Ch 5: Structure (Click on Structure at the top black bar of the NCBI homepage)
Structural databases such as Entrez Structure at NCBI contain details of protein structure based on X-ray crystallographic and NMR studies. From this database it is possible to retrieve and examine a particular three-dimensional structure in a viewer called Cn3D. In this tutorial, we will examine some structures and learn to use the Cn3D structural viewer.

Download Cn3D v4.1 by clicking on Cn3D v4.1 on the left-hand side menu.

Type 1JM6 (the ID for rat pyruvate dehydrogenase in the PDB protein database)-Click Go.

When the result appears, click 1JM6 to see the NCBI Molecular Modeling Database (MMDB) Structure Summary page

Click "View 3D Structure"
You will see alpha helices are shown as green cylinders and beta pleated sheets as gold flat arrows. The connecting amino acid chain is in blue.

Use your mouse to drag the molecule and rotate it. Note that it consists of two mirror image complexes consisting of the A and B chains. Notice the bound ADP molecule in each complex (partly colored in red and complexed with a Mg ion)? Can you identify the adenine ring structure in the ADP molecule? You can zoom in using the Zoom feature under View in top menu.

The lower pop-up window (Sequence/Alignment Viewer) shows the primary sequence of the two amino acid chains. Note that the sequence is color coded to match the 3D structure.

On the top menu, try style such as **frame** and **spacefill**

Go back to Structure by clicking Structure on the very top
Do another search with GCN4 and yeast-Go, you will get a list (4 pages)
Click on 1YSA (on page 4)
Click View 3D-you will see both protein chains interacting with DNA
Go back to Structure
[**Click VAST (Vector Alignment Serach Tool)**

VAST allows an investigator to search the database for structures similar to the one of interest. This allows a crystallographer with a newly acquired sequence to search for structurally related proteins utilizing the VAST program.

Search for **1G5S, then try click domain 2, click VAST]-optional**

Ch 6: OMIM (Online Mendelian Inheritance in Man)
Click on statistics on the left (under OMIM facts)
A Table shows all the genes entered in OMIM (about half of the 35,000 human genes are shown)

- **Click on X-linked**
- **Click on the first entry**-get the description about the gene
- **Go back to OMIM, Click on Update Log (just below Statistics)**
  - See the record is updated every month
- **Go back to OMIM, enter "Huntington" in the search window-Go**
  - You will get 107 entries
- **Click on the the first entry (OMIM number *143100)**
  - See the wealth of info on this disease
- **Click on Map "4p16.3" -**get a table- **click 4p16.3 in the top of table**

By zooming in on the locus (use the zoom in feature just above the chromosome graphic on the very left), we can display the genes that are located close to the Huntington locus. Under the Morbid column are various loci associated with disease phenotypes.

Click on HD under the "symb" column

Led to Entrez Gene record for the Huntington disease gene with links to many information resources

Click HGMD (the human genetic diseases database) on the right under LINK. HGMD is specializing in the nature of characterized mutations for various loci. Note the trinucleotide repeat for HD

Go back to Entrez Gene,

Scroll down, see the Genomic context, click "see HD in Mapview"

Click "sv" (sequence view)**-**get to detailed molecular info on HD

Ch 7: Cancer Genome Anatomy Project (NCI-CGAP)

Click on NCI-CGAP under Hot Spot on the NCBI Home page

Click on Cancer Genome Anatomy Project

Click "Gene"

Click "Gene Finder" (third in the list)

Enter "BRCA1" (Breast Cancer Associated1) and Submit query

Click "Gene Info"

Under Database Links, **Click UniGene** (UniGene entry is a set of transcript sequences that appear to come from the same transcription locus) together with information on protein similarities, gene expression, cDNA clone reagents, and genomic location.

Click "Entrez Gene", explore

Click "OMIM", explore

Get back to CGAP by clicking to panel

Click "Pathway"

Click on the BioCarta Pathways

Click on "ATM Signaling Pathway"

The ATM pathway is important for delaying cell cycle progression to allow time for repair if there has been damage to DNA. This helps to prevent permanent damage or chromosome breakage and the consequent genomic instability. Maps of this type help the researcher place a particular gene product into a broader context. BRCA1 is shown just to the left of center.

Clicking on any of the icons in the map will takes us back to the Gene Info page for that gene

Get back to CGAP-Click "genes" again

Click on the Gene Ontology (GO) browser

GO defines function in a hierarchical fashion

Click "+" sign next to the three terms in turn to open up the next level of the hierarchy

Click + next to Molecular Function

Clicking + sign next to 'binding' and then 'nucleic acid binding'

Click on the number to see the list of genes belonging to that category

Get back to CGAP-click "chromosomes"

Click on FISH-mapped BACs, click on chromosome 1

Click on Physical SNP map, click on chromosome 1