Recap From Last Time:

- Bioinformatics is computer aided biology.
  - Deals with the collection, archiving, organization, and interpretation of a wide range of biological data.
- There are a large number of primary, secondary and tertiary bioinformatics databases (see handout!).
- The NCBI and EBI are major online bioinformatics service providers.
- Introduced Gene, UniProt and PDB databases as well as a number of 'boutique' databases including PFAM and OMIM.
- Introduced the notion of *controlled vocabularies* and *ontologies* via exploring GO annotations.
- Also covered: Course structure; Introductions, Software setup and Database Vignette…

Example Vignette Questions:

- What chromosome location and what genes are in the vicinity of a given query gene? NCBI **GENE**
- What can you find out about molecular functions, biological processes, and prominent cellular locations? EBI **GO**
- What amino acid positions in the protein are responsible for ligand binding? EBI **UniProt**
- What variants of this gene are associated with gastric cancer and other human diseases? NCBI **OMIN**
- Are high resolution protein structures available to examine the details of these mutations? How might we explain their potential molecular effects? RCSB **PDB**
- What is known about the protein family, its species distribution, number in humans and residue-wise conservation? EBI **PFAM**

TODAYS MENU

- More hands-on exploration of these databases and their associated tools (searching with a propose!)
- Major hands-on sections include:
  1. BLAST, GenBank and OMIM @ **NCBI** [~35 mins]
  2. GENE database @ **NCBI** [~15 mins]

     — BREAK —
  3. UniProt & Muscle @ **EBI** [~25 mins]
  4. PFAM, PDB & NGL [~30 mins]

     — BREAK —
  5. Optional extension exercises [~20 mins]

  - Please do answer the last review question (**Q19**).
  - We encourage discussion and exploration!

SideNote: Bioinformatics Databases

AATDB, AceDb, ACUTS, ADB, AFDB, AGIS, AMSdb, ARR, AsDb,BBDB, BCGD, Beanref, BioImage, BioMagResBank, BIOMDB, BLOCKS, BovGBASE, BOVMAP, BSORF, BTKbase, CANSITE, CarbBank, CARBHYD, CATH, CAZY, CCDC, CD4OLbase, CGAP, ChickGBASE, Colibri, COPE, CottonDB, CSNDB, CUTG, CyanoBase, dbCFC, dbEST, dbSTS, DDBJ, DGP, DictyDb, Picty_cDB, DIP, DOGS, DOMO, DPD, DPInteract, ECDC, ECGC, EC02DBASE, EcoCyc, EcoGene, EMBL, EMD db, ENZYME, EPD, EpoDB, ESTHER, FlyBase, FlyView, GCRDB, GDB, GENATLAS, Genbank, GeneCards, Genlilesne, GenLink, GENOTK, GenProtEC, GIFTS, GPCRDB, GRAP, GRBase, gRNAsdb, GRR, GSDB, HAEMB, HAMSTERS, HEART-2DPAGE, HEXAdb, HGMD, HIDB, HIDC, HIVdb, HotMolecBase, HOVERGEN, HPDB, HSC-2DPAGE, ICN, ICTVDB, IL2RGbase, IMGT, Kabat, KDNA, KEGG, Klotho, LGIC, MAD, MaizeDb, MDB, Medline, Mendel, MEROPS, MGDB, MGI, MHCPEP5 Micado, MitoDat, MITOMAP, MJDB, MmtDB, Mol-R-Us, MPDB, MRR, MutBase, MycDB, NDB, NRSub, 0-lycBase, OMIA, OMIM, OPD, ORDB, OWL, PAHdb, PatBase, PDB, PDD, Pfam, PhosphoBase, PigBASE, PIR, PKR, PMD, PPDB, PRESAGE, PRINTS, ProDom, Prolysis, PROSITE, PROTOMAP, RatMAP, RDP, REBASE, RGP, SBASE, SCOP, SeqAnaiRef, SGD, SGP, SheepMap, Soybase, SPAD, SRNA db, SRPDB, STACK, StyGene,Sub2D, SubtiList, SWISS-2DPAGE, SWISS-3DIMAGE, SWISS- MODEL Repository, SWISS-PROT, TelDB, TGN, tmRDB, TOPS, TRANSFAC, TRR, UniGene, URNADB, V BASE, VDRR, VectorDB, WDCM, WIT, WormPep, etc ..... !!!!

