Molecular Biology 5

- iClicker 26A
- Gene Mutations
  - Missense
  - Nonsense
  - Frame-shift
  - Promoter
- iClicker 26B

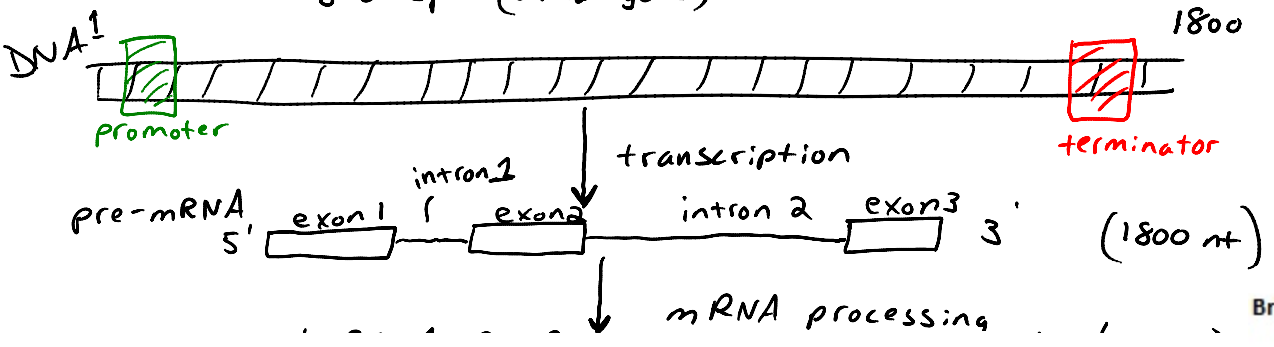
- Due in Lab this week
  - No lab next week (Thanksgiving)

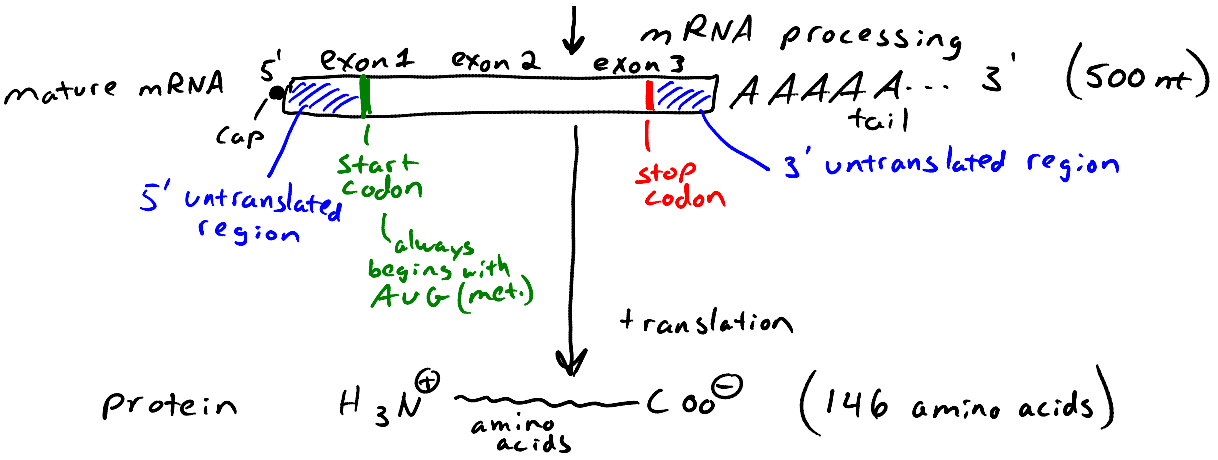
- Exam 2 solutions posted this afternoon

- Extra credit assignment will be announced and posted Monday

Mutations

ex. β-globin, which is a subunit of hemoglobin
- on chromosome 11
- ~ 1800 bp (small gene)





mutations are alterations in DNA that cause alterations in mRNA that <u>may</u> cause alterations in protein

mutations cause changes in DNA (allele) → changes in protein structure → changes in protein function

Bio 111 Selected β-globin Mutations

Changes shown in outline type.

