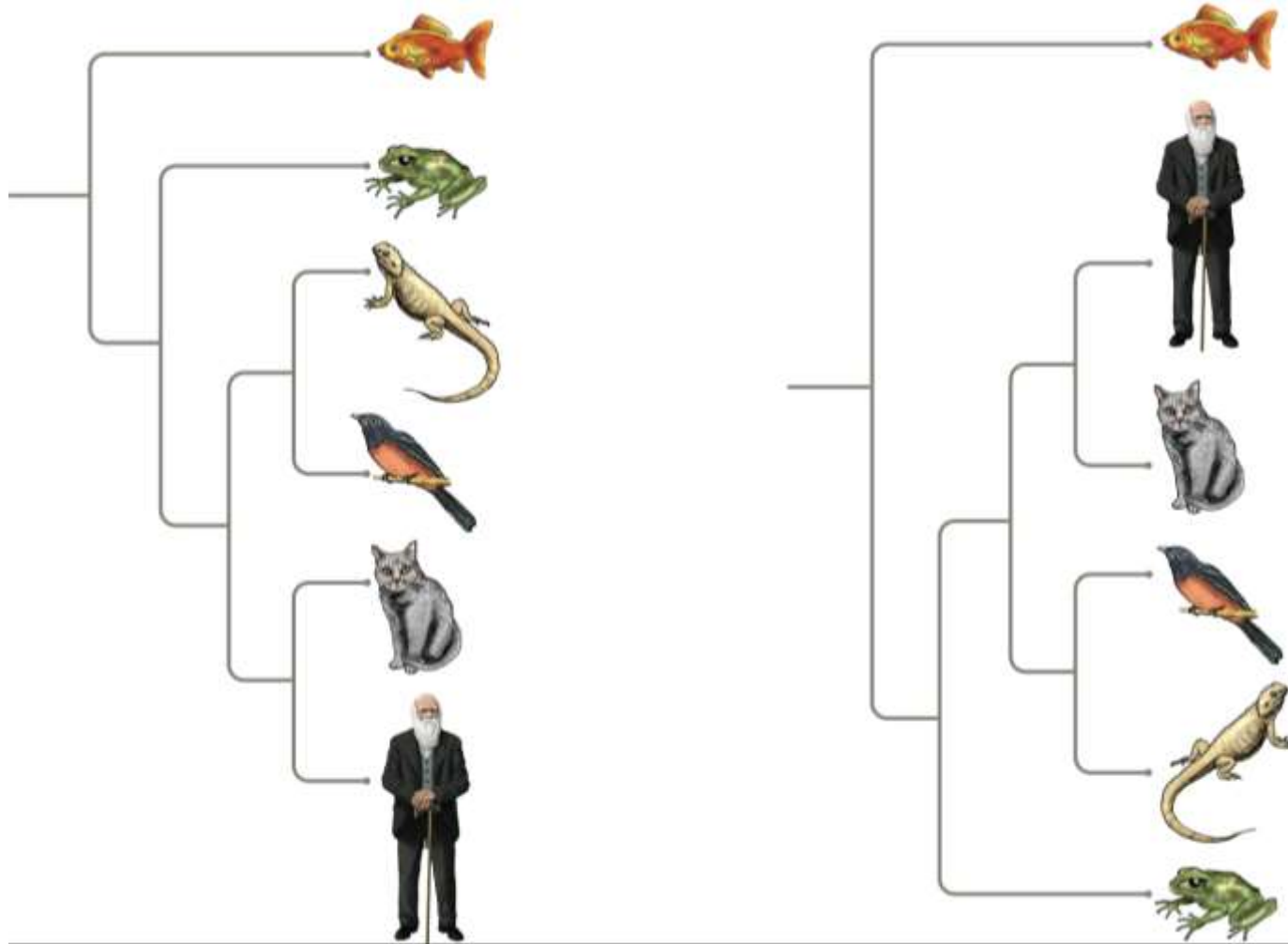




No currently existing species is ancestral to any other

