

Model organisms: the genes we share

Introduction

In this activity you will discover why scientists use different organisms to study human genetics and human disease.

Model organisms can be used to test hypotheses or treatments such as new drugs. With model organisms, answers to scientific questions can usually be obtained faster and without as many ethical dilemmas as would be caused by using human subjects. As part of the Human Genome Project, the DNA sequences of these model organisms have been deposited in a genetic bank at the National Center for Biotechnology Information (NCBI), along with data from the human genome.

You will use computer tools developed by the NCBI to analyze genetic similarities between humans and various model organisms.

Problem

Huntington disease is a heritable disorder that affects the nervous system of individuals, usually after the age of 30. There is no cure and the clinical outcome is death. Carriers of this gene appear to be healthy and live normal lives; sometimes not even aware they have the disorder. For a complete overview of the disease, go to the following page on the Internet site *Your Genes Your Health*:

<http://www.ygyh.org/hd/>

The human gene that is mutated in Huntington disease (HD) is located on chromosome 4. People with HD have an enlarged version of a gene called *huntingtin*.

Do mice have this gene? If so, could a mouse model be developed to study HD?

To find the answers to these questions, you need to use NCBI's gene search tool *Homologene*. This site searches genetic databases for homologous genes - genes shared by organisms due to our common evolution. Follow the directions below and answer the questions that follow.

Solve the problem:

1. Go to the Internet site: <http://www.ncbi.nlm.nih.gov/HomoloGene/>
2. Type "Huntington disease" into the space provided.
3. Click "go." When the search is complete, there will be many results.
4. Choose the first result from the top. It should be "HomoloGene:1593. Gene conserved in Coelomata"
5. Click the first entry.

6. Look under "Genes."

List the four organisms that are shown to possess a gene homologous to the HD gene. Then search the Internet to find the common name of each organism.

Organism 1. _____

Organism 2. _____

Organism 3. _____

Organism 4. _____

7. Look under "Alignment Scores." Click on "Show Table of Pairwise Scores."

Which organism has the closest nucleotide sequence to the mouse HD gene? (Look under nt% ID.)

What percentage of the DNA sequence of the mouse HD gene matches the human HD gene?

8. How similar is the mouse HD protein to the human and the rat HD protein? (Look under aa% ID.)

Why are the human and mouse protein (amino acid) sequences here similar than their nucleotide sequences?

9. In mice the HD gene is found on chromosome 5, whereas in humans it is found on chromosome 4.

Explain why this gene is not found on the same chromosome in both organisms.

10. Based on your computer analysis of the HD gene in mice, what would happen if scientists mutated this gene the same way that the human gene is mutated in HD?
Do you think the mice would develop HD? How could you determine if the mice are affected?

11. Explain why drug companies would be interested in mice or rats with Huntington disease.

12. Is it ethical to create a mouse model to study Huntington disease? Defend your argument.