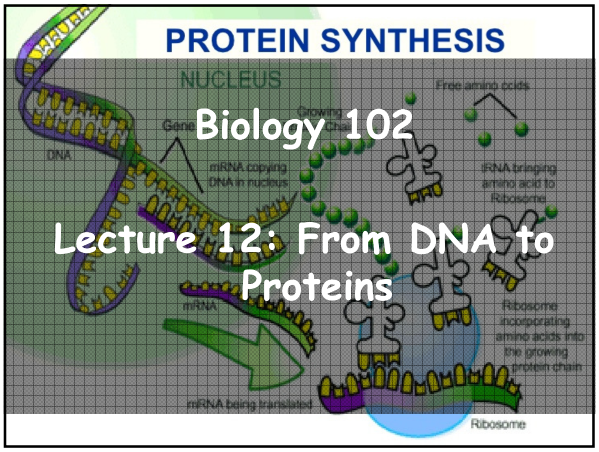
Biology 102

Lecture 12: From DNA to Proteins



Genes

- Sequence of nucleotide bases in DNA is a code for making proteins
- To uniquely code for each of the 20 amino acids, how many bases must code for a single amino acid?

	Total number of unique codes
1 base forms code pattern	4 unique codes - A, T, C, G (4^1)
2 bases form code pattern	4^2 = 16 unique codes (too few)
3 bases form code pattern	4^3 = 64 unique codes (just right)
4 bases form code pattern	4^4 = 256 unique codes (too many)

Genes

- A group of 3 DNA bases is called a *triplet*
- Each triplet codes for one amino acid in a protein's primary structure (more on this later)

second base in codon

first base in codon	T	C	A	G	third base in codon
T	TTT Phe	TCT Ser	TAT Tyr	TGT Cys	T
	TTC Phe	TCC Ser	TAC Tyr	TGC Cys	C
	TTA Leu	TCA Ser	TAA stop	TGA stop	A
	TTG Leu	TCG Ser	TAG stop	TGG Trp	G
C	CTT Leu	CCT Pro	CAT His	CGT Arg	T
	CTC Leu	CCC Pro	CAC His	CGC Arg	C
	CTA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CTG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	ATT Ile	ACT Thr	AAT Asn	AGT Ser	T
	ATC Ile	ACC Thr	AAC Asn	AGC Ser	C
	ATA Ile	ACA Thr	AAA Lys	AGA Arg	A
	ATG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GTT Val	GCT Ala	GAT Asp	GGT Gly	T
	GTC Val	GCC Ala	GAC Asp	GGC Gly	C
	GTA Val	GCA Ala	GAA Glu	GGA Gly	A
	GTG Val	GCG Ala	GAG Glu	GGG Gly	G

Transcription

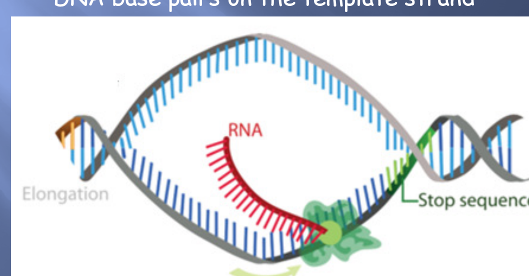
- DNA is too large, too valuable to leave the nucleus
- Can't get to the ribosomes to give instructions for making proteins
- Sends a temporary copy made of RNA
- Process of making this copy is called *transcription*
- Specific type of RNA produced in transcription is messenger RNA (mRNA)

Steps in Transcription

1. *Initiation*
   - Chromatin unwinds to expose DNA
   - DNA "unzips"
   - Enzymes bind to gene of interest

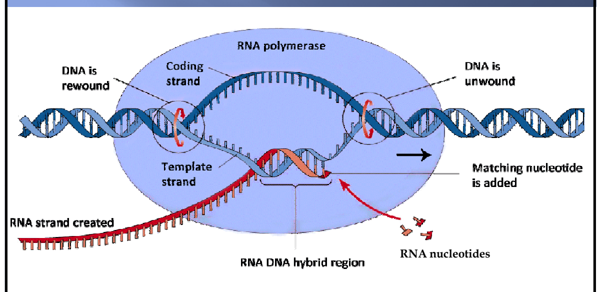
Steps in Transcription

2. *Elongation*
   - RNA nucleotides are added to compliment the DNA base pairs on the template strand