SideNote: Bioinformatics Databases

AATDB, AceDb, ACUTS, ADB, AFDB, AGIS, AMSdb, ARR, AsDb,BBDB, BCGD, Beanref, BioImage, BioMagResBank, BIOMDB, BLOCKS, BovGBASE, BOVMAP, BSORF, BTKbase, CANSITE, CarbBank, CARBHYD, CATH, CAZY, CCDC, CD4OLbase, CGAP, ChickGBASE, Colibri, COPE, CottonDB, CSNDB, CUTG, CyanoBase, dbCFC, dbEST, dbSTS, DDBJ, DGP, DictyDb, Picty_cDB, DIP, DOGS, DOMO, DPD, DPInteract, ECDC, ECGC, EC02DBASE, EcoCyc, EcoGene, EMBL, EMD db, ENZYME, EPD, EpoDB, ESTHER, FlyBase, FlyView, GCRDB, GDB, GENATLAS, Genbank, GeneCards, Genlilesne, GenLink, GENOTK, GenProtEC, GIFTS, GPCRDB, GRAP, GRBase, gRNAsdb, GRR, GSDB, HAEMB, HAMSTERS, HEART-2DPAGE, HEXAdb, HGMD, HIDB, HIDC, HIVdb, HotMolecBase, HOVERGEN, HPDB, HSC-2DPAGE, ICN, ICTVDB, IL2RGbase, IMGT, Kabat, KDNA, KEGG, Klotho, LGIC, MAD, MaizeDb, MDB, Medline, Mendel, MEROPS, MGDB, MGI, MHCPEP5 Micado, MitoDat, MITOMAP, MJDB, MmtDB, Mol-R-Us, MPDB, MRR, MutBase, MycDB, NDB, NRSub, 0-lycBase, OMIA, OMIM, OPD, ORDB, OWL, PAHdb, PatBase, PDB, PDD, Pfam, PhosphoBase, PigBASE, PIR, PKR, PMD, PPDB, PRESAGE, PRINTS, ProDom, Prolysis, PROSITE, PROTOMAP, RatMAP, RDP, REBASE, RGP, SBASE, SCOP, SeqAnaiRef, SGD, SGP, SheepMap, Soybase, SPAD, SRNA db, SRPDB, STACK, StyGene,Sub2D, SubtiList, SWISS-2DPAGE, SWISS-3DIMAGE, SWISS- MODEL Repository, SWISS-PROT, TelDB, TGN, tmRDB, TOPS, TRANSFAC, TRR, UniGene, URNADB, V BASE, VDRR, VectorDB, WDCM, WIT, WormPep, etc ..... !!!!

There are lots of Bioinformatics Databases

For a annotated listing of major bioinformatics databases please see the online handout

< Major_Databases.pdf >

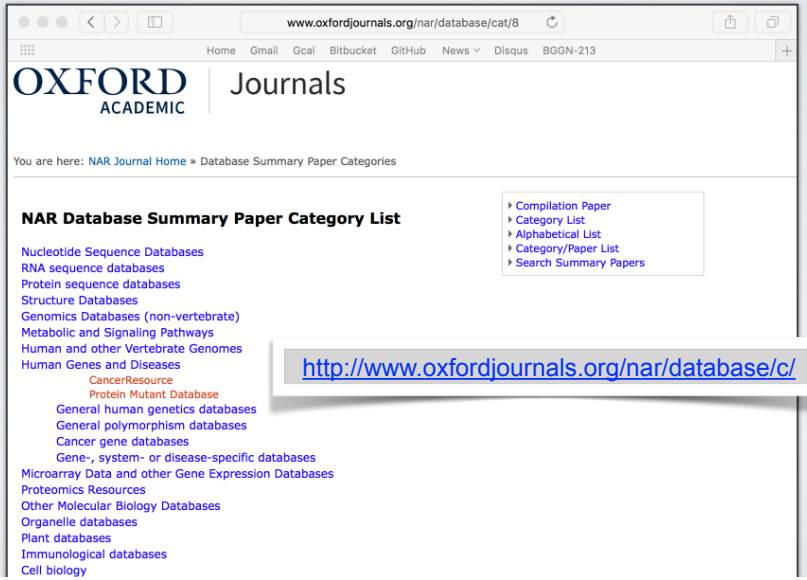
Side-note: Databases come in all shapes and sizes





Databases can be of variable quality and often there are multiple databases with overlapping content.

Finding Bioinformatics Databases



http://www.oxfordjournals.org/nar/database/c/

GENBANK & REFSEQ: NCBI'S NUCLEOTIDE SEQUENCE DATABASES

What is GenBank?

