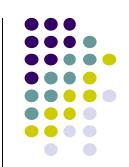




## Introduction to Bio-Informatics Lecture 6

Lecture by: Ahmad R. Naghsh-Nilchi, PhD
Department of Artificial Intelligence
Faculty of Computer Engineering
University of Isfahan





## In the last session, we discussed:

- Prokaryotes and Eukaryotes are introduced.
- GenBank information on Prokaryotes is explained.
- One Prokaryote gene type: dUPase with Accession code (X01714) is searched on GenBank and information is discussed one by one.



#### GenBank: X01714.1

#### FASTA Graphics



LOCUS X01714 1609 bp DNA linear BCT 23-OCT-2008

DEFINITION E. coli dut gene for dUTPase (EC 3.6.1.23) (deoxyuridine

5'-triphosphate nucleotidohydrolase).

ACCESSION X01714

VERSION X01714.1

KEYWORDS dUTPase; unidentified reading frame.

SOURCE Escherichia coli

ORGANISM <u>Escherichia coli</u>

Bacteria; Pseudomonadati; Pseudomonadota; Gammaproteobacteria;

Enterobacterales; Enterobacteriaceae; Escherichia.

REFERENCE 1 (bases 1 to 1609)

AUTHORS Lundberg, L.G., Thoresson, H.O., Karlstrom, O.H. and Nyman, P.O.

TITLE Nucleotide sequence of the structural gene for dUTPase of

Escherichia coli K-12

JOURNAL EMBO J. 2 (6), 967-971 (1983)

PUBMED 6139280

COMMENT Data kindly reviewed (25-NOV-1985) by L. Lundberg.





FEATUMES Location/Qualiflers

Source 1..1689

/organism="Escherichia coll" /mol\_type="genomic DMA" /db\_xrsf="taxon:561"

regulatory 286...291.

/regulatory class-"premoter"

/note="-35 region"

regulatory \$10..318

/regulatory\_class-"promoter"

/mits+"-18 region"

wise feature 322: 324

/note="put. transcription start region"

regulatory 3380,333

/regulatory\_class-"ribosoms\_binding\_site"

/note="put. rMNA bindles site"

CDS 343..798

/nuts="unnamed protein product; diff">-ase (as 1-151)"

/codon start-1

/transl\_table=ii

/protein id+"CAA25859.1"

/db: xnef+160A:P869681

/db sref-"IntarPro: Dwamming"

/db\_aref+"InterProc199888181"

/db arrof\*\*\*PDB:10U0\*\*

/db aref="108:10.0"

/db: xnef+"708:1845"

/db\_kmef="NOB::IEU/"

/db\_xref+"908:1888"

/db snof="PD6c1861"

/db.xnef="F0B:15EH"

/db xref+"908:15YL"

/db/sref="708:2H65"

/db:\xref+"908:248%"

/db:xnof="IniProtEB/Sales-Prot:PBNISB"

/translation="MEXIDAKIDAKIDPHYGKEFPLPTYAT5GSAGLDLRACUMDAVELAP

**Protein Sequence** 

GETTLYFTGLAZHLADFSLAAMYLFRSGLIDHKHGZYLIMLYGLZISIJYQGQLMZSVAN

RISQUIST LIGHGER LAGRITY VVV QAEFNILVED FDATORS & GCFGHSGRO".

at the first transfer of the





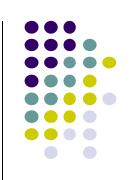








## GenBank Entry of an eukaryotic mRNA



- Continue with the dUPase gene, but an eukaryotic!
- dUPase presents both prokaryotes and eukaryotes.
- Human have it too!
- A simple eukaryote dUPase gene version is U90223.
- Selecting dUPase for both types, allows us to better feel and understands the complexity differences





Log in

Nucleotide

Nucleotide

U90223

. . .

