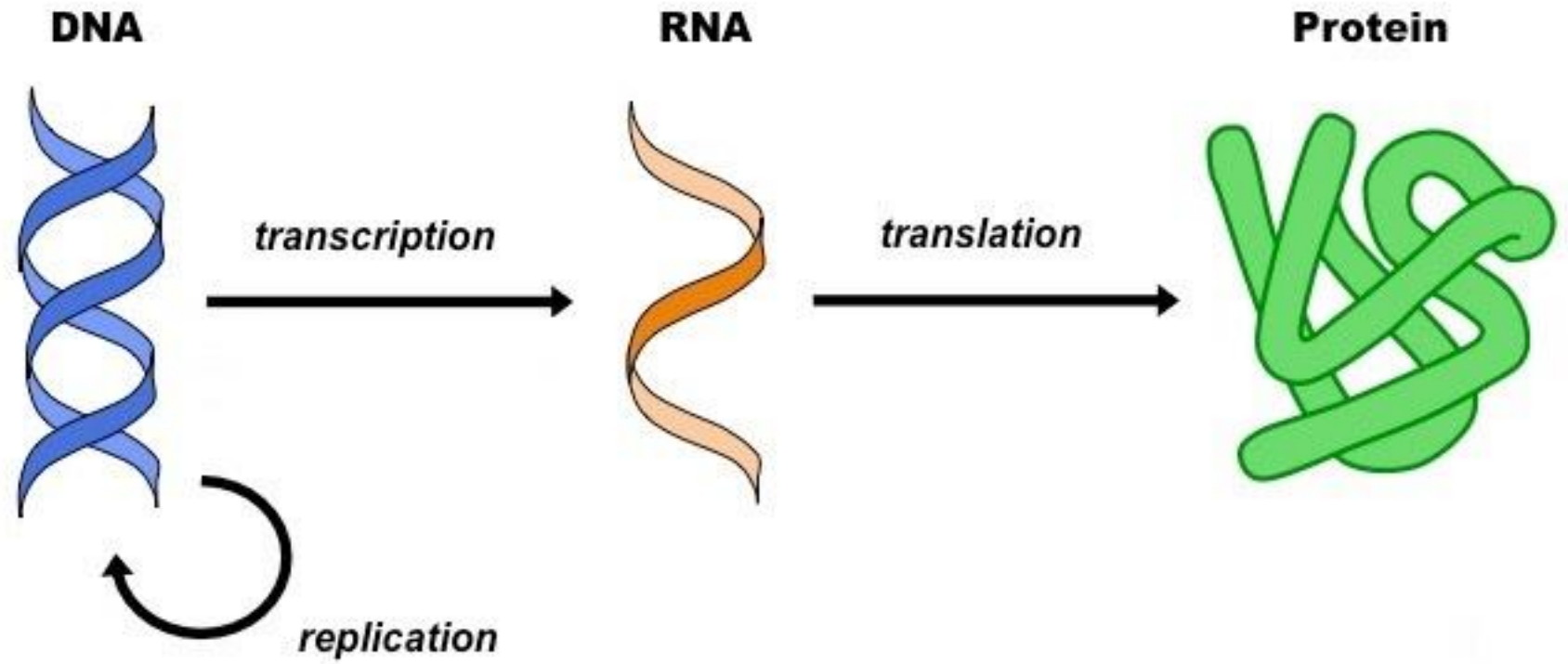
Slides for October 31 through November 3, 2017

Cell Biology – where are we?

- Cell parts
- Crossing Cell Membranes (Diffusion)
- Photosynthesis & Respiration
- Cell Division (Mitosis)
- Heredity (Mendel)
- Meiosis
- Genes to Proteins (Central Dogma)
- Separating DNA by Gel Electrophoresis

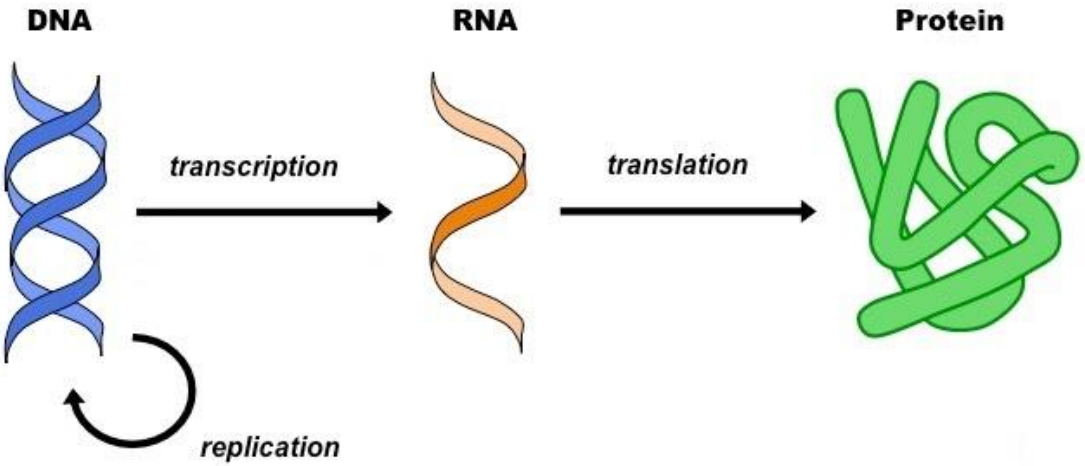
Genes to Proteins:
The "Central Dogma of Molecular Biology"



Today's LO: Explain how the information in DNA is copied into a "messenger" form (RNA).

SLE: Meet NGSS.