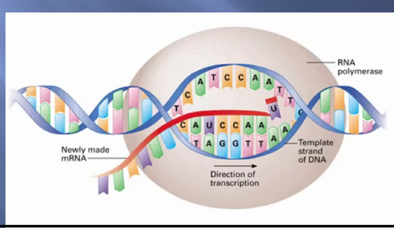
Steps in Transcription

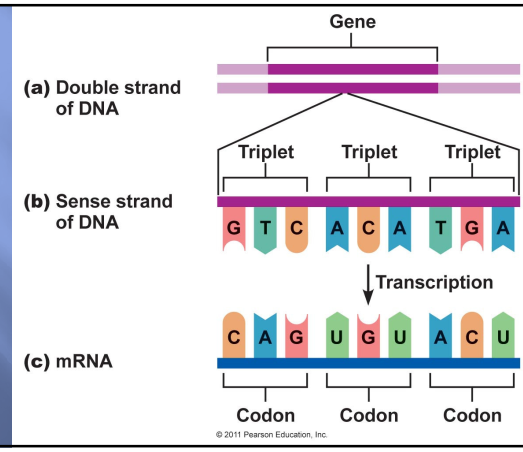
3. *Termination*
   - Enzymes and mRNA strand released



Transcription

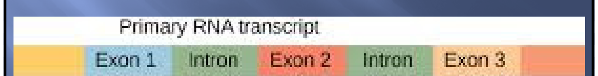
- DNA triplets have been re-coded as mRNA *codons*
  - But in mRNA, T is replaced with U





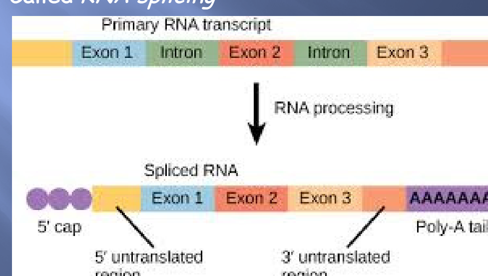
mRNA Processing

- mRNA is not yet ready to direct protein synthesis
- Protein-coding DNA sections of genes are called *exons*
- Genes are further protected with interspersed non-coding regions called *introns*



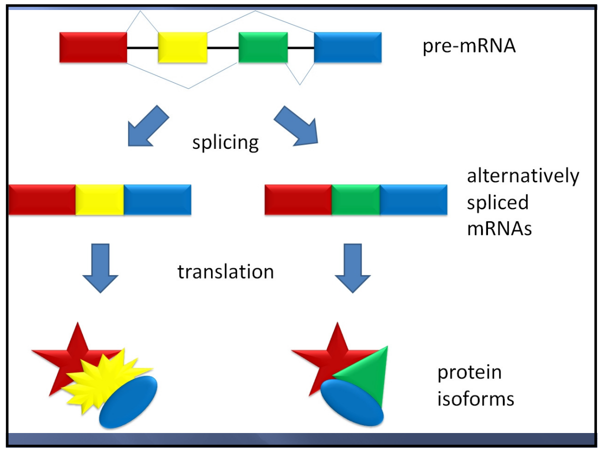
mRNA Processing

- Introns must be removed and exons joined together
- Called *RNA splicing*



mRNA Processing

- Some genes can be spliced together in multiple ways
  - Called *alternative splice products* or *splice isoforms*
- One gene can code for more than one protein
- One protein may have multiple forms



Protein Synthesis

- Once a strand of mRNA has been spliced, it is ready to be decoded to build a protein
- This process is called *translation*
- The genetic code is translated from the language of nucleic acids to the language of proteins

Genetic Linguistics

- Think about different written languages
- Do the same letter combinations mean the same thing in all languages?

<u>Examples</u>	<u>French</u>
Ours	
Pain	
Pet	

Genetic Linguistics

- What about the language of DNA and proteins?
- Will every species read DNA the same way?
- If we put the gene for a human protein into another species, will it make the same protein?

