

Using Bioinformatics to Explore Genotype/Phenotype Correlations

This laboratory will be held on Monday, November 4, in Wilcox 073. There are 15 workstations in Wilcox. All students should log in with:

username - cheme355

password - giagyu

The database OMIMTM - Online Mendelian Inheritance in ManTM is available through the World Wide Web at <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>. The database is a compilation of data on human diseases and their genetic basis, and it allows the investigator to probe the origin of diseases and their within-species and between-species similarities and differences. OMIM is now a part of the Entrez System developed and maintained by NCBI (National Center for Biotechnology Information). The OMIM page has links to help sections and tutorials.

1. **Exercise 1: Become familiar with OMIM.** Start by going through the simple introduction to OMIM available at <http://www.ornl.gov/hgmis/posters/chromosome/omim.html>. Supplement that with the OMIM help at <http://www.ncbi.nlm.nih.gov/entrez/Omim/omimhelp.html>. Once you have gone through this material, you should be able to define and enter basic queries in OMIM. A mutation in the Type I collagen molecule (which makes up about 90% of total body collagen) is responsible for Osteogenesis Imperfecta (OI). Learn more about collagen at http://www.rcsb.org/pdb/molecules/pdb4_1.html. By far, collagen is the most plentiful protein in the body, and up to now, 15 types of collagen molecules have been discovered. Use OMIM to document the link between a mutation in Type I collagen and OI, and describe your findings. Be sure to support your findings with literature citations (using PUBMED, which is linked to OMIM), and precisely indicate how these citations corroborate your conclusions.
2. **Exercise 2: Disorders with similar clinical manifestations can have different molecular basis.** Consider now a clinical manifestation best described as a connective tissue disorder characterized by frequent rupturing of tissues with minimal mechanical force applied. This disease is known as Ehlers-Danlos (ED) syndrome. Describe the clinical symptoms of ED. Use OMIM to link ED syndrome to mutations that affect collagen, and document your findings. How many varieties of ED have been discovered? Do they share the same genetic basis? Document your answers.
3. **Exercise 3: Disorders with different clinical manifestations can have similar molecular basis.** Homocystinuria is a metabolic disorder due to the absence of a key enzyme in protein breakdown. Describe the clinical symptoms of homocystinuria. How does it relate to mutations in collagen Type I? Report your findings, corroborating them with literature citations.