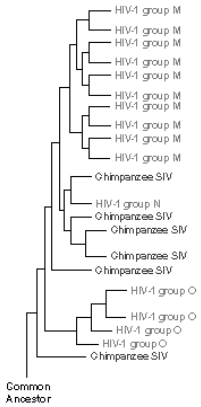
Why should anyone care about phylogeny?

- One of the best tools for understanding the spread of contagious disease

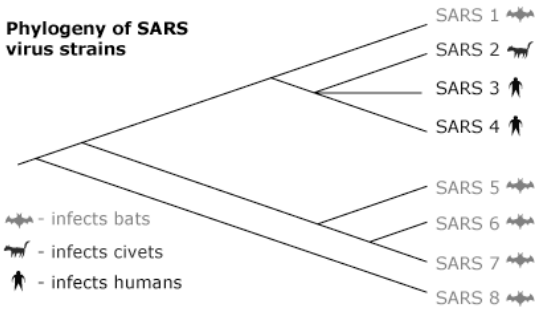
Uses of phylogenies: Medicine



- Learn about the origin of diseases
- Look for disease resistance mechanisms in other hosts to identify treatment and therapy in humans

Multiple origins of HIV from SIV (Simian Immunodeficiency Virus)

Example of disease phylogeny



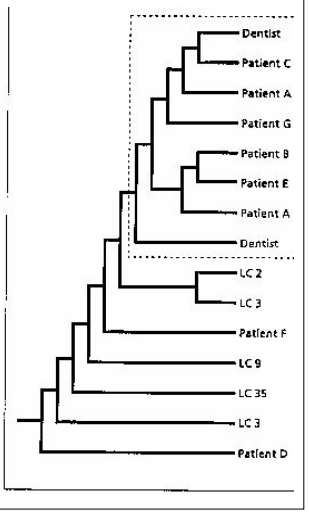
Source of Severe Acute Respiratory Syndrome coronavirus was unknown… phylogenetic analyses traced it to civets and bats.

USING PHYLOGENY TO SOLVE A HEALTH MYSTERY

In 1990, a woman with no HIV risk factors contracted HIV. The hypothesis was put forward that she contracted it from her HIV positive dentist.

A phylogenetic tree of HIV sequences from the dentist, seven patients, and several local controls clearly shows that 5 of the patients had HIV virus sequences closest to those of the dentist.

Fig. 1.2 The case of the Florida dentist. Each branch represents the sequence from part of the envelope (*env*) gene of HIV-1. Viral sequences were obtained from the dentist and seven of his former patients (labelled A to G), also infected with the virus. Five of these patients (A, B, C, E and G), have sequences very closely related to those of the dentist (boxed), suggesting that he infected them. Two of his other former patients (D and F) had other risk factors for HIV infection and their viruses are separated from the dentist by sequences taken from local controls (LC)—HIV-infected individuals living within a 90-mile radius of the dentist's surgery. Because HIV-1 is so variable, two different sequences are included for the dentist and patient A. Data taken from Ou *et al.* (1992).



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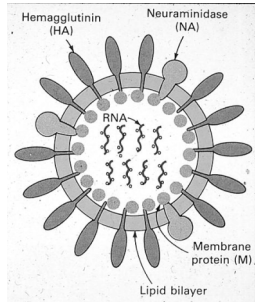
Beating Flu with Evolutionary Biology

Human Flu Viruses (Influenza A and B) cause frequent flu epidemics

Flu viruses evolve very rapidly; this is why there is a new flu vaccine each year

The body protects itself against flu by producing antibodies to hemagglutinin on the flu virus protein coat

One might hypothesize that flu viruses with novel hemagglutinins would be favored under natural selection

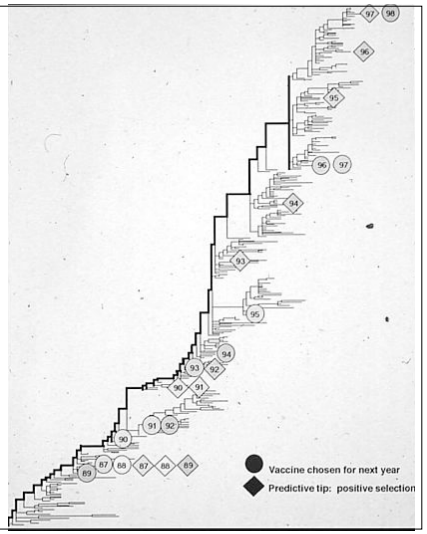


In the late 90's, Walter Fitch, Robin Bush, and co-workers produced a phylogeny of flu viruses over more than 10 years using DNA from frozen viral samples.

The resulting phylogenetic tree showed a non-random pattern of which flu strain from each year would become the dominant strain in the next year.

Indeed, they found that strains with amino acid changes at hemagglutinin sites tended to become the dominant strain next year.

This has since been helpful in selecting flu vaccines



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Plant secondary chemicals have proven to be a vast reservoir for useful pharmaceuticals — these include analgesics, diuretics, laxatives, tranquilizers, contraceptive agents, and cough drops.