- GenBank is NCBI's primary **nucleotide only** sequence database
  - Archival in nature - reflects the state of knowledge at time of submission
  - Subjective - reflects the submitter point of view
  - Redundant - can have many copies of the same nucleotide sequence
  - GenBank is actually three collaborating international databases from Europe, US and Japan

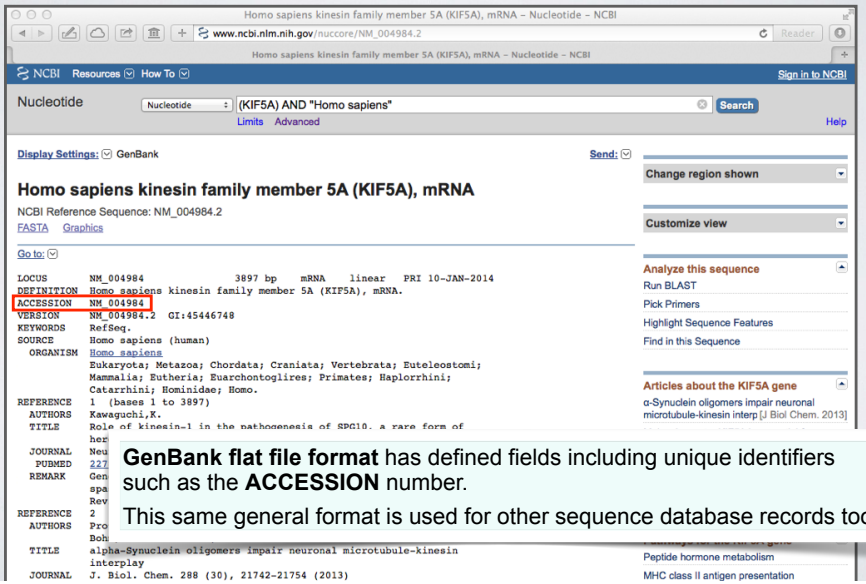
ENA ⟷ **GenBank** ⟷ **DDBJ**

ENA Housed at EBI

GenBank Housed at NCBI

DDBJ Housed in Japan

GenBank sequence record



GenBank flat file format has defined fields including unique identifiers such as the **ACCESSION** number.

This same general format is used for other sequence database records too.

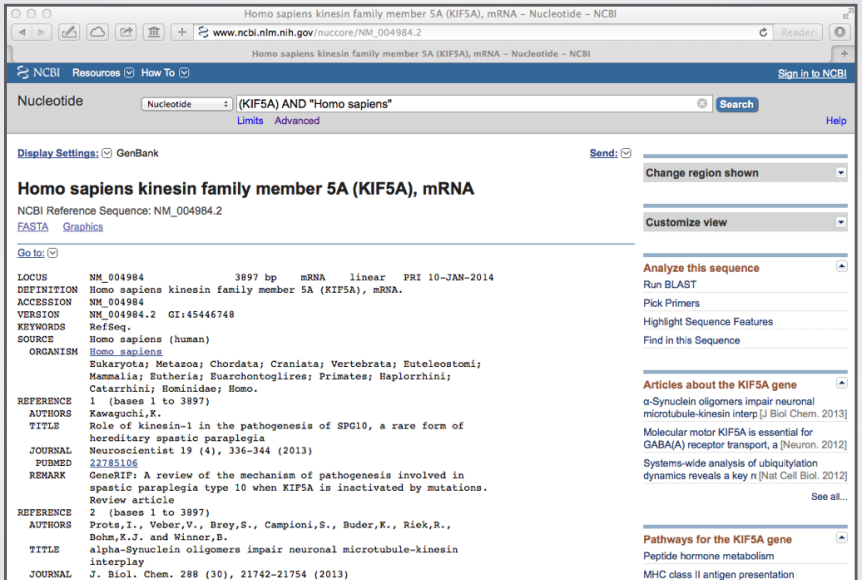
Side node: Database accession numbers

Database **accession numbers** are strings of letters and numbers used as **identifying labels** for sequences and other data within databases