Advanced

Halr

Search

Help

GenBank -

#### Human deoxyuridine triphosphate nucleotidohydrolase precursor mRNA, nuclear gene encoding mitochondrial protein, complete cds

GenBank: U90223.1

FASTA Graphics

Go to: ☑

LOCUS

HSU90223

96

mRNA

mRNA linear

linear PRI 03-JAN-1998

DEFINITION Human deoxyuridine triphosphate nucleotidohydrolase precursor mRNA,

nuclear gene encoding mitochondrial protein, complete cds.

ACCESSION U90223

VERSION U90223,1

KEYWORDS

SOURCE Homo sapiens (human)

Customize view

Send to: -

Analyze this sequence

Change region shown

Run BLAST

Pick Primers

Highlight Sequence Features

Find in this Sequence

Related information

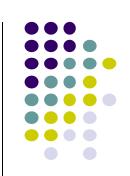
Protein

+





## Reading the GenBank header of a Eukaryotic entry



- Although it is related to a human gene, GenBank entry U90223 doesn't look very different from entry X01714, which describes its bacterial homologue.
- The top part of the entry follows the general information keywords order: Locus, Accession, Definition, and Version!
- The Keyword line, which is supposed to list relevant and searchable terms (such as dUPase), is empty for U90223!!!)



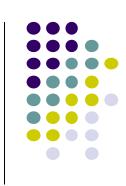
## What? How that is possible?



- Unfortunately, this is not an accident!
- It shows a common problem in sequence databases: Annotations may be incomplete!
- Information on databases may be missing or incomplete!
- A word to the wise: You should never expect GenBank (or any other sequence databases) annotations to be up-to-date!



## Feature Section of U90223 Entry



- The CDS keyword indicates a coding region (63-821) sequence that corresponds to the mitochondrial form of human dUTPase.
- Mitochondria are referred to as the "powerhouses" part of the cells
  of most eukaryotes because this part of the cell generates most of
  the chemical energy required for cellular functions.
- Following the conceptual amino-acid translation of the open reading frame, ORF, the sig peptide keyword indicates the location of a mitochondrial targeting sequence
- The mat peptide keyword provides the exact boundaries of the mature peptide (A molecule that contains two or more amino acids)



FEATURES Location/Qualifiers

source 1..960

/organism="Homo sapiens"

/mol\_type="mRNA"

/db\_xref="taxon:9606"

CDS 63..821

/note="mitochondrial dUTPase isoform; DUT-M"

/codon\_start=1

/product="deoxyuridine triphosphate nucleotidohydrolase

precursor"

/protein\_id="AAB94642.1"

/translation="MTPLCPRPALCYHFLTSLLRSAMQNARGTAEGRSRGTLRARPAP

RPPAAQHGIPRPLSSAGRLSQGCRGASTVGAAGWKGELPKAGGSPAPGPETPAISPSK

RARPAEVGGMQLRFARLSEHATAPTRGSARAAGYDLYSAYDYTIPPMEKAVVKTDIQI

ALPSGCYGRVAPRSGLAAKHFIDVGAGVIDEDYRGNVGVVLFNFGKEKFEVKKGDRIA

QLICERIFYPEIEEVQALDDTERGSGGFGSTGKN"

sig\_peptide 63..269

/note="mitochondrial targeting presequence"

mat\_peptide 270..818

/product="deoxyuridine triphosphate nucleotidohydrolase"

#### ORIGIN

1 ggtggaagcc tggcgcacgt ccggaggtgc cgaggaccca accagcccaa actctggggg 61 aaatgactcc cctctgccct cgccccgcgc tctgctacca tttccttacg tctctgcttc