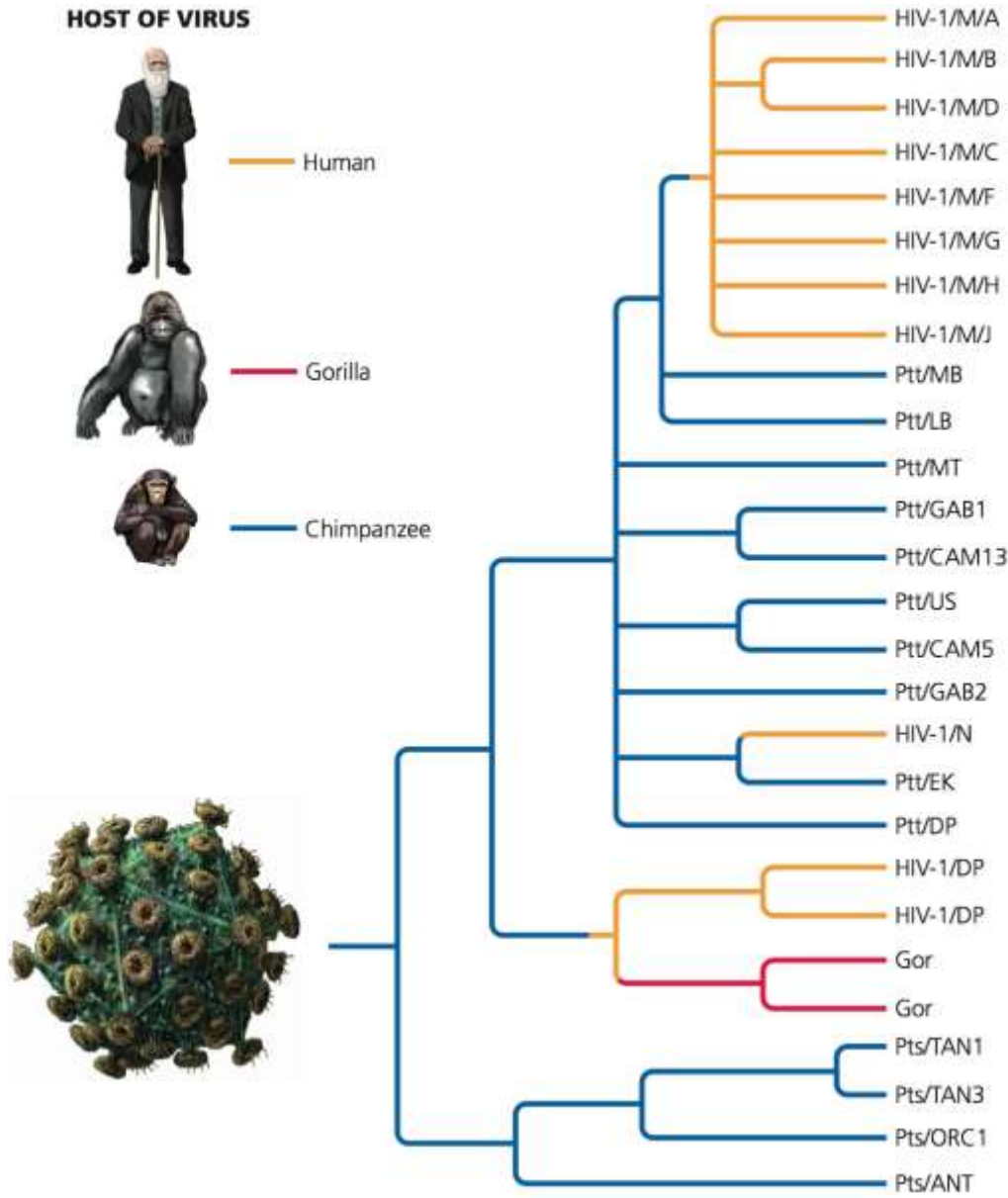


# Different arrangements show the same relationships



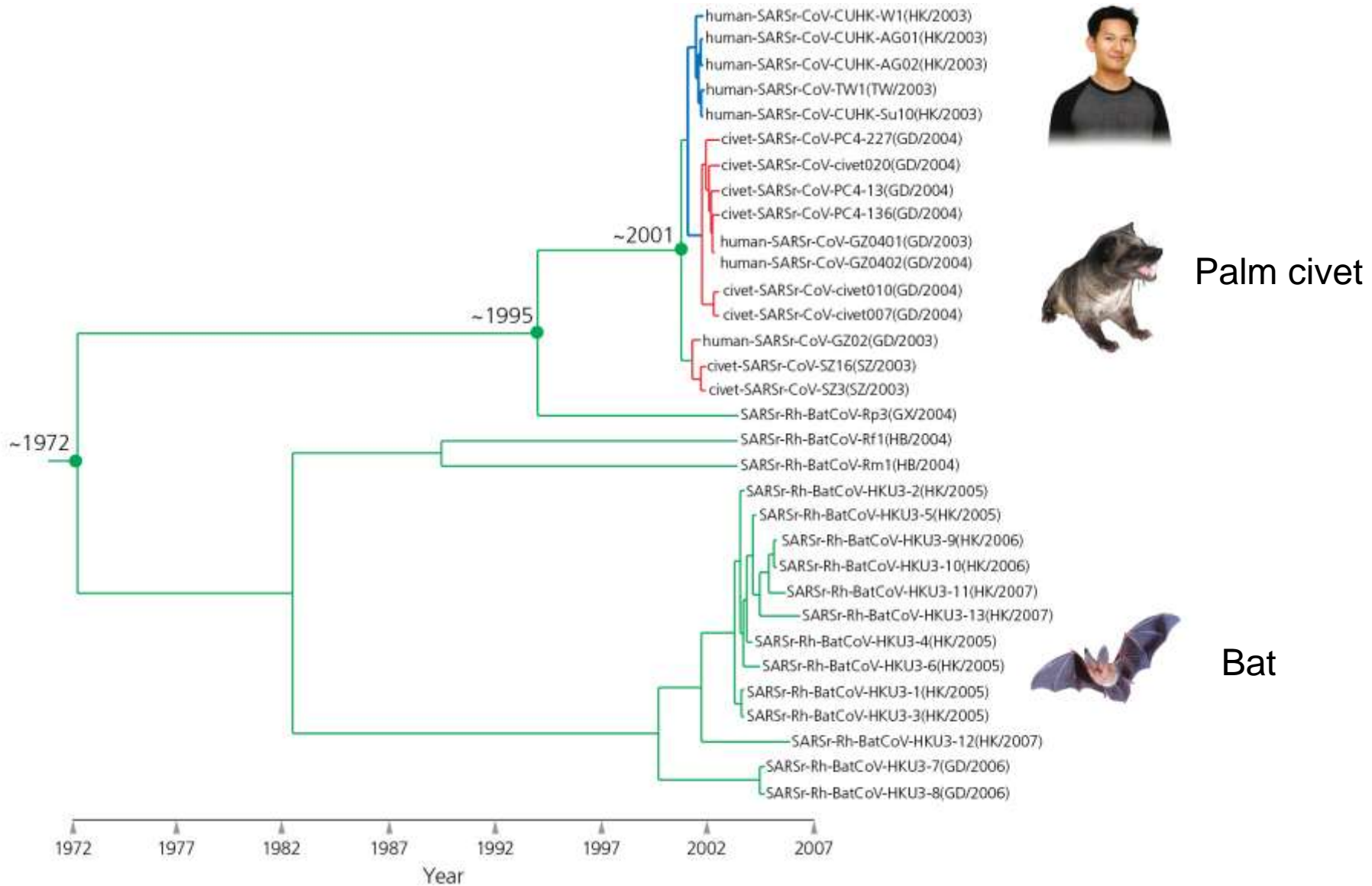
There is no linear ancestor-descendent relationship! Humans did not evolve from cats or fish!