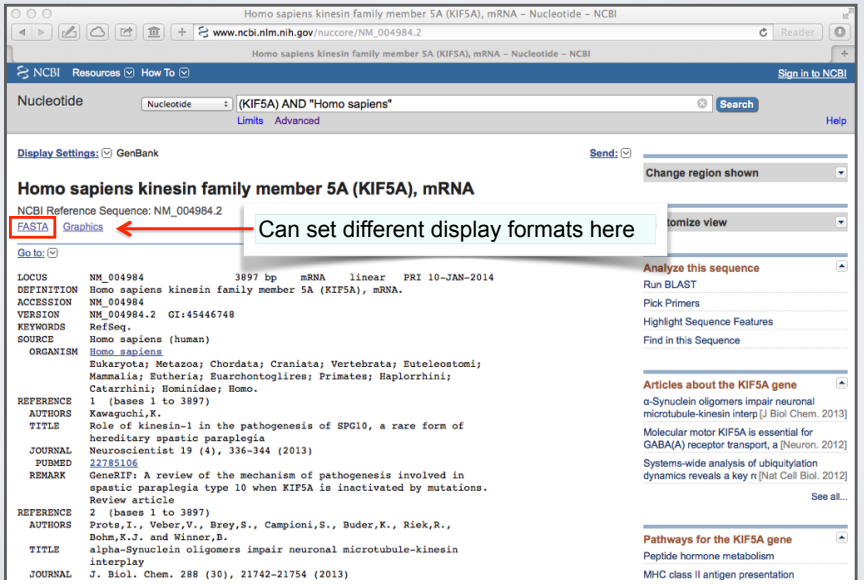
- Examples (all for retinol-binding protein, RBP4):

X02775	GenBank genomic DNA sequence	DNA
NT_030059	Genomic contig	
N91759.1	An expressed sequence tag (1 of 170)	RNA
NM_006744	RefSeq DNA sequence (from a transcript)	
NP_007635	RefSeq protein	Protein
AAC02945	GenBank protein	
Q28369	UniProtKB/SwissProt protein	
1KT7	Protein Data Bank structure record	
PMID: 12205585	PubMed IDs identify articles at NCBI/NIH	Literature