Clinically proven drugs derived from higher plants include morphine, codeine, atropine, quinine, digitalis, and many others.

Scientists have only examined about 1 percent of existing plant species for such useful pharmaceuticals.

The powerful anti-cancer drug Paclitaxel (Taxol) caused a sensation when it was discovered in the bark of Pacific Yew Trees, *Taxus brevifolia.*

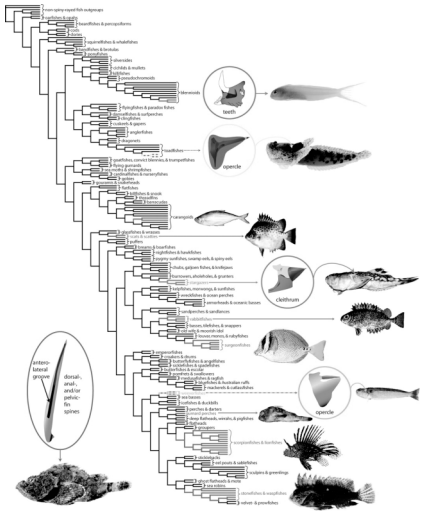
However, almost 100,000 pounds of bark were needed for clinical trials alone, and bark collection kills the tree. It was estimated that if Paclitaxel were used regularly to treat melanomas and ovarian cancer in the U.S., 360,000 trees would have to be destroyed each year. (!!!!!)

In the 90's, phylogenetic studies of yew trees guided scientists to other species of *Taxus* that could be used as sources for taxol (including *Taxus baccata*)

Now *Taxus* genes in transformed bacterial genomes produce paclitaxel at large scales

Currently, spider, snake, and fish phylogenies are being used in a survey to search for medically valuable compounds in the venoms of these animals.

Powerful anticancer and antistroke drugs have already been isolated from venoms of snakes



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- In gene and protein research, phylogeny allows one to make scientifically sound comparisons between different genes, proteins, and species

Question:

Pretend you are a medical researcher interested in the expression and function of a particular human gene.

You are interested in comparing the gene with homologous genes in other species, to compare their similarities and differences. Which species would have a gene most similar to the human gene of interest?

a.) chimpanzee

b.) rat

c.) cow

d.) puffer-fish

Answer: it depends entirely on which 2 genes you are comparing. Species relatedness alone is *not* a reliable guide!

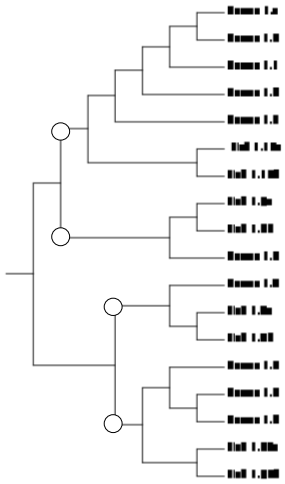
Example: Consider the voltage-gated sodium channels. Vertebrate animals can have ten or more sodium channel genes in their genomes, each of which has specialized expression in different excitable tissues.

$Na_v1.1$	$Na_v1.2$	$Na_v1.3$	$Na_v1.7$	$Na_v1.4$	$Na_v1.5$	$Na_v1.8$	$Na_v1.9$	$Na_v1.6$
CNS PNS	CNS	embryonic CNS	PNS	skeletal muscle	heart & skeletal muscle	PNS	PNS	CNS PNS

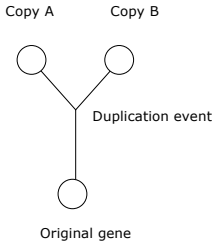
Gene nomenclature and expression profile in mammals.
CNS=Central Nervous System. PNS=Peripheral Nervous System.
Chromosomal locations: Blue, HC2; Black, HC17; Orange, HC3; Green, HC12

Because of gene families, a human sodium channel gene can be more closely related to a sodium channel gene in another species, than to another sodium channel in the human genome. For example, Nav1.4 (from skeletal muscle) is more closely related, evolutionarily, to the Nav1.4 gene of fish, than it is to any other human gene.

The common ancestor to fish and mammals had only four of these genes. Gene duplications occurred in the two lineages *after* the evolutionary split between them. This is what the phylogeny looks like, for 10 mammalian genes and 8 fish genes. Depending on which pair of genes you compare, sometimes a mammal gene is more closely related to a fish gene, than to another mammal gene.



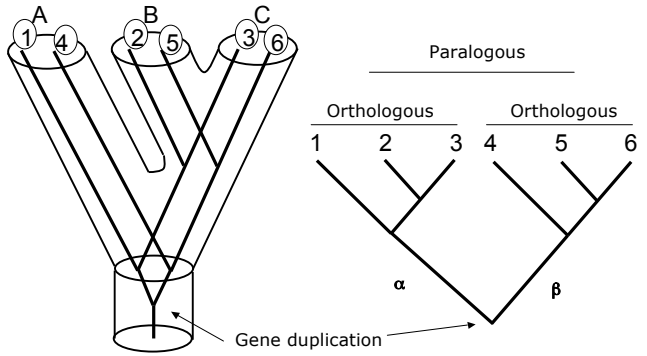
Gene duplication



So why are they interesting?