# Phylogeny of HIV



Three separate introductions from chimpanzees

# Back to our case study: the emergence of SARS



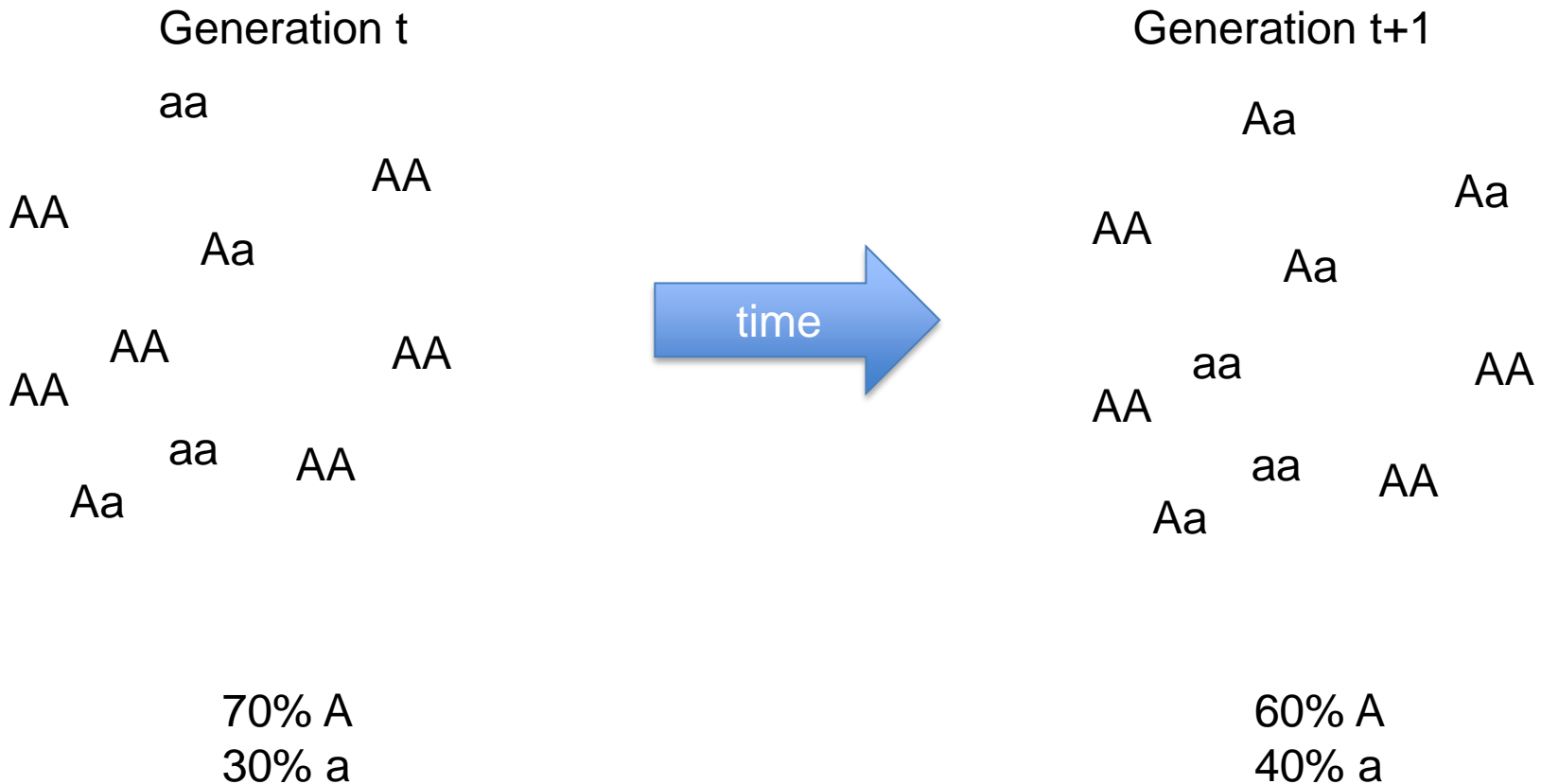
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# What is evolution?

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



# Natural selection is one mechanism of evolution

Natural selection: differential reproductive success

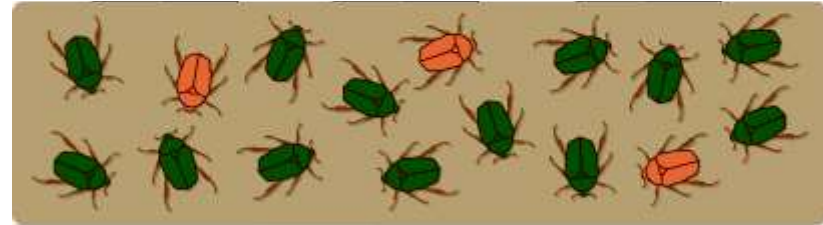
- Non-random
- Not forward-looking, can only work with existing variation
- Only adaptive mechanism of evolution