Image: http://ib.bioninja.com.au/standard-level/topic-2-molecular-biology/27-dna-replication-transcri/central-dogma.html

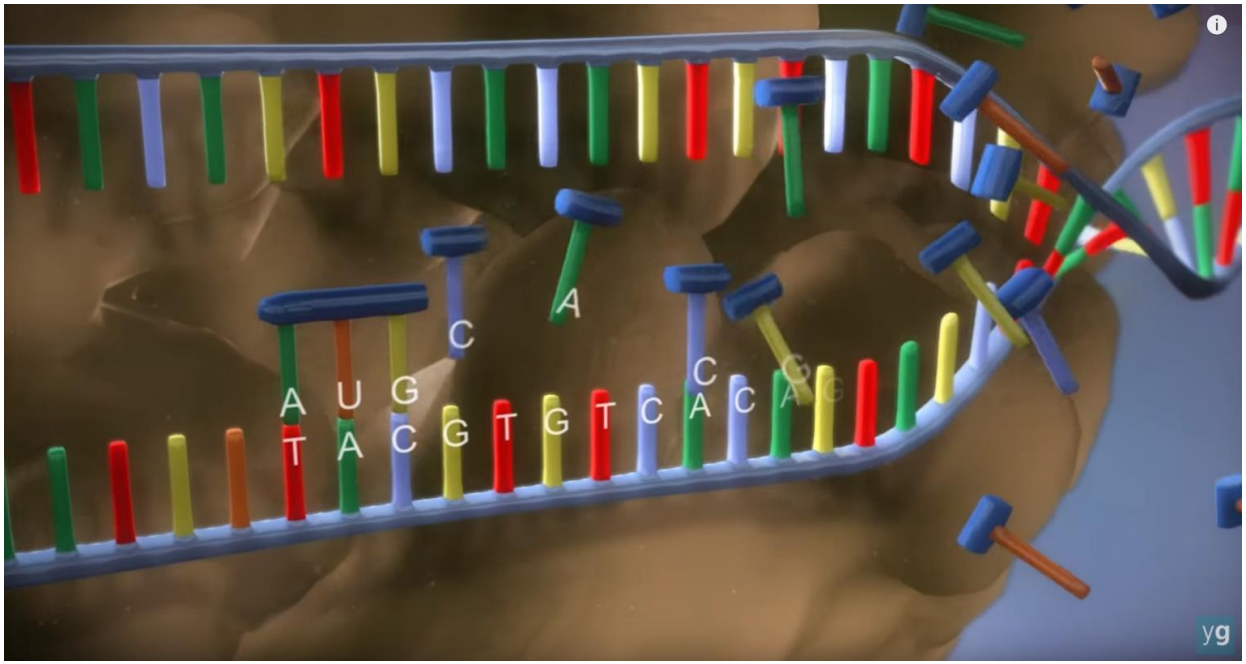


What you already know

What you need to know

Image: http://ib.bioninja.com.au/standard-level/topic-2-molecular-biology/27-dna-replication-transcri/central-dogma.html

Video: DNA to RNA to protein

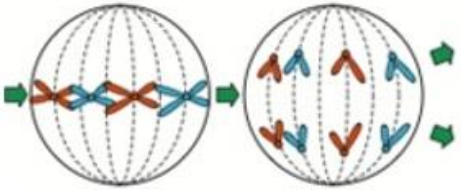


How is RNA made (during transcription)?

How is protein made (during translation)?

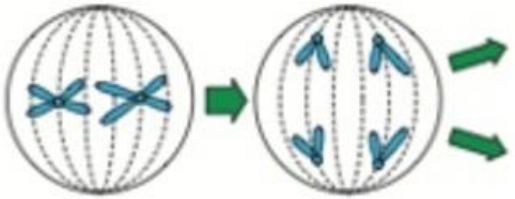
https://www.youtube.com/watch?v=gG7uCskUOrA

Imagine an organism whose cells (aside from egg and sperm) normally have **4 chromosomes**, i.e., **2 pairs of 2 chromosomes**. Look at each of the images shown below (taken from https://sites.google.com/a/mgsd.k12.nc.us/smith-s-super-science-spot/daily-news/mitosismeiosis; original source unknown). For each one, say (a) what phases of mitosis and/or meiosis they could be and (b) why you think that.



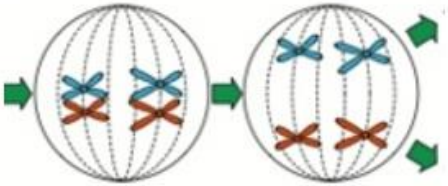
(1a)

(1b)



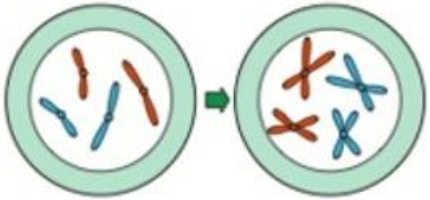
(2a)

(2b)



(3a)

(3b)



(3a)

(3b)

(5a) Do 2 sister chromatids normally contain the same alleles?

(5b) Do 2 homologous chromosomes normally contain the same alleles?