Experiment

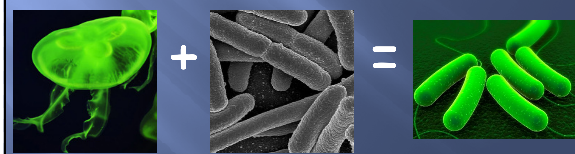
- Jellyfish are cool
- Some of them make a protein known as GFP that glows green when exposed to UV light

Experiment

- What if we take the gene for this protein and put it into bacteria?
- Will the bacteria make GFP? Or will they translate the genetic code differently?

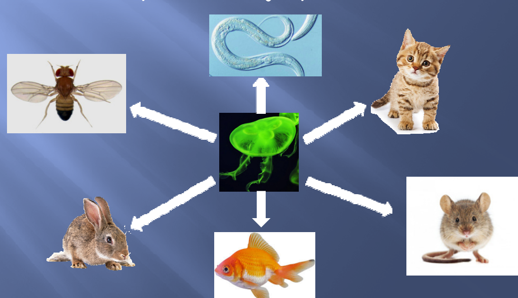
Experiment

- They make GFP!



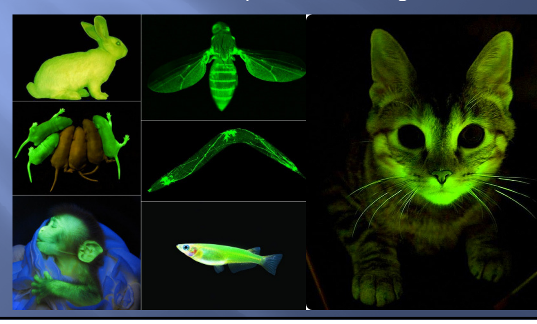
Experiment

- What about other species?
- How will they translate jellyfish DNA?



Experiment

- They make the same protein!
- What does this tell you about the genetic code?

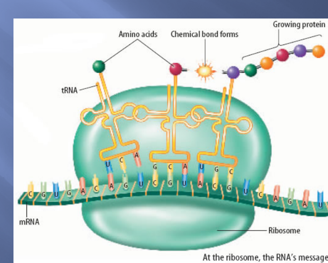


Experiment

- They make the same protein!
- What does this tell you about the genetic code?
- It's universal! An mRNA codon will be translated into the same protein, no matter the species
- We exploit this is so many, very cool ways
  - Recombinant DNA technology

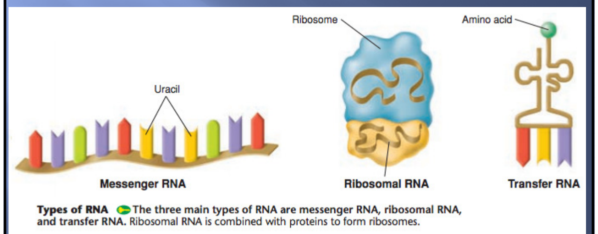
Translation

- How do we get from DNA to protein?
- The process is pretty complicated, but let's take a look…



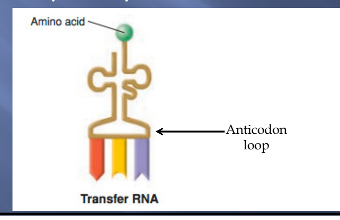
Protein Synthesis

- All 3 types of RNA are involved in this process



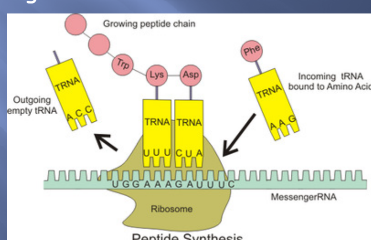
Protein Synthesis

- Let's take a closer look at tRNA
- Note the anticodon loop at the bottom
- Note the amino acid attached to the other end
- Each tRNA will carry a specific amino acid determined by the specifc anticodon



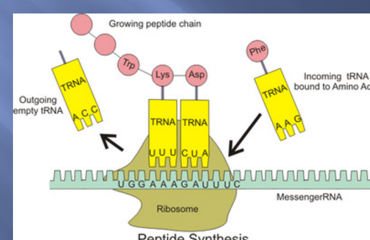
Protein Synthesis

- 3 exosed bases on the anticodon loop bind to a codon in mRNA through complimentary base-pairing
  - Hydrogen bonds