# Evolution by natural selection

## Ingredients needed for evolution by natural selection

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



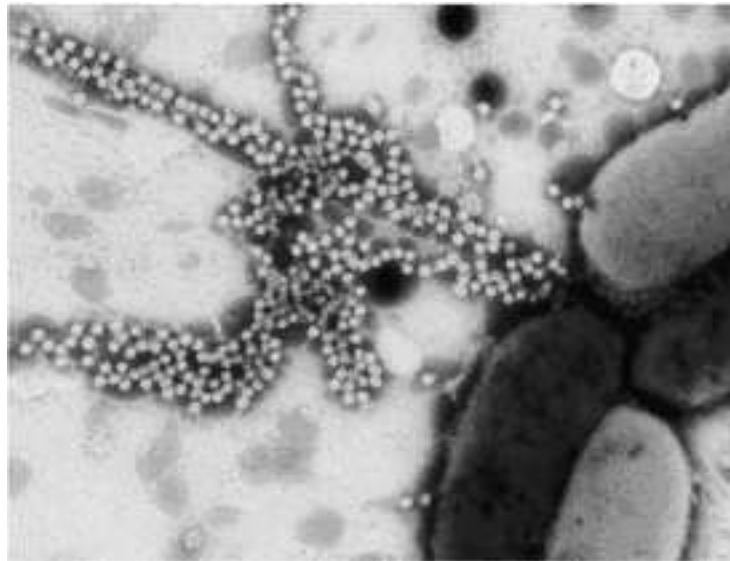
End result: Traits that increase reproductive success increase in frequency in a population.

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- **How do pathogens shift hosts?**
- The evolution of virulence

# 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.

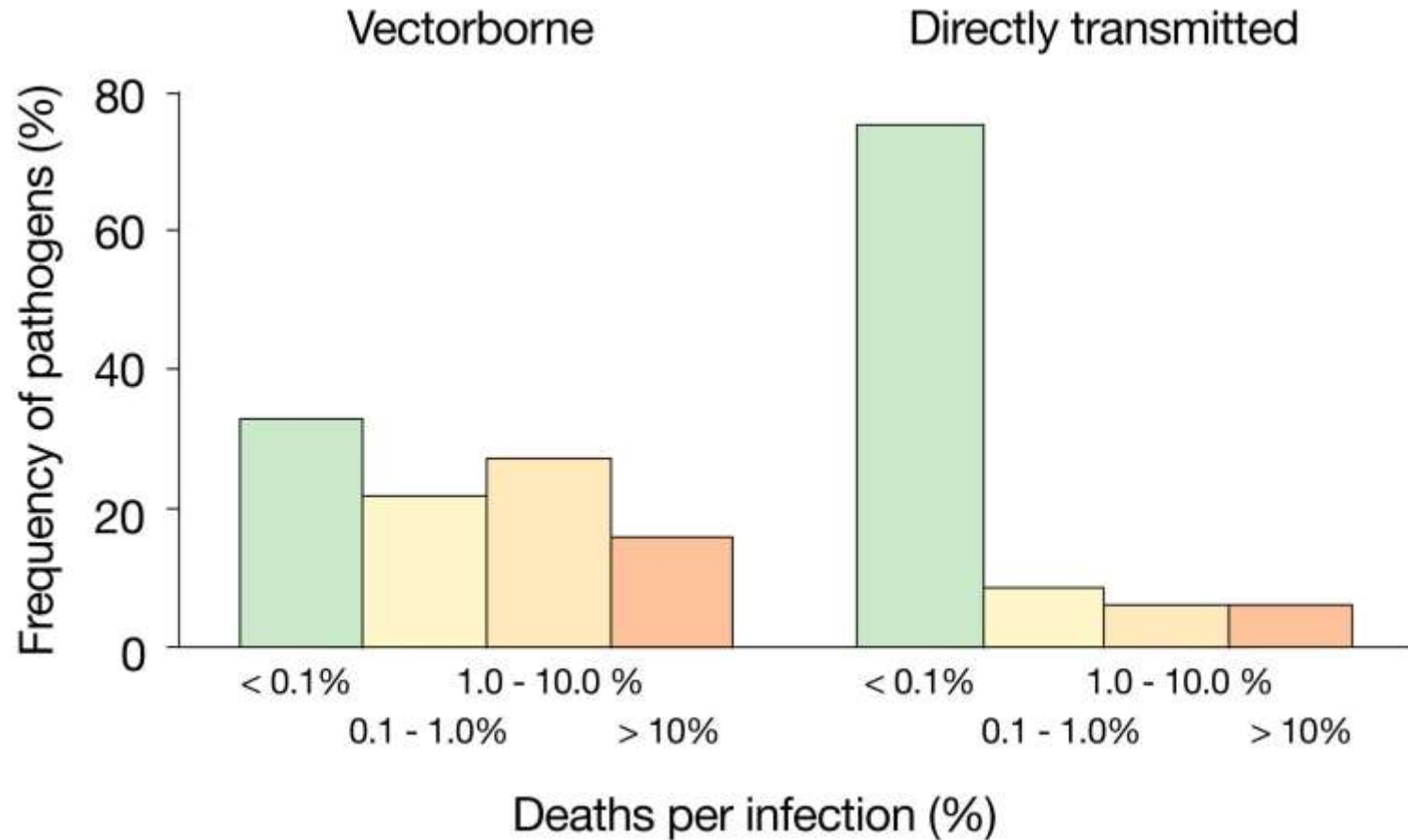
# Mode of transmission affects virulence