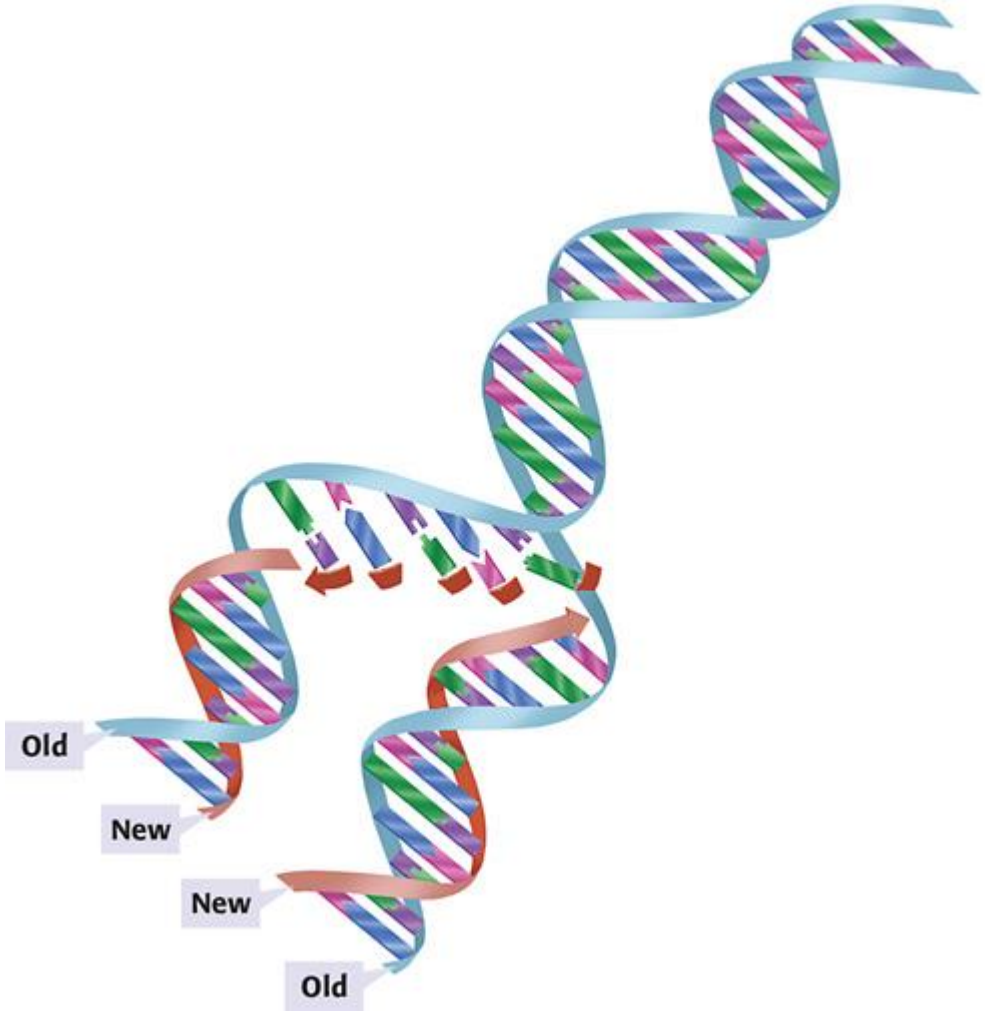
Key vocabulary

- “Central Dogma”
- RNA
- Transcription
- Translation

The structure of DNA

Figure from page 88 of your textbook

DNA replication … and transcription



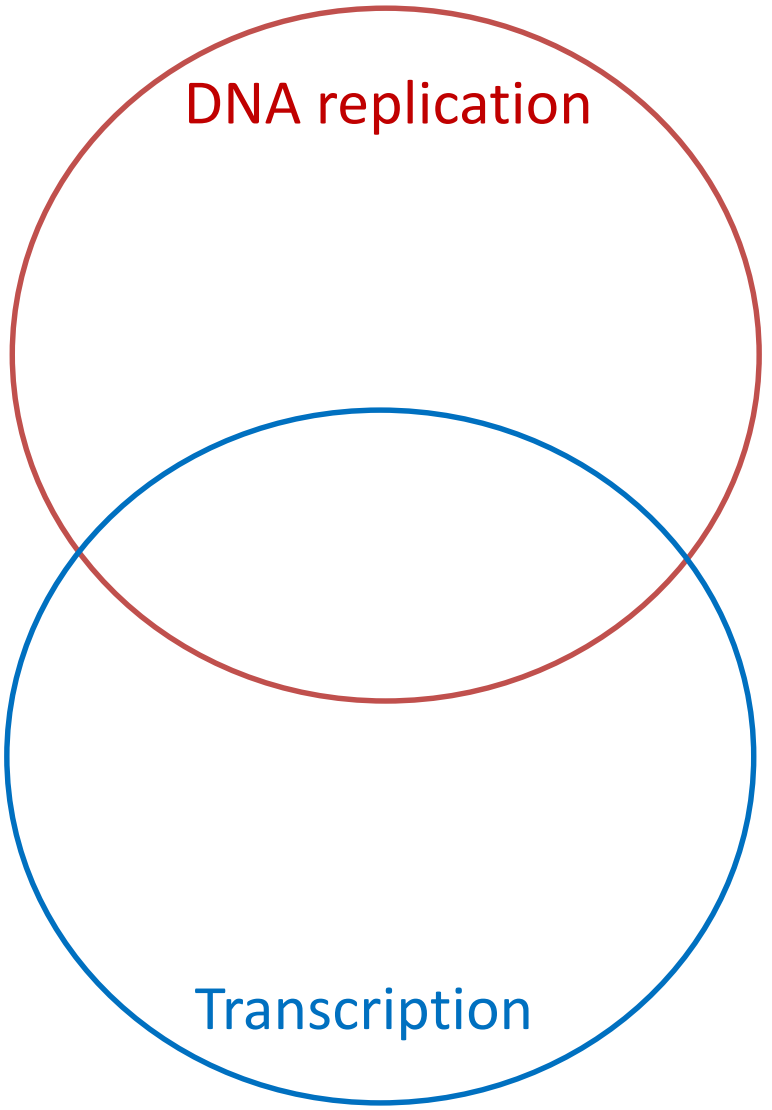


Figure from page 88 of your textbook

REMINDERS about TOMORROW

- Science Inquiry Project proposals are due
  - One paragraph (3 to 5 sentences) on what you want to do and why.
- Quiz on Central Dogma stuff
  - through yesterday's material