121 gctcagcgat gcaaaacgcg cgaggcacgg cagagggccg aagccgcggt actctccggg

181 ccaggcccgc ccctcggccg ccggcggcgc agcacgggat tccccggccg ctgtccagcg

241 ctggccgcct gagccaaggc tgccgcggag ccagtacagt cggggccgct ggctggaagg

301 gcgagcttcc taaggcgggg ggaagcccgg cgccggggcc ggagacaccc gccatttcac

361 ccagtaagcg ggcccggcct gcggaggtgg gcggcatgca gctccgcttt gcccggctct

421 ccgagcacgo cacggcccco acccggggct ccgcgcgcgc cgcgggctac gacctgtaca

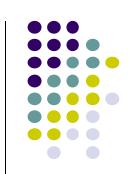


#### Protein Sequence





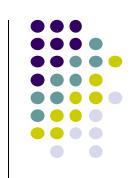
## Not much differencet between: X01714 – U90223



- Human GenBank entry is not more complex than its bacterial homologous – Because U90233 is mRNA sequence, not a genomic one!
- The relationship between a eukaryotic protein and its nucleotide sequences is as collinear as its prokaryotic counterpart.
- Next, we are showing genomic data, which is a bit trickier!



## Eukaryotic Genomic Entry on GenBank



- AH005568, a GenBank entry related to the gene sequence (as it is on the chromosome) is examined.
- This human genomic entry is mRNA-originated by dUTPase (DUT gene).
- This human genomic entry contains some of the specifications only encountered in eukaryotic entries.







GenBank •

#### Homo sapiens dUTPase (DUT) gene, complete cds, alternatively spliced

GenBank: AH005568.2

FASTA Graphics

#### Go to: ₪

LOCUS AH005568 5507 bp PRI 10-JUN-2016 DNA linear DEFINITION Homo sapiens dUTPase (DUT) gene, complete cds, alternatively spliced. AH005568 AF018429 AF018430 AF018431 AF018432 ACCESSION AH005568.2 VERSION KEYWORDS. SOURCE Homo sapiens (human) ORGANISM: Homo sapiens

> Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.

Change region shown

Customize view

Send to: -

Analyze this sequence

Run BLAST

Pick Primers

Highlight Sequence Features

Find in this Sequence

### Articles about the DUT gene

Multisite phosphorylation dictates selectivε [Mol Cell. 202

Discovery of two new isoforms



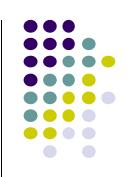
## Reading AH005568



- LOCUS: the locus name is AH005568. The rest of this line says it is 5507 bp, and it is Linear DNA. Its last update was in 2016.
- Note that this is a complete version of previous genes developed since 1997.
- DEFINITION: the gene is DUT.
- ACCESSION line is standard.
- VERSION is 2.
- KEYWORDS lines are standard. No Keywords means one can not retrieve this entry using keyword searches.



## Reading AH005568 Continued ...



- SOURCE: Homo sapiens
  - ORGANISM: It includes varieties of human organisms, such as Mammalia; Eutheria; Primate, Homo.
- REFERENCE:
  - Authors: given
  - Title: given
  - Journal: unpublished
- COMMENT: This sequence version replaced many Genomes listed in 2016.



## **Features Table**

**FEATURES** 

source

gene

CD5



- Features table is what makes an eukaryotic genomic entry different!
- It is much longer than the one for prokaryotic organisms.
- Its GenBank page is shown here and on the next slide.
- It contains many elements described as follows.

```
Location/Oualifiers
1.,5507
/organism="Homo sapiens"
/mol_type="genomic DNA"
/db xref="taxon:9606"
/map="15q15-q21.1"
<1..>5236
/gene="DUT"
join(<282..561,1034..1172,2395..2486,3113..3157,
4447..4521,4673..4743,5180..>5236)
/gene="DUT"
/product="dUTPase"
/note="alternatively spliced; encodes mitochondrial form
of the protein"
join(282..561,1034..1172,2395..2486,3113..3157,4447..4521,
4673..4743,5180..5236)
/gene="DUT"
/note="DUT-M; alternatively spliced; mitochondrial form of
the protein; similar to H. sapiens dUTPase encoded by
GenBank Accession Number U90224"
/codon start=1
/product="dUTPase"
/protein id="AAB71393.1"
/translation="MTPLCPRPALCYHFLTSLLRSAMQNARGTAEGRSRGTLRARPAP
RPPAAQHGIPRPLSSAGRLSQGCRGASTVGAAGWKGELPKAGGSPAPGPETPAISPSK
RARPAEVGGMOLRFARLSEHATAPTRGSARAAGYDLYSAYDYTIPPMEKAVVKTDIOI
ALPSGCYGRVAPRSGLAAKHFIDVGAGVIDEDYRGNVGVVLFNFGKEKFEVKKGDRIA
```