- New gene functions
- Gene duplications structure genomes
- Important for comparative genetics

Orthology and Paralogy



Why orthology matters

- Inference of structure or function is best made between orthologous sequences (paralogues may be more greatly divergent).
- For phylogenetic analyses, inference of species relationships should be based on orthologous genes

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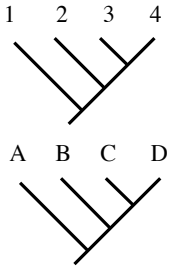
- In gene and protein research, phylogeny allows one to make scientifically sound comparisons between different genes, proteins, and species
- Phylogenetic information plus knowledge of coevolutionary symbioses can help in the design of strategies for biological control of agricultural pathogens and pests

USING PHYLOGENY FOR BIOPROSPECTING

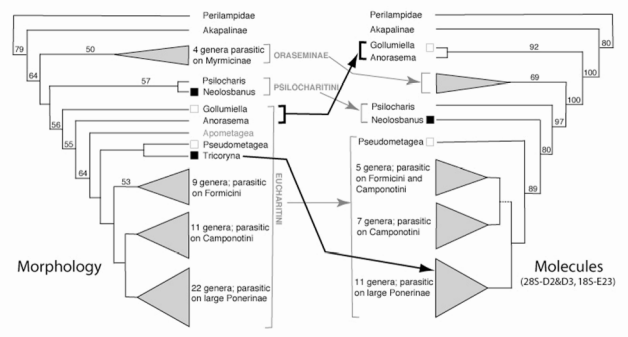
Many plants and animals are beneficial to human beings for medicine, or for biological control of pests, parasites, or pathogens

Phylogeny can help guide a search for potentially beneficial species based on what is known about their close relatives



For example, if a valuable medicine can be produced from natural compounds in plant species 3, it would make sense to search for similar compounds in the closely related plant species 4.

Or, if wasp species 3 helps control pest caterpillar C, then wasp species 4 may be a good candidate for natural control of pest caterpillar D.



Phylogeny reveals specialized parasite/host relationships. Eucharatid wasps can be used for biological control of imported red fire ants

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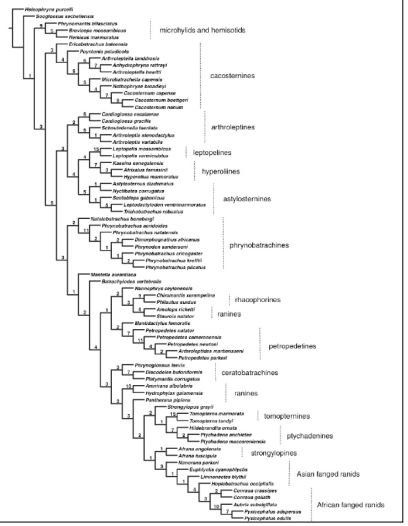
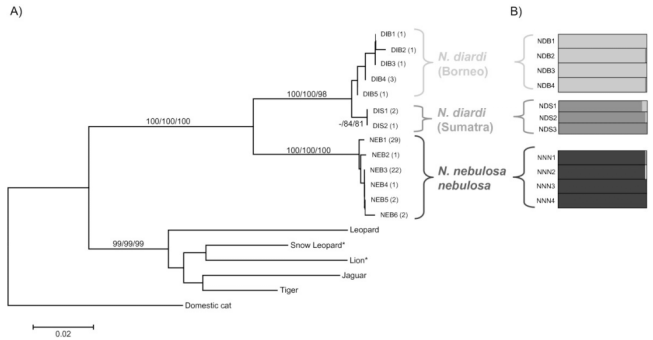
- To conserve biological diversity in threatened ecosystems or habitats, phylogeny can aid in selecting priority species for monitoring and protection

For example: frogs are undergoing a worldwide mass extinction, due to several factors. It is unlikely that we can save them all -- but which ones should we save?

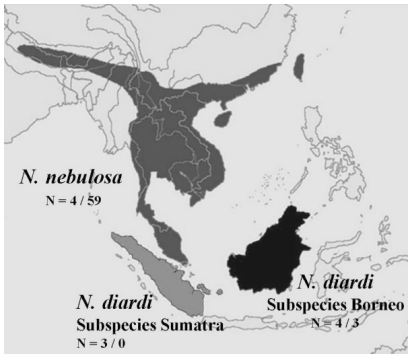
Use phylogeny to choose conservation strategies that maximize biological diversity… and choose geographic areas that contain the most diversity



The clouded leopard (*Neofelis nebulosa*) lives in parts of southeast Asia, Malaysia, and Indonesia.



The clouded leopard was long treated as a single species, but recent phylogenetic analyses indicate that leopards on Borneo and Sumatra are different. This is supported by new morphological evidence as well.



As a result of information provided by phylogeny, two species are now recognized and have separate conservation status. The new species *Neofelis diardi* has even been designated into Sumatran and Bornean subspecies.