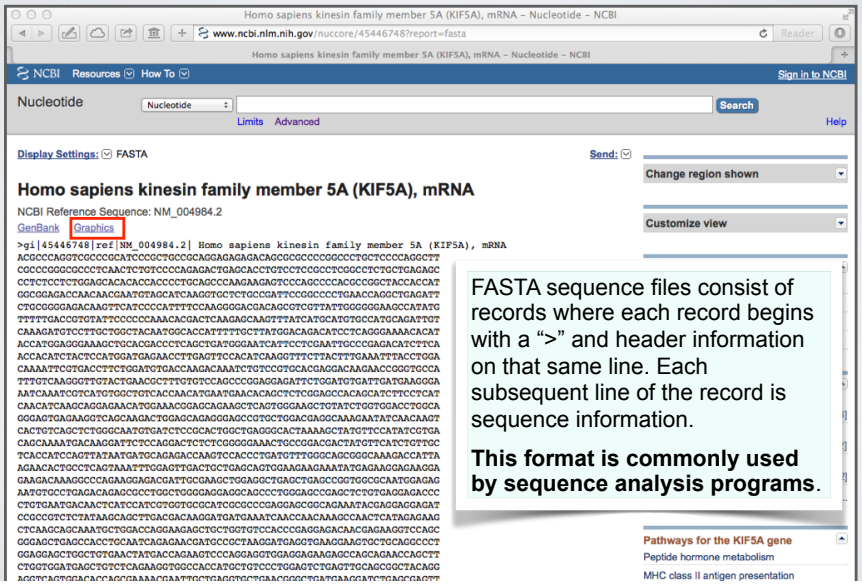
GenBank sequence record



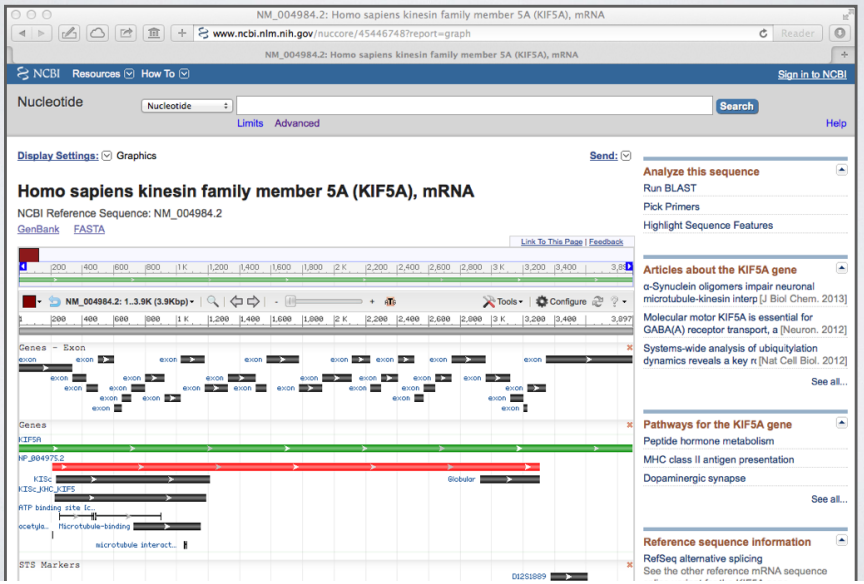
GenBank sequence record



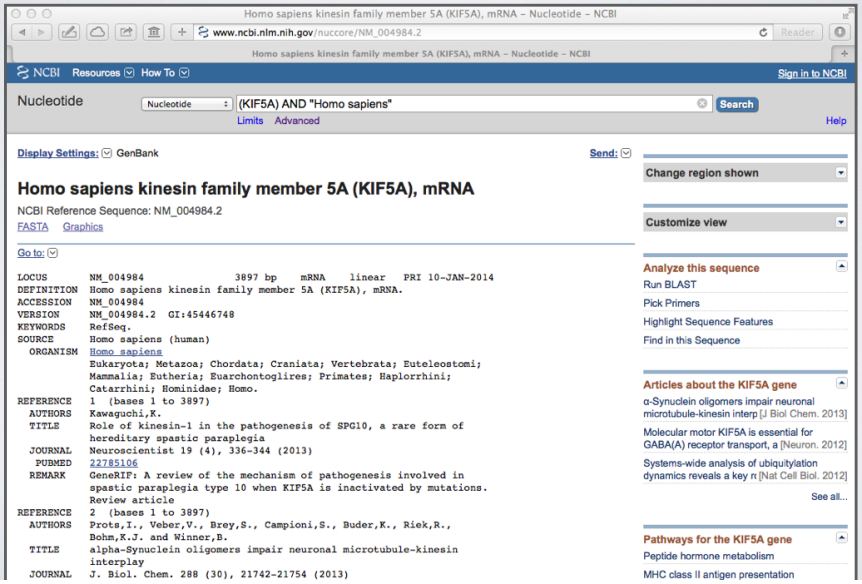
FASTA sequence record



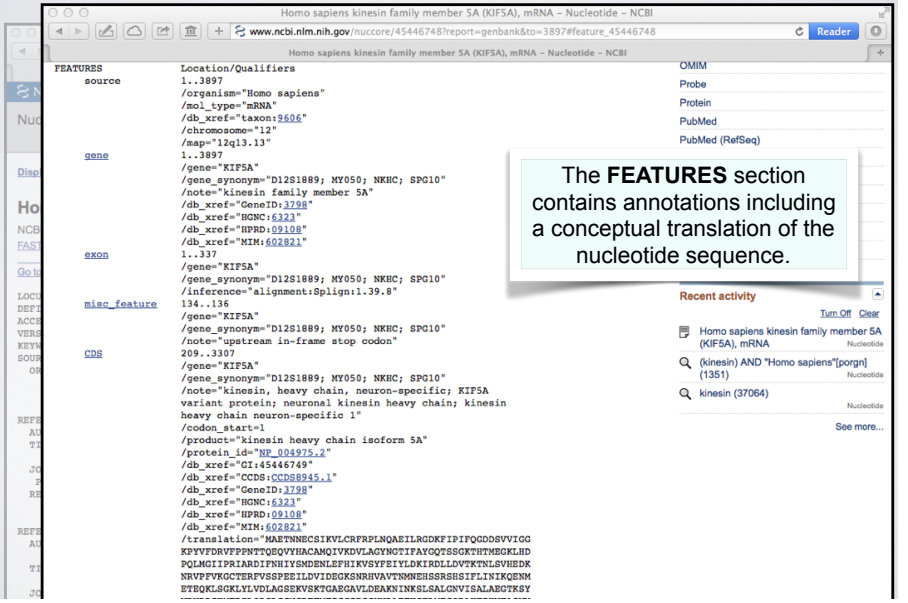
GenBank ‘graphics’ sequence record



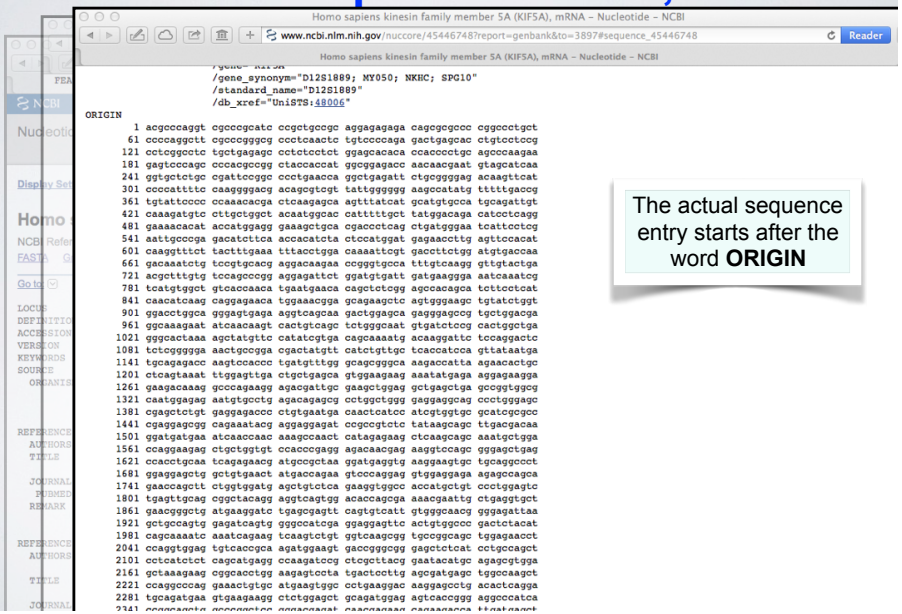
GenBank sequence record, cont.