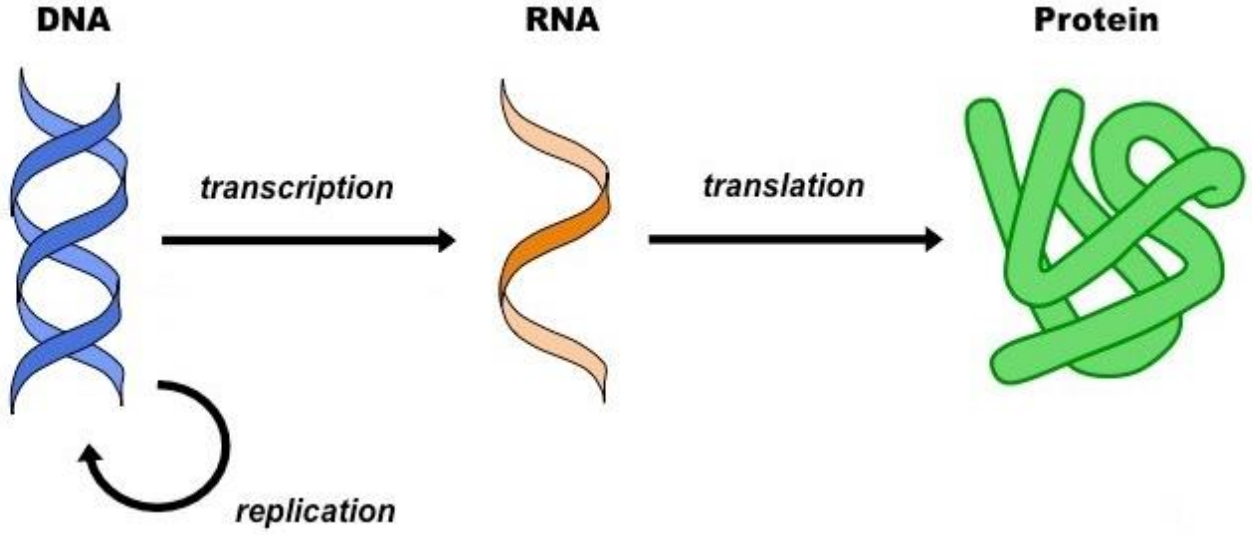


Image: http://ib.bioninja.com.au/standard-level/topic-2-molecular-biology/27-dna-replication-transcri/central-dogma.html

5. Now show the sequence of the transcribed RNA:

(Template) DNA:	A	A	G	C	T	T	A	T	C	C	G	A	A	A	A	G	G	C	G	A	T
RNA:																					

6. What will happen to this strand of RNA once it is made?

7. Describe one aspect of today's material that is currently confusing to you.

OPTIONAL. Do you think that all of the cells in your body contain the same RNA? Explain.

Translation: RNA to protein

- The sequence of bases in an RNA specifies the sequence of amino acids in the protein … according to the **genetic code**.

LO: Crack the genetic code! SLE: Meet NGSS.

› Science

Common cold cure a step closer after scientists 'crack' genetic code

share

7

The common cold has multiple strains CREDIT: NICK GREGORY

HOME » NEWS » SCIENCE » SCIENCE NEWS

Scientists crack the genetic code for rice

By Roger Highfield

12:00AM GMT 01 Feb 2001

Misuses of the term “genetic code” taken from telegraph.co.uk

As you know, RNA consists of a sequence of 4 bases:

1-letter abbreviation:	A	C	G	U
Full name:	Adenine	Cytosine	Guanine	Uracil

You are also learning that proteins are made up of amino acids, of which there are 20 (they have both 1-letter and 3-letter abbreviations):

1-letter:	A	C	D	E	F	G	H	I	K	L
3-letter:	Ala	Cys	Asp	Glu	Phe	Gly	His	Ile	Lys	Leu
Full:	Alanine	Cysteine	Aspartate	Glutamate	Phenyl-alanine	Glycine	Histidine	Isoleucine	Lysine	Leucine

1-letter:	M	N	P	Q	R	S	T	V	W	Y
3-letter:	Met	Asn	Pro	Gln	Arg	Ser	Thr	Val	Trp	Tyr
Full:	Methionine	Asparagine	Proline	Glutamine	Arginine	Serine	Threonine	Valine	Tryptophan	Tyrosine

As of about 1960, the big question was, how does the genetic code works?

(1) In your own words, please elaborate on this question. What does the phrase "genetic code" really mean?