QLICERIFYPEIEEVQALDDTERGSGGFGSTGKN"



## Features Table Continued ...



exon	<282561	exon	<10181172
	/gene="DUT"		/gene="DUT"
	/note="exon used only in the mitochondrial form of the		/note="alternative exon used in nuclear form of the
	protein"		protein"
	/number=1		/number=2
protein bind	898983	exon	10341172
	/gene="DUT"		/gene="DUT"
	/bound_moiety="SP-1"		/note="alternative exon used in mitochondrial form of the
protein_bind	935943		protein"
	/gene="DUT"		/number=2
	/bound_moiety="E2F"	gap	17361835
mRNA	join(<10181172,23952486,31133157,44474521,		/estimated_length=unknown
	46734743,5180>5236)	exon	23952486
	/gene="DUY"		/gene="DUT"
	/product="duTPase"		/number=3
	/note="alternatively spliced; encodes nuclear form of the	gap	30133112
	protein"		/estimated_length=unknown
CDS	join(10181172,23952486,31133157,44474521,	exon	31133157
	46734743,51805236)		/gene="DUT"
	/gene="DUY"		/number=4
	/note="DUT-N; alternatively spliced; nuclear form of the	gap	36903789
	protein; similar to H. sapiens dUTPase encoded by GenBank		/estimated_length=unknown
	Accession Number U90224"	exon	44474521
	/codon_start=1		/gene="DUT"
	/product="dUTPase"		/number=5
	/protein_id="AAB71394.1"	exon	46734743
	/translation="MPCSEETPAISPSKRARPAEVGGMQLRFARLSEHATAPTRGSAR		/gene="DUT"
	AAGYDLYSAYDYTIPPMEKAVVKTDIQIALPSGCYGRVAPRSGLAAKHFIDVGAGVID		/number=6
	EDYRGNVGVVLFNFGKEKFEVKKGDRIAQLICERIFYPEIEEVQALDDTERGSGGFGS	exon	51805236
	TGKN"		/gene="DUT"
			/number=7



## AH005568 Features Table



- Features table element includes source section.
- The source section contains a /map section.
- For this genome, it indicates that the sequence belongs to chromosome 15, and is mapped on the long arm (q) of this chromosome, within the q21.1 cytogenetic band.
- The mRNA: The AH005568 entry has two mRNA fields, which are interesting.
- This is a common property of higher eukaryotic gene expression.

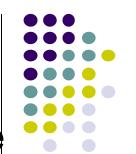




- These two mRNA include type 1 (for mitochondria) and type 2 (for the nucleus).
- The type 1 contains the first exon, but type 2 does not.
- Type 2 uses a part of the second exon in a different reading frame from its type 1 counterpart.
- The two protein sequences become identical on the third exon.
- The exon section indicates the position of the sole exon present in this sequence.
- The page ends with ORIGIN, which is the genomic sequence of the entry.



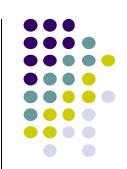
## **Exon in the Feature table**



- The term "exon" holds significant importance in the context of gene structure and function.
- Exons are defined as the segments of a gene that are transcribed into messenger RNA (mRNA) and subsequently translated into proteins.
- In eukaryotic organisms, genes are often composed of both exons and introns.
- The latter are non-coding regions merged out during the post-transcriptional processing of mRNA.
- The presence of exons enables the coding sequences required for protein synthesis, serving as the blueprint for the biological activities essential for life.