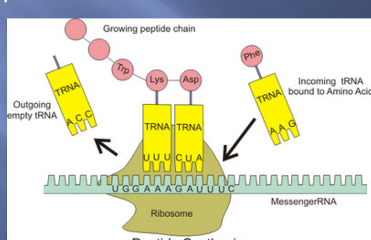
Protein Synthesis

- Ribosome moves long mRNA to sequentially expose each codon
- Base-pairing brings amino acids to the ribosome in the correct order



Protein Synthesis

- Amino acids joined together to form a protein's primary structure
- Takes about 20 seconds to form the whole protein



Protein Synthesis

- The signal for where to begin translation is the start codon: AUG
  - Codes for the amino acid methionine
  - All proteins begin with methionine
- Translation ends when a STOP codon is reached
  - Codes for no amino acid
  - No corresponding tRNA
  - Ribosome comes apart and releases mRNA, protein

Universal Genetic Code

Second letter

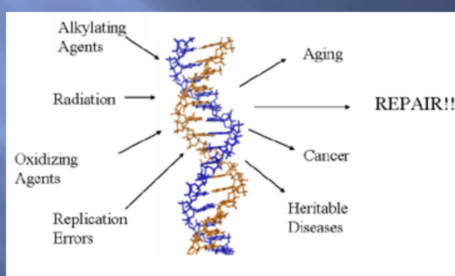
First letter	U		C		A		G		Third letter
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
U	UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys	C
U	UUA	Leu	UCA	Ser	UAA	Stop	UGA	Stop	A
U	UUG	Leu	UCG	Ser	UAG	Stop	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
C	CUC	Leu	CCC	Pro	CAC	His	CGC	Arg	C
C	CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg	A
C	CUG	Leu	CCG	Pro	CAG	Gln	CGG	Arg	G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
A	AUC	Ile	ACC	Thr	AAC	Asn	AGC	Ser	C
A	AUA	Ile	ACA	Thr	AAA	Lys	AGA	Arg	A
A	AUG	Met	ACG	Thr	AAG	Lys	AGG	Arg	G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
G	GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly	C
G	GUA	Val	GCA	Ala	GAA	Glu	GGA	Gly	A
G	GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly	G

DNA

- DNA is PRECIOUS!!
- If the code is changed, another amino acid could be made
- A change in just one nucleotide base can be devastating

DNA Damage, Repair, and Mutation

- Many factors lead to DNA damage
- Happens CONSTANTLY – yet usually we're fine!

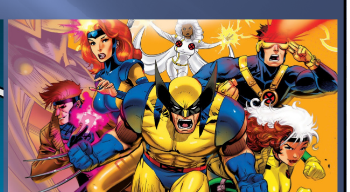


DNA Damage, Repair, and Mutation

- Many different DNA repair enzymes exist
- Replace damaged piece by…
  - Direct repair
    - Methylation defects
  - Referencing complimentary strand
    - Single base or nucleotide excision, mismatch repair
  - Referencing homologous chromosome
    - Double-strand breaks

DNA Damage, Repair, and Mutation

- Rarely, DNA damage is undetected or improperly repaired
- This is called a *mutation*
- Several types of mutations exist



Point Mutations

- Changing one base
- Could change an amino acid
- Lots of other things could happen
  - Nothing
    - Example: ACC to ACA
    - Both code for THR
  - Could cause truncation (protein gets cut short)
    - Example: UGG to UGA
    - UGG = TRP   UGA = Stop
  - Could make a protein too long, could miss a Start codon, etc

Frameshift Mutations

- When a mutation changes how codons are grouped and read
- Changes every amino acid following the mutation
- Example: Take a sentence with all 3-letter words

  THE DOG SAW THE CAT
- If we delete the E at position 3 and re-group the words, it no longer makes sense

  THD OGS AWT HEC AT
- Which mutations in our previous examples produced a frameshift?

Other Mutations

- Additions
- Deletions
- Inversions and translocations
  - Large pieces of DNA (sometimes most of a chromosome) broken apart and reattached
  - Sometimes within a chromosome
  - Sometimes to another chromosome

Other Mutations

- May be benign
  - Entire genes with their promoters simply moved from one place to another
- Gene may split into pieces
  - No longer codes for a functional protein
  - Example: most severe hemophilia is caused by an inversion of the gene for a blood-clotting protein