The REAL code-breaker: Marshall Nirenberg

https://www.youtube.com/watch?v=fODwXbtysqQ&t=400s

The Nirenberg Concerto

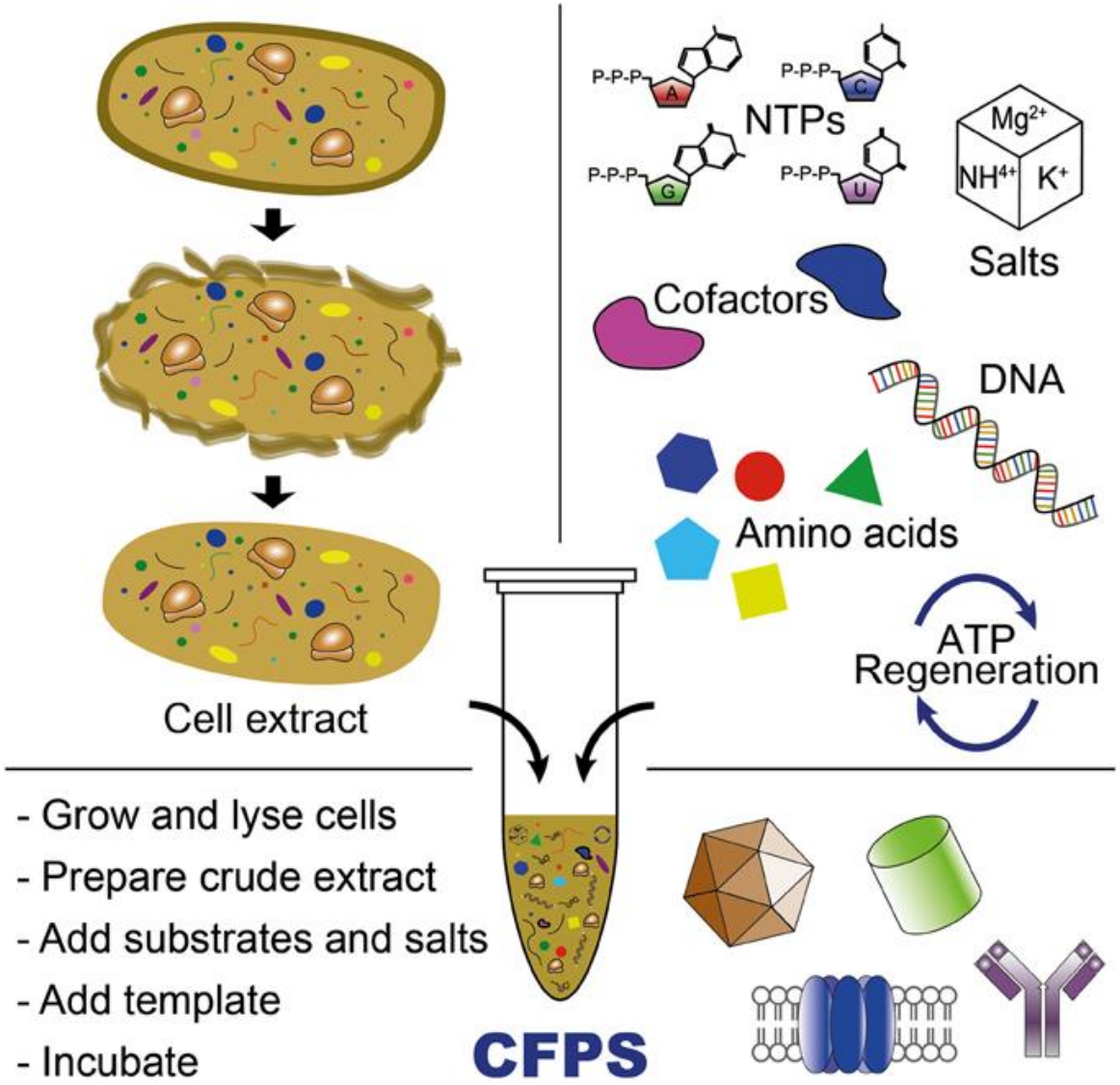
Nirenberg. (Can you crack…)
Marshall Warren Nirenberg! (Can you crack the code?)
Nirenberg. (Can you crack…)
Marshall Warren Nirenberg! (Can you crack the code?)

From bases . . . to amino acids.
From UUU . . . to phenylalanine.
From bases . . . to amino acids.
From mRNA . . . to a new protein!

Nirenberg. (Can you crack…)
Marshall Warren Nirenberg! (Can you crack the code?)
Nirenberg. (Can you crack…)
Marshall Warren Nirenberg! (Can you crack the code?)
Nirenberg!

http://faculty.washington.edu/crowther/Misc/Songs/nirenberg.shtml

Nirenberg's experiments: cell-free protein synthesis!

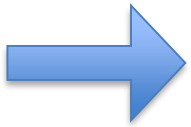


https://www.frontiersin.org/articles/10.3389/fchem.2014.00034/full

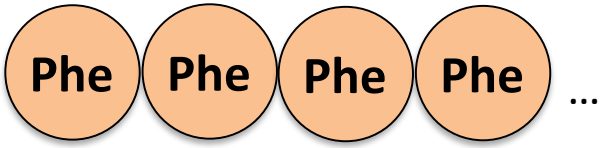
Nirenberg's breakthrough

RNA input

U-U-U-U-U-U-U-U-U-U-U-U-U-U…



Protein output



Simulated experiment: take the next step!

- Design another RNA molecule to be translated into protein, in order to continue deciphering the genetic code.

Results of simulated experiments

- Your worksheets will be returned with the results of translating your RNA sequence(s).

- What can you conclude from these results?

Quiz on the Central Dog…

Class results: cracking the genetic code

Group	RNA submitted	Resulting protein	Interpretation
Marshall	U-U-U-U-U-U-U-U…	Phe-Phe-Phe…	U, UU, UUU, or UUUU codes for Phe
Chloe, Grace L., Hannah K.	A-A-A-A-A-A-A-A-A…		
Cullen, Ella, Garett, Grace W.	C-C-C-C-C-C-C-C-C…		
Cullen, Ella, Garett, Grace W.	G-G-G-G-G-G-G-G…		

Class results: cracking the genetic code

- How many bases code for each amino acid? (1? 2? 3? 4?)

