BIO00056I Revision exercises
Week 6: Phylogenies and The Molecular Clock

This exercise describes a scenario where you can use phylogeny to solve a problem of an unidentified infectious agent (a pathogen). To solve this, you will need to have some fundamental knowledge of pathogens that we have not taught in this module, so we start with this.

Pathogens and epidemiology (the study of the causes of disease)

There are many types of pathogenic organisms; viruses, bacteria and protozoans are common types. Protozoans are single-celled eukaryotes, such as *Plasmodium* species that cause malaria. Here we consider *Leishmania* and *Endotrypanum*, protozoan pathogens that cause skin lesions that do not heal. **Figure 1** shows some examples.

Figure 1. Skin lesions caused by *Leishmania* pathogens.
The disease is called cutaneous leishmaniasis.

Three facts about protozoan pathogens are important here.

1. **Breeding:** They undergo meiosis and sexual recombination. ie: they breed sexually.
2. **Vectors:** They are almost always transmitted by insects. The insects feed on human and/or animal blood. They pick up the pathogen from the skin of an infected person or animal when they feed, and transfer the pathogen to another person or animal. Such insects are called **the vector of the pathogen**.
3. **Reservoirs:** Some pathogens and the insect vectors feed on animals as well as people. A large number of pathogens can be present in the animal population. An animal that contains pathogens is called a **reservoir species.** A pathogen can have more than one reservoir species.

The problem

In a remote island in the pacific there appears to be a new disease. Its symptoms are similar to the cutaneous leishmaniasis (Figure 1), but with larger lesions. It is spreading, and doctors suspect it is caused by the spread of a pathogen because it comes in clusters of cases within specific villages and households. You have received a grant to investigate the cause. Could this be a new protozoan?

The main questions that you have to answer are:

1. Is this a new protozoan or a more virulent strain of an already known protozoan?
2. Is there an insect vector? If so, what is it?
3. Is there a potential reservoir? If so, what is it?

What is already known:

1. On this island, only two protozoans were known to cause symptoms like cutaneous leishmaniasis *Leishmania major* and *Endotrypanum colombiensis.* They are quite different pathogens, and can be distinguished genetically.
2. There are only three potential reservoirs: rats, dogs and pigs
3. There are two sandflies species that could be the vector
4. Both *L. major* and *E. colombiensis* and the mystery protozoan can be isolated from patients, cultured in a laboratory, and DNA extracted.

You have a team of clinicians and laboratory technicians that can do parasite isolation, culturing and DNA extractions.

What to think about

- How can phylogeny help to solve question 1?
- How do you design experiments so that you can find out the answers to questions 2 and 3?
- Would there be a spatial, temporal, or seasonal component to your experiments?
- Could the situation be more complex than we suppose? How would you ensure you have robust answers?

What to write

To create a solution:

1. Write an experimental plan that includes sampling numbers, locations and time scales. This can be one paragraph, or a list of tasks.
2. Explain how phylogeny can give you concrete answers.
3. Explain a scenario where phylogenetic analysis might return less-convincing or more complex answers.