

Mutations

This is tricky, though it shouldn't be. To compare the original gene to a mutant version of it, it is necessary to figure out what the mutation(s) does to the protein. This requires translating the protein that would be produced by the original and the protein that would be produced by the mutant. This is easy, but students don't usually bother to do it (!).

Here, I've constructed two mutant genes that produce the identical protein to the original. There is no effect on the protein. Then, I give two mutant genes that have frameshifts--which change the protein completely, and cause premature termination. (Students usually don't "stop" translating when they get to "stop," however.) The effect on the protein is simple: it is completely changed, so the original is simply not there. Last, I give a simple base change that changes one amino acid. Here, and only here, is it difficult to predict what will happen. Will the protein be unchanged? Will it fold a little differently, so that it works a little differently? It's hard to tell.

The last example is important because it gets at the notion that "mutations are always bad." The frameshifts are important because they provide examples of how mutations can "inactivate a gene," which is necessary to understand genetics. The first examples are important because they demonstrate that DNA changes don't necessarily result in protein changes.

What do mutations do to a gene?

Here's a DNA sequence for a very short gene:

ATGAAGCTCTGGATAGCCGATAACCCCCCTCTCAGACAGTAA

_____ name

This would give the following RNA

AUGAAGCUCUGGAUAGCCGAUAACCCCCCUCUCAGACAGUAA

The nearly-universal genetic code is shown on the right. This is how cells of almost all organisms translate the RNA code. The table shows which amino acid is specified by each 3-letter "word" in the RNA.

		2nd position				
		U	C	A	G	
1st position	U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
		UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
		UUA Leu	UCA Ser	UAA STOP	UGA STOP	A
	C	UUG Leu	UCG Ser	UAG STOP	UGG Trp	G
		CUU Leu	CCU Pro	CAU His	CGU Arg	U
		CUC Leu	CCC Pro	CAC His	CGC Arg	C
	A	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
		CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
		AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	G	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
		AUA Ile	ACA Thr	AAA Lys	AGA Ser	A
		AUG Met	ACG Thr	AAG Lys	AGG Ser	G
	GUU Val	GCU Ala	GAU Asp	GGU Gly	U	
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C	
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A	
		GUG Val	GCG Ala	GAG Glu	G	

If you translate this RNA, what protein sequence do you get?

Here's a hint about how to do this most easily:

Met Lys
 AUGAAGCUCUGGAUAGCCGAUAACCCCCCUCUCAGACAGUAA
 [][][] [][][] [][][] [][][] [][][] [][][] [][][] [][][] [][][]

put brackets on the 3-base units that the ribosome would read, then write the amino acid above it.

Now, here are some RNAs from mutant versions of this gene. The mutations are indicated with arrows. Translate each of these gene versions...what happens?

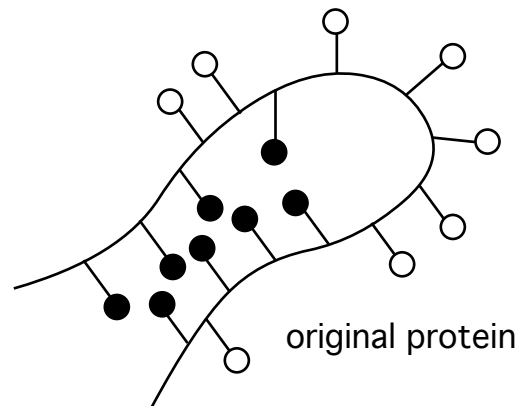
<p>base change ↓ AUGAAGCUAUGGAUAGCCGAUAACCCCCCUCUCAGACAGUAA</p> <p>7 base changes ↓ ↓ ↓ ↓ ↓ ↓ ↓ AUGAAGCUGUGGAUCGCAGACAAUCCGCCACUCAGACAGUAA</p> <p>insert 1 base ↓ AUGAAAGCUCUGGAUAGCCGAUAACCCCCCUCUCAGACAGUAA</p> <p>delete 1 base ↓ AUGAACUCUGGAUAGCCGAUAACCCCCCUCUCAGACAGUAA</p> <p>base change ↓ AUGGAGCUCUGGAUAGCCGAUAACCCCCCUCUCAGACAGUAA</p>	<p>Effect on protein:