Group	RNA submitted	Resulting protein	Interpretation
Abigail, Charlie, Owen, Sofia	A-C-A-C-A-C-A-C…		
Claire, Nick, Mac, Portia	U-C-A-U-C-A-U-C-A…		
Allie, Eric, Katey, Sam	A-C-G-A-C-G-A-C-G…		

Class results: cracking the genetic code

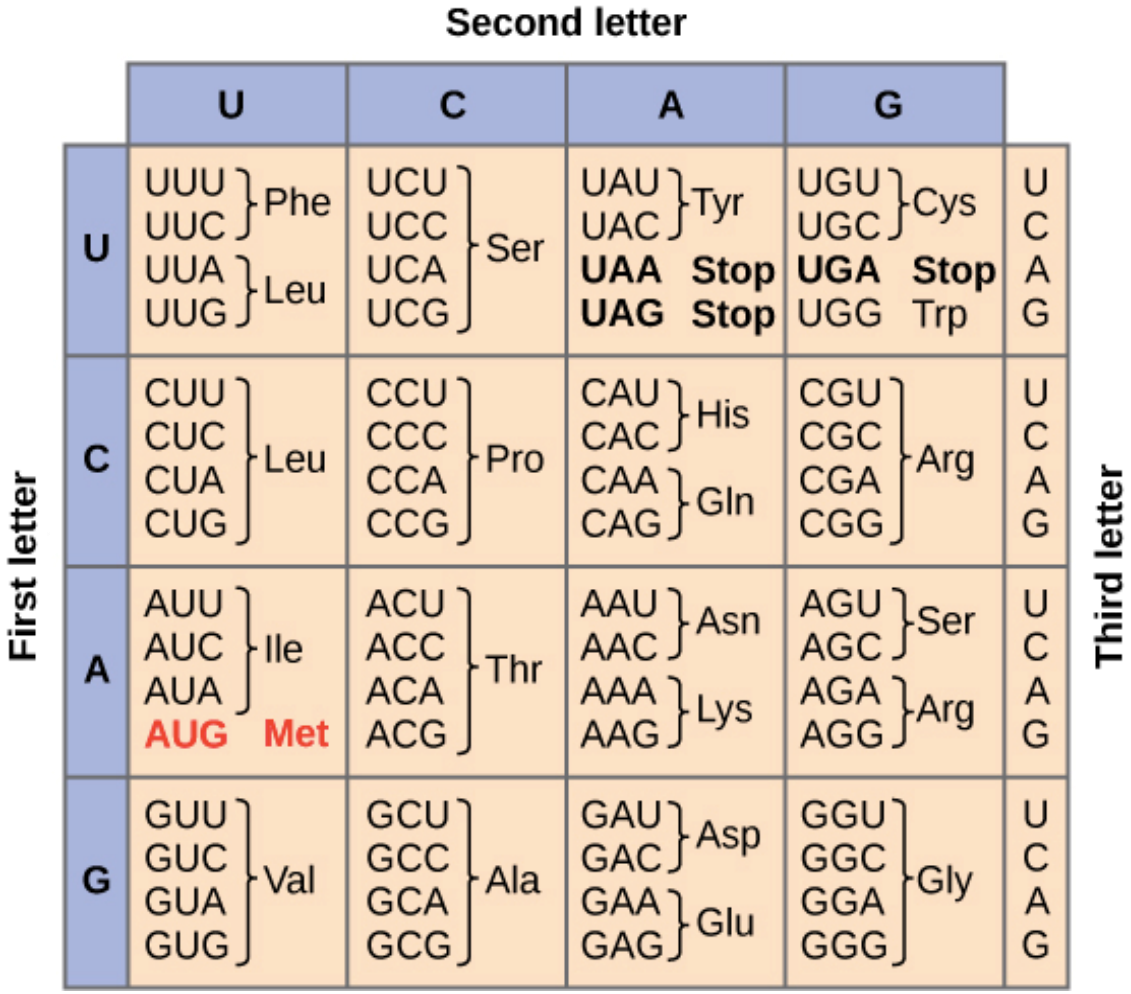
Group	RNA submitted	Resulting protein	Interpretation
Marshall	U-U-U-U-U-U…	Phe-Phe-Phe…	U, UU, UUU, or UUUU codes for Phe
Eliyah, Keawa, Malia, Mick	A-A-A-A-A-A-A…		
Casey, Kade, Olivia, Valerie	A-A-A-A-A-A-A…		
Emmett, John, Jourdan	G-G-G-G-G-G-G…		
Adam, Frankie, Rachel	C-C-C-C-C-C-C-C…		

Class results: cracking the genetic code

- How many bases code for each amino acid? (1? 2? 3? 4?)

Group	RNA submitted	Resulting protein	Interpretation
Benj, Elise, Natalie, Zac	G-U-A-G-U-A-G-U-A…		
Henry, Jane, Mimi	U-U-G-U-U-G-U-U-G…		

The complete genetic code



Key vocabulary:

- **Codon**
- **Stop Codon**
- **Redundancy**

Table: https://openstax.org/details/biology

1. Where in the cell does transcription occur?

2. Where in the cell does translation occur?

3. Starting with the piece of DNA below, write the RNA sequence and the amino acid sequence that result from this DNA sequence.

DNA sequence: T A C C G G C C C G G G A G G G A G...

RNA sequence:

Amino acid sequence:

4. If this gene contains additional codons beyond those shown here, can you tell what the very last amino acid in the protein will be?

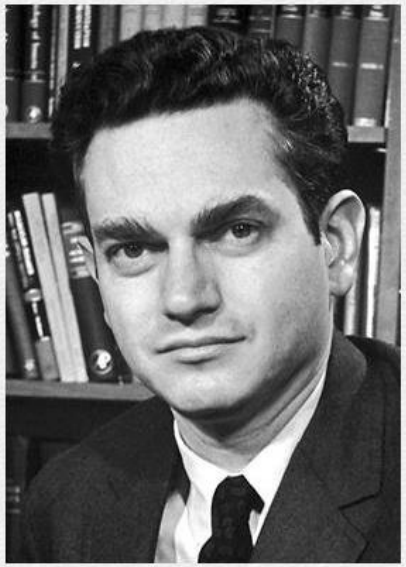
5. If a typical protein contains about 500 amino acids, how many bases long would you expect the corresponding gene to be?