1) Hemoglobin Christchurch (missense mutation: one amino acid changed to another)

T to C
A to G

	normal allele	mutant allele	
DNA:	5′...TTT...3′ 3′...AAA...5′	5′...TCT...3′ 3′...AGA...5′	all others unchanged
mRNA:	5′...UUU...3′	5′...UCU...3′	all others unchanged
protein:	H_3N^+-...phenylalanine...COO^- #71	H_3N^+-...serine...COO^- #71	all others unchanged

genetic code

phobic

philic → mis-folded protein
↳ Heintz bodies
↳ hemolytic anemia

not changing the protein after it is made

Silent mutation → mutation that does not change the amino acid

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2) Nonsense mutation (one amino acid codon changed to a stop codon)

	normal allele	mutant allele	
DNA:	5′...TGG...3′ 3′...ACC...5′	5′...TAG...3′ 3′...ATC...5′	all others unchanged
mRNA:	5′...UGG...3′	5′...UAG...3′	all others unchanged
protein:	H_3N^+-...leu-trp-(132 more)-COO^- #14 15	H_3N^+-...leu-COO^- #14	all others missing

146 amino acids

protein is only 14 amino acids long
∴ non-functional protein
→ genetic disease: β^0-thalassemia
nofunctional hemoglobin
autosomal rec.

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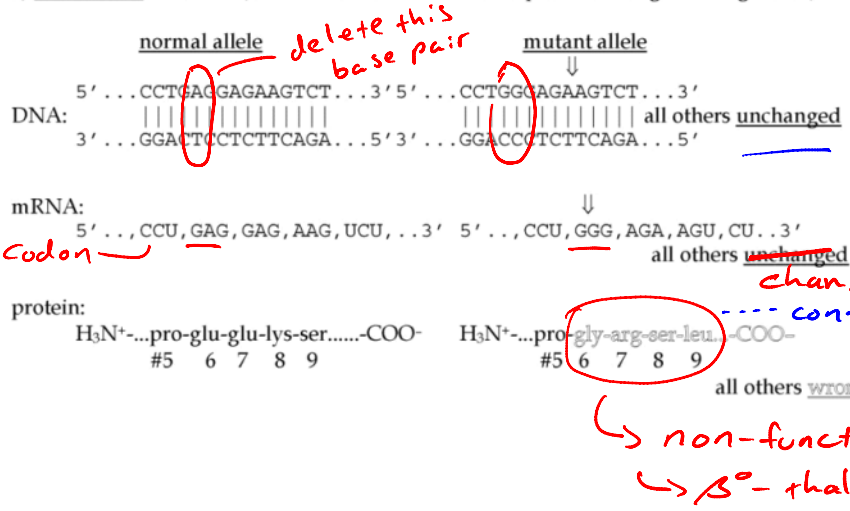
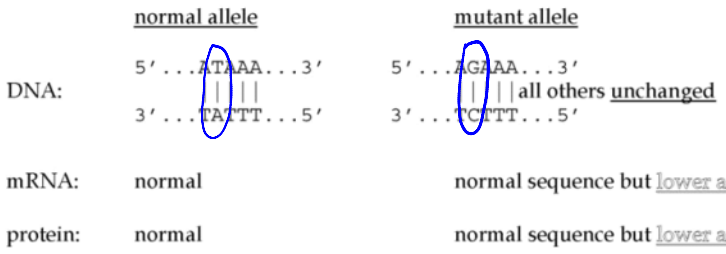
3) Frame-shift mutation (add or delete 1 or more base pairs ⇒ change reading frame)



4) Promoter mutation - change DNA sequence so RNA pol no-longer recognizes it as well



β⁺- thalassemia
make some β-globin, but not 100%

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other mutations
- splice site mutations
  alter start intron site → intron 1 is not removed
  - add more codons

- deletions of an entire gene
- insertions of random DNA (1- 1,000's n.t.)