## **Working with Related Entries**



- So far, we know the accession number for the entries we wanted to study: X01714, U90223, HA005568.
- Normally, we get these numbers by reading articles mentioning them.
- A good strategy is to start with an accession number of a known genome entry out of these articles, and continue exploring by clicking the links of articles, related information, etc. on the right side of the GenBank page.



### **Retrieving without Accession Number**

- Searching GenBank by using gene or protein keywords rather than accession numbers is possible.
- Suppose you want to find the nucleotide sequence encoding the human dUTPase, without accession number.
- Type human [organism] and dUTPase (protein name) in the search window.
- The next slide shows the search results. It gives 6752 outputs, the first three are shown.
- You may see the accession number HA005568.2 as the second result.



Release date Custom range...

Revision date Custom range...

Clear all

Show additional filters

#### Items: 1 to 20 of 6752

<< First < Prev Page 1 of 338 Next> Last>>

Human betaherpesvirus 6A tp/cap, mdbp, U42 orf, U43 orf, U44

orf, and dUTPase genes

10,601 bp linear DNA

Accession: X92436.1 GI: 1044869

Protein Taxonomy

GenBank FASTA Graphics

Homo sapiens dUTPase (DUT) gene, complete cds,

alternatively spliced

5,507 bp linear DNA

Accession: AH005568.2 GI: 1036029938

Protein Taxonomy

GenBank FASTA Graphics

Mus musculus endogenous retroviral sequence MuERV-L gag,

5. pol and dUTPase genes

6,471 bp linear DNA

Accession: Y12713.1 GI: 2065208

Protein PubMed Taxonomy

GenBank FASTA Graphics

#### Search details

("Homo sapiens" [Organism] OR human[All Fields]) AND dUTPase[All Fields]

Search

See more...

#### Recent activity

Turn Off Clear

human dUTPase (6752)

Nucleotide

RefSeq RNA Links for Gene (Select 34529) (4) Nucleotide

A human UTPase (4)

Nucleotide

human duppies accession (513353) Nucleotide

human dutpase (6752)

Nucleotide

See more...



## **Using a Gene-Centric Database**

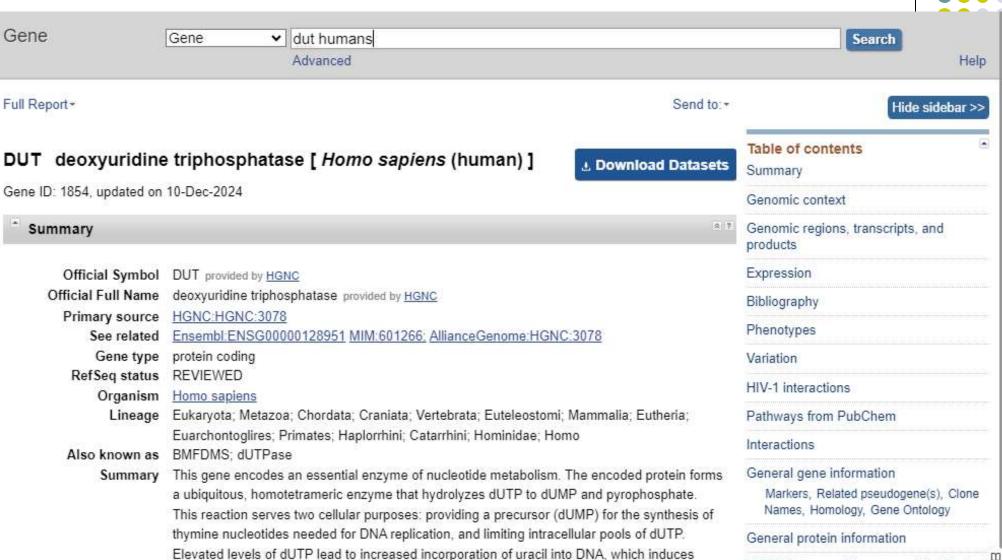
- Besides GenBank, NCBI has developed other databases more adapted to gene-centric searches.
- Making a gene-centered query involves asking a question that relates directly to a specific gene, rather than going through all known pieces of sequences related to that gene.
- Main advantage: it returns results that are more synthetic than a long list of GenBank entries.
- For that search NCBI "Gene database" rather than GenBank.