Cracking the code: a “Nobel” pursuit

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE 1968

Robert W. Holley
(1922-1993)
Prize share: 1/3

H. Gobind Khorana
(1922-2011)
Prize share: 1/3



Marshall W. Nirenberg
(1927-2010)
Prize share: 1/3

"for their interpretation of the genetic code and its function in protein synthesis".

Nobelprize.org
The Official Web Site of the Nobel Prize

How translation actually happens

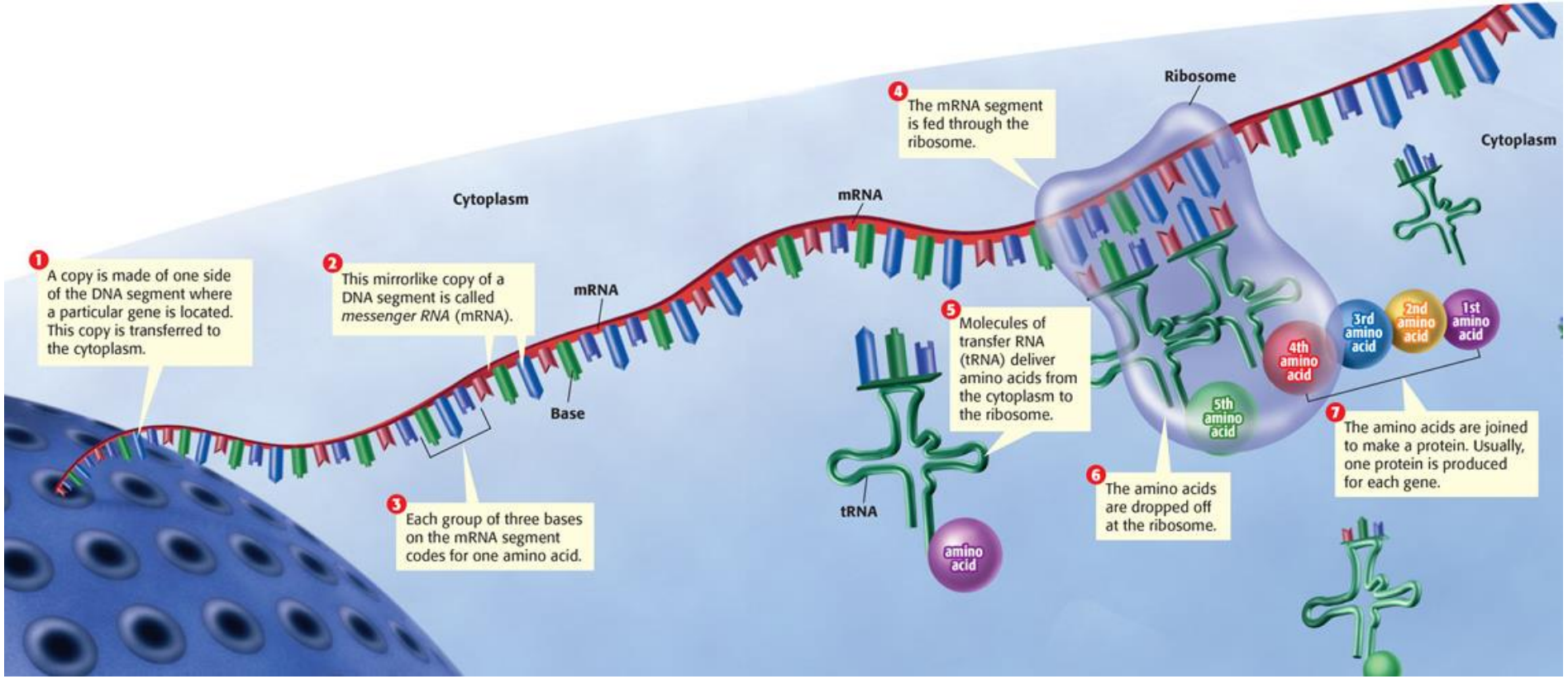


Figure from pages 92-93 of your textbook

Genetic Mutations!

LO: Predict whether a mutant protein will still work! SLE: Work collaboratively.

- Definition of a genetic mutation?

- From Amoeba Sisters video:
  - Causes of mutations?
  - Types of mutations?