Direct transmission, vectorborne, waterborne

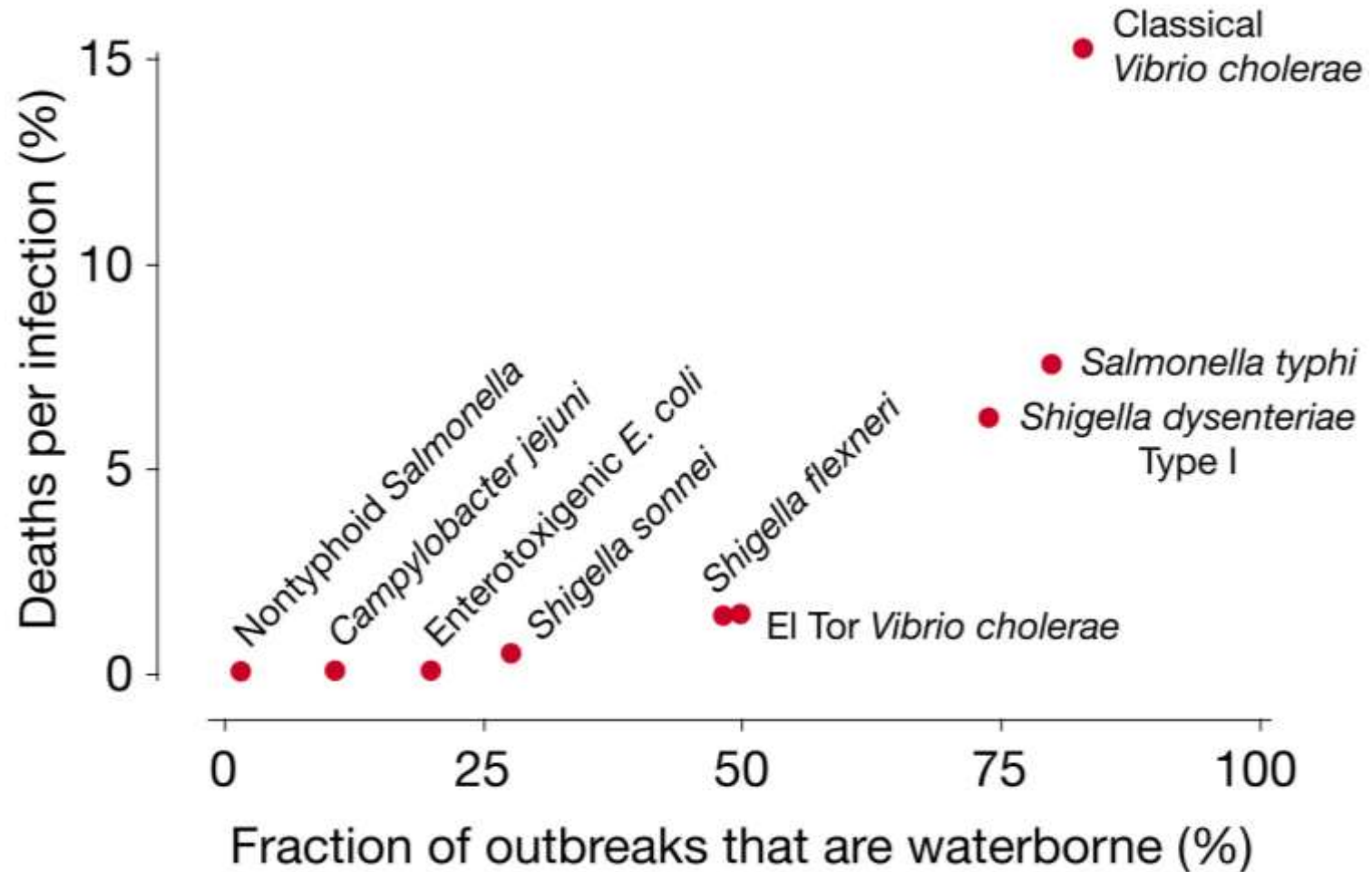




# Mode of transmission affects virulence



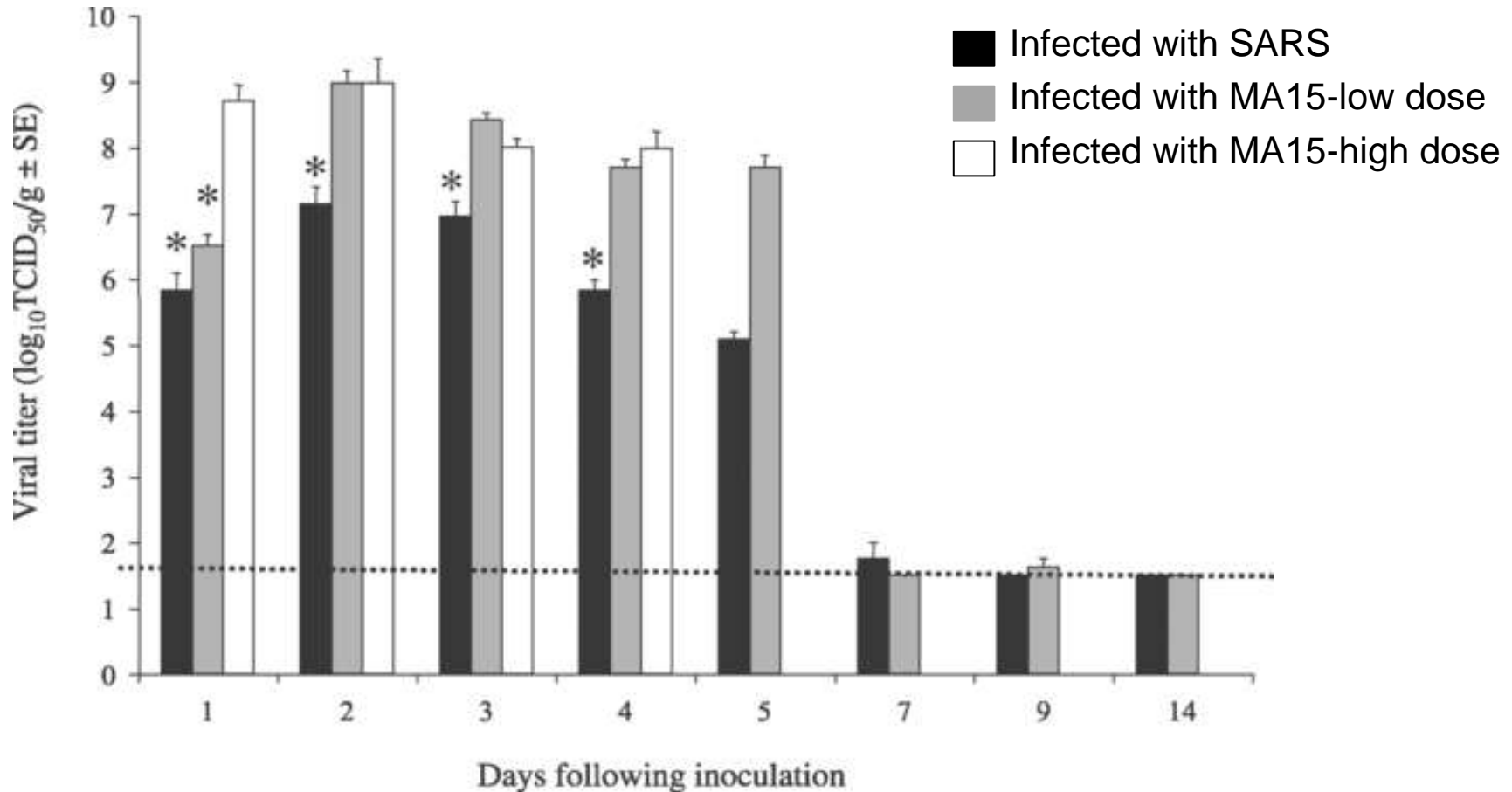
# Mode of transmission affects virulence



# 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



# Evolution of virulence: implications for public health

Select for lower virulence by interfering with transmission

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

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



Selection **across hosts** favors reduced virulence.





# 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