GenBank sequence record, cont.



GenBank sequence record, cont.



The actual sequence entry starts after the word **ORIGIN**

RefSeq: NCBI's Derivative Sequence Database

- RefSeq entries are hand curated best representation of a transcript or protein (in their judgement)
- Non-redundant for a given species although alternate transcript forms will be included if there is good evidence

- Experimentally verified transcripts and proteins
  accession numbers begin with "NM_" or "NP_"
- Model transcripts and proteins based on bioinformatics predictions with little experimental support
  accession numbers begin with "XM_" or "XP_"
- RefSeq also contains contigs and chromosome records

UNIPROT:
THE PREMIER PROTEIN SEQUENCE DATABASE

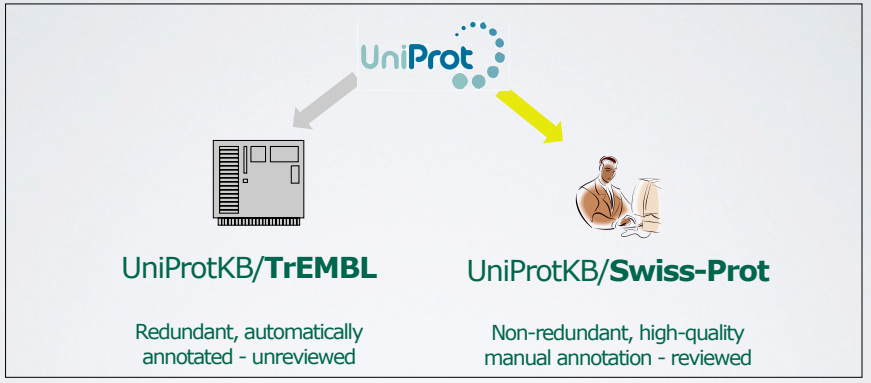
UniProt: Protein sequence database

UniProt is a comprehensive, high-quality resource of protein sequence and functional information

- UniProt comprises four databases:

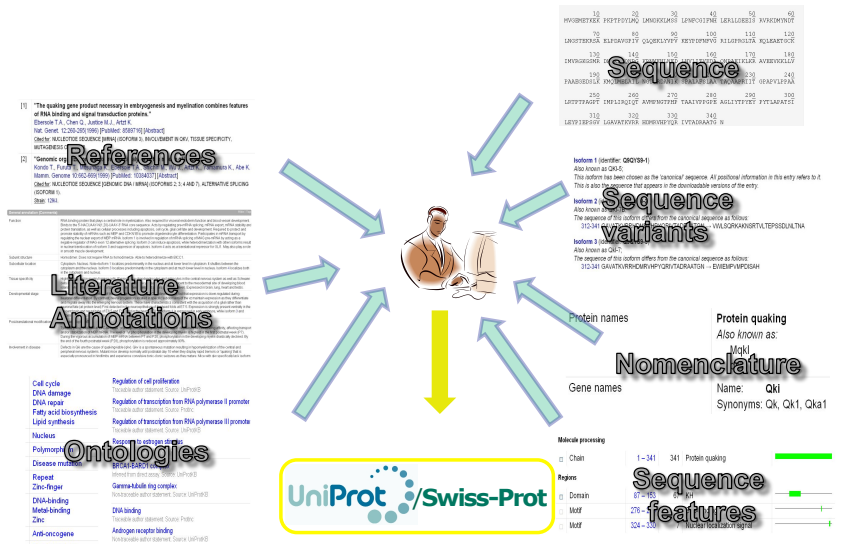
1. **UniProtKB** (Knowledgebase)
   Containing **Swiss-Prot** and **TrEMBL** components
   (these correspond to hand curated and automatically annotated entries respectively)
2. **UniRef** (Reference Clusters)
   Filtered version of UniProtKB at various levels of sequence identity
   e.g. UniRef90 contains sequences with a maximum of 90% sequence identity to each other
3. **UniParc** (Archive) with database cross-references to source.
4. **UniMES** (Metagenomic and Environmental Sequences)