Amoeba Sisters video: https://www.youtube.com/watch?v=GieZ3pk9YVo

Name that mutation

original sequence → new sequence

(a) …ACGTACGTACGT… → …ACGTAGTACGT…

(b) …ACGTACGTACGT… → …ACGTAGGTACGT…

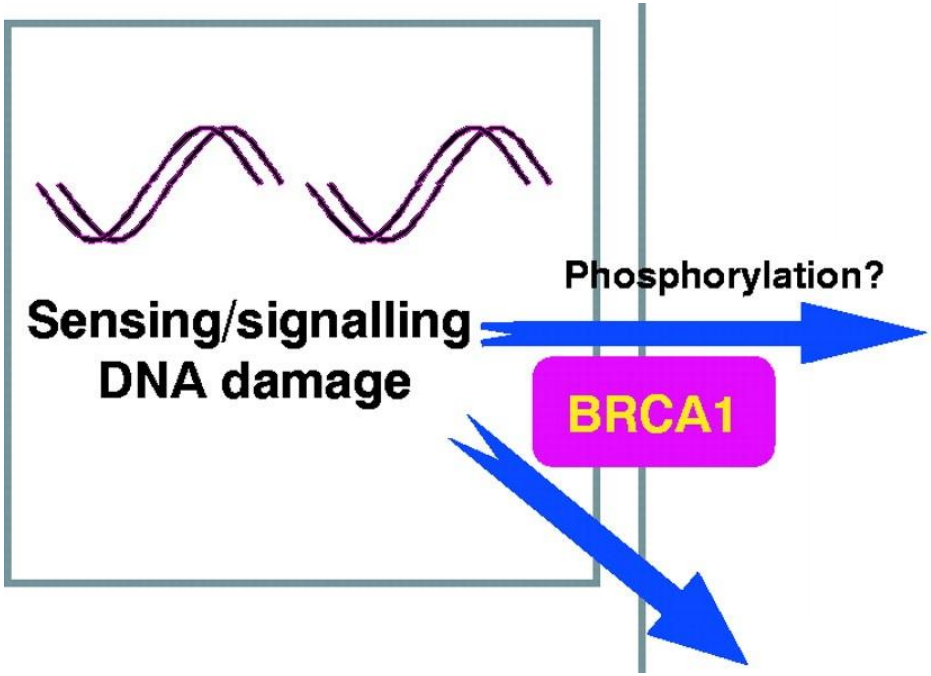
(c) …ACGTACGTACGT… → …ACGTTACGTACGT…

Which is/are most likely to disrupt the function of the protein?

Mutations in the real world: BRCA1

- BRCA1 gene codes for a tumor suppressor protein, which repairs damaged DNA
- If BRCA1 gene is mutated, chance of getting breast cancer may increase greatly

Dr. Mary-Claire King discovered BRCA1

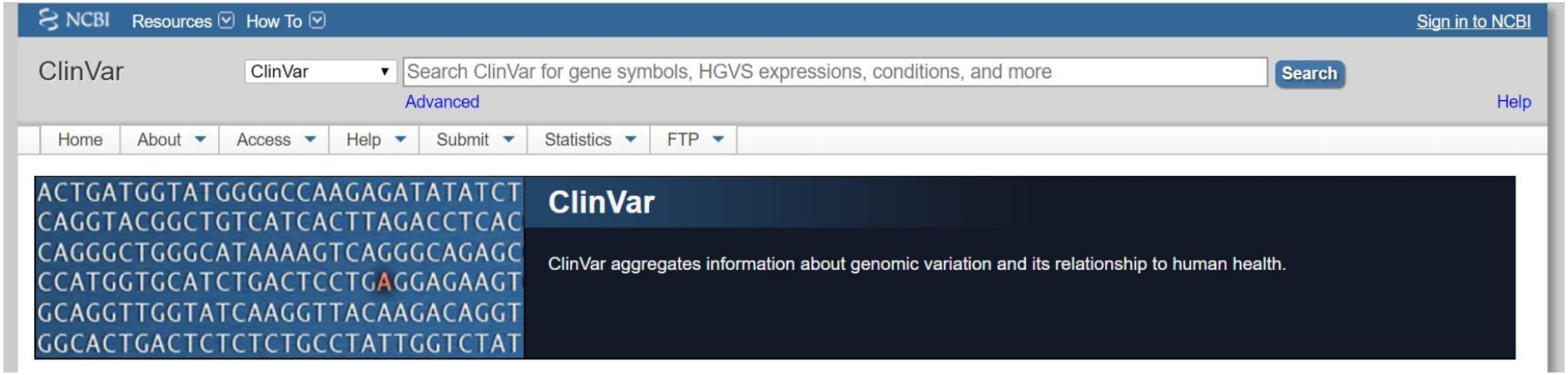


https://www.youtube.com/watch?v=tOP5pUIYhv4

Figure: http://jcs.biologists.org/content/114/20/3591

Your challenge

- Find your group's BRCA1 mutation on the next worksheet.
- Classify your BRCA1 mutation as an insertion, deletion, or substitution (missense).
  - Predict whether your mutation is likely to disrupt the protein's function, and thus likely to be pathogenic (cause disease).
- Check your prediction at the ClinVar (Clinical Variant) database: https://www.ncbi.nlm.nih.gov/clinvar/



Group assignments

- Halley homeroom
  - 1: Clouse & Moriarty
  - 2: Douglas & Ellis
  - 3: Embry & Fairchild
  - 4: Gilbert & Gilbrough
  - 5: Henricksen & Johnson
  - 6: Kahn & Kineman
  - 7: Krawchik & Linke
  - 8: Lipscomb & Martinez
  - 9: Melder & Miller
  - 10: Muenzberg & DeLong
  - 11: Schuler & Smith
  - 12: Sorrick & Stewart
  - 13: Tiritilli & Wiseman
- Thomas homeroom
  - Arruela: choose a group below
  - 1: Bergman & Branley
  - 2: Brecht & Brouns-Prince
  - 3: Brumback & Clouse
  - 4: De Ryan & Deines
  - 5: Deubler & Drechsler
  - 6: Fay & Finnan
  - 7: Givens & Helser
  - 8: Kineman & Lamb
  - 9: McCallum & Nenninger
  - 10: Pelfrey & Petre
  - 11: Randall & Sabiers
  - 12: Schumer & Spear
  - 13: Tramountanas & Wiseman

Class results: BRCA1

Group	Mutation type	Pathogenic?

Group	Mutation type	Pathogenic?

BRCA mutation analysis

- Which type(s) of mutation was/were most likely to be pathogenic (cause disease)?
  - Is this consistent with what you know about the genetic code?

- Homework: use ClinVar database to quickly analyze lots of BRCA1 and BRCA2 mutations!
  - https://www.ncbi.nlm.nih.gov/clinvar/