NCBI Reference Sequences (RefSeq)

Related sequences



extensive excision repair mediated by uracil glycosylase. This repair process, resulting in the removal and reincorporation of dUTP is self-defeating and leads to DNA fragmentation and





01 000 00

mitochondrion or nucleus. A related pseudogene is located on chromosome 19. [provided by

RefSeq, Jul 2008]

Expression Ubiquitous expression in bone marrow (RPKM 16.5), lymph node (RPKM 14.4) and 25 other

tissues See more

Orthologs mouse all

NEW Try the new Gene table

Try the new Transcript table

#### Genomic context

Location: 15q21.1

Exon count: 8

See DUT in Genome Data Viewer

Annotation release	Status	Assembly	Chr	Location	
RS_2024_08	current	GRCh38.p14 ( <u>GCF_000001405.40</u> )	15	NC_000015.10 (4833109548343373)	
RS_2024_08	current	T2T-CHM13v2.0 (GCF_009914755.1)	15	NC_060939.1 (4613935646151634)	
RS_2024_09	previous assembly	GRCh37.p13 (GCF_000001405.25)	15	NC_000015.9 (4862329248635570)	

#### Chromosome 15 - NC\_000015.10

[48206802] [48652260 | L0012898852# +L00124903488 + L00127829489 + L00125478478 + L00139457418 + Stictions -**→** DUT → FONI . LOC128862123 DUT-ASI L00126582124 100130957919 100122399898 LOCIL0239244 100130957920 100122861577 100124943486 100150957921 L00127829488 100150957922-100128892125 L00121539500 -100127829490 100150957917 FERG-DT

#### Additional links







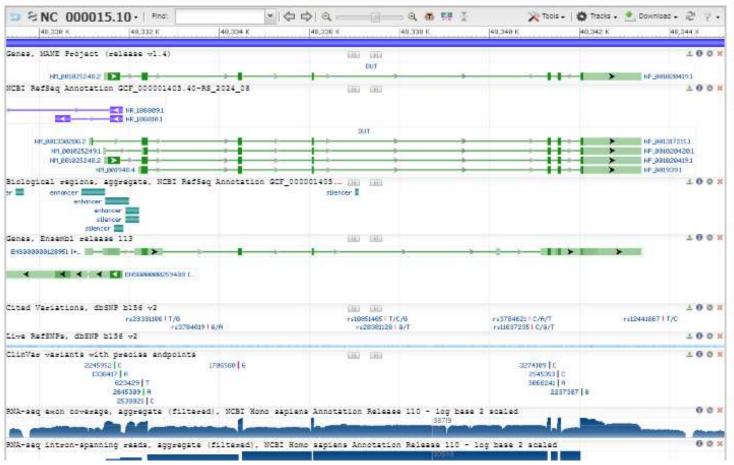


#### Genomic regions, transcripts, and products

Go to reference sequence details

Genomic Sequence: NC\_000015.10 Chromosome 15 Reference GRCh38.p14 Primary Assembly ▼

Go to nucleotide: Graphics FASTA GenBank



Full text in PMC

Full text in PMC\_nucleotide

Functional Class

Gene neighbors

Genes with a similar H3K4me3 profile

Genome

**GEO Profiles** 

GTR

MedGen

Nucleotide

OMIM

Probe

Protein

PubChem Compound

PubChem Substance

PubMed

PubMed (GeneRIF)