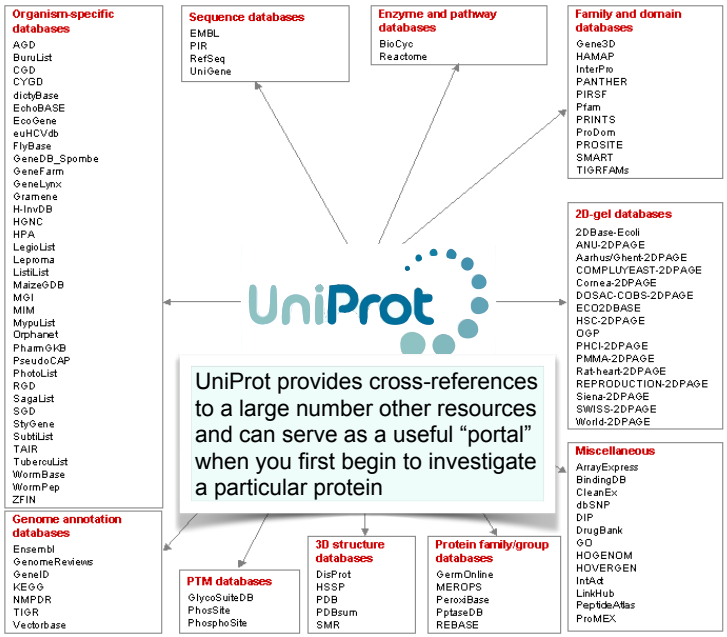
The two sides of UniProtKB



Indicators of which part of UniProt an entry belongs to include the color of the stars and the ID

The main information added to a UniProt/Swiss-Prot entry

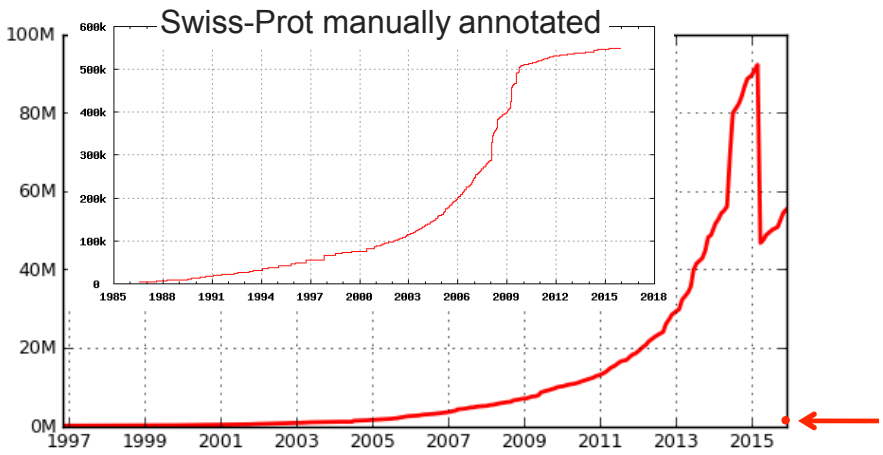




UniProt/Swiss-Prot *vs* UniProt/TrEMBL

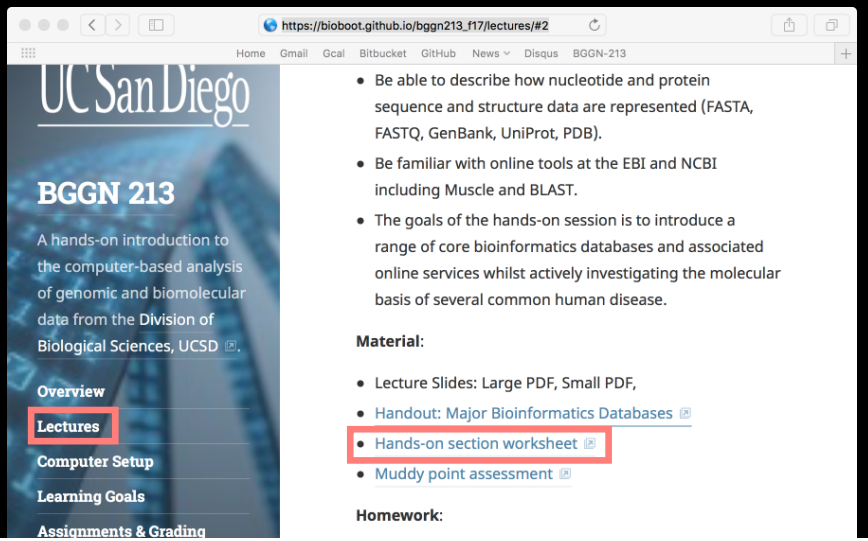
- *UniProtKB/Swiss-Prot* is a **non-redundant** database with one entry per protein
- *UniProtKB/TrEMBL* is a **redundant** database with one entry per translated ENA entry (ENA is the EBI's equivalent of GenBank)
  - Therefore TrEMBL can contain multiple entries for the same protein
  - Multiple UniProtKB/TrEMBL entries for the same protein can arise due to:
    - Erroneous gene model predictions
    - Sequence errors (Frame shifts)
    - Polymorphisms
    - Alternative start sites
    - Isoforms
    - OR because the same sequence was submitted by different people

Side note: **Automatic Annotation (a.k.a. sharing the wealth)**



Your Turn!

https://bioboot.github.io/bggn213_f17/lectures/#2



BGGN-213: FOUNDATIONS OF BIOINFORMATICS (Lecture 2)

Bioinformatics Databases and Key Online Resources
https://bioboot.github.io/bggn213_f17/lectures/#2
Dr. Barry Grant
Oct 2017

Overview: The purpose of this lab session is to introduce a range of bioinformatics databases and associated services available on the Web whilst investigating the molecular basis of a common human disease.

Sections 1 and 2 deal with querying and searching GenBank, GENE and OMIM databases at NCBI. Sections 3 and 4 provide exposure to EBI resources for comparing proteins and visualizing protein structures. Finally, section 5 provides an opportunity to explore these and other databases further with additional examples.

Side-note: The Web is a dynamic environment, where information is constantly added and removed. Servers "go down", links change without warning, etc. This can lead to "broken" links and results not being returned from services. Don't give up - give it a second go and try a search engine using terms related to the page you are trying to access.

Section 1
The following transcript was found to be abundant in a human patient's blood sample.

```
>example1
ATGGTGCATCTGACTCCTGTGGAGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAG
TTGGTGGTGAGGCCCTGGGCAGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGG
GGATCTGTCCACTCCTGATGCAGTTATGGGCAACCCTAAGGTGAAGGCTCATGGCAAGAAAGTGCTCGGT
GCCTTTAGTGATGGCCTGGCTCACCTGGACAACCTCAAGGGCACCTTTGCCACACTGAGTGAGCTGCACT
GTGACAAGCTGCACGTGGATCCTGAGAACTTCAGGCTCCTGGGCAACGTGCTGGTCTGTGTGCTGGCCCA
TCACTTTGGCAAAGAATTCACCCCACCAGTGCAGGCTGCCTATCAGAAAGTGGTGGCTGGTGTGGCTAAT
GCCCTGGCCCACAAGTATCACTAAGCTCGCTTTCTTGCTGTCCAATTT
```

The only information you are given is the above sequence so you must begin your investigation with a sequence search - for this example we will use NCBI's **BLAST** service at: http://blast.ncbi.nlm.nih.gov/

Note that there are several different "basic BLAST" programs available at NCBI (including nucleotide BLAST, protein BLAST, and BLASTx).

YOUR TURN!

- There are five major hands-on sections including:

1. BLAST, GenBank and OMIM @ **NCBI** [~35 mins]
2. GENE database @ **NCBI** [~15 mins]

— BREAK —

3. UniProt & Muscle @ **EBI** [~25 mins]
4. PFAM, PDB & NGL [~30 mins]

— BREAK —

5. Extension exercises [~30 mins]

- Please do answer the last review question (**Q19**).
- We encourage discussion and exploration!

YOUR TURN!

- There are five major hands-on sections including:

	End times:
1. BLAST, GenBank and OMIM @ **NCBI**	[9:45 am]
2. GENE database @ **NCBI**	[10:00 am]
— BREAK —	— 10:10 am —
3. UniProt & Muscle @ **EBI**	[10:35 am]
4. PFAM, PDB & NGL	[11:05 am]
— BREAK —	— 11:15 am —
5. Extension exercises	[11:45 am]

- Please do answer the last review question (**Q19**).
- We encourage discussion and exploration!

HOMEWORK

https://bioboot.github.io/bggn213_f17/lectures/#2

☑ Please do answer the last review question from today (**Q19**)

☑ Complete the **lecture 1 homework questions** for Thur.

☑ Check out the "**Background Reading**" material online.