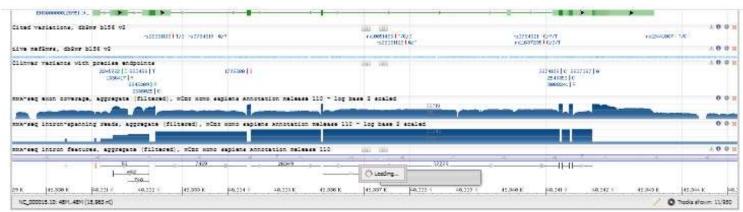
PubMed (OMIM)

PubMed(nucleotide/PMC)

RefSea Proteins







Expression

HPA RNA-seq normal tissues

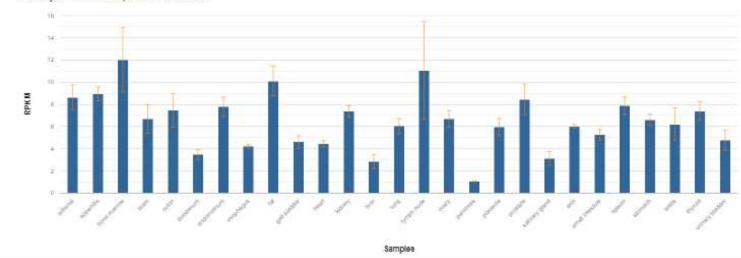
Project title: HPA RNA-seq normal tissues

Description: RNA-seq was performed of tissue samples from 95 human individuals representing 27 different tissues in order to determine tissue-specificity of all protein-coding genes

BioProject PRJEB4337

Publication: PMID 24309898

Analysis date: Wed Apr 4 07:08:55 2018



MedGen Nucleotide. OMIM Probe Protein PubChem Compound PubChem Substance PubMed PubMed (GeneRIF) PubMed (OMIM) PubMed(nucleotide/PMC) See details RefSeq Proteins RefSeq RNAs RefSeaGene Related gene-specific medical variations

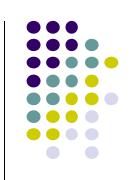
SNP

Taxonomy
Variation Viewer

Links to other resources
HGNC
Ensembl
AllianceGenome
AceView
PharmGKB
MGC
HuGE Navigator
KEGG



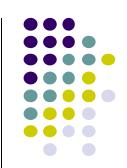
## Guanine (G) and Cytosine (C)



- "GC" typically refers to the GC content of a DNA sequence, which is the proportion of guanine (G) and cytosine (C) bases in the DNA.
- High GC content can influence the stability and structure of DNA, as well as affect gene expression

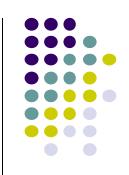






- یک ارگانیسم پروکاریوتی و یک ارگانیسم یوکاریوتی را انتخاب کنید
   بطوریکه هر دو متعلق به یک منشاء باشند. با استفاده از GenBank ،
   دنباله نوکلئوتیدی یک ژن خاص از هر موجود زنده را پیدا و تجزیه و
   تحلیل کنید. برای موجودات انتخابی خود، موارد زیر را انجام دهید:
  - نام علمی و سلسله مراتب طبقه بندی هر دو موجود زنده را مشخص کنید.
    - توالی نوکلئوتیدی ژن انتخاب شده را از GenBank بازیابی کنید و Accession number ها را برای مرجع ارائه دهید.
- طول و ویژگی های قابل توجه (مانند اینترون/اگزون در ژن یوکاریوتی) توالی
   های به دست آمده را مقایسه کنید.
- در مورد اهمیت بیولوژیکی ژن ها در رابطه با ارگانیسم های مربوطه بحث کنید.





# Thank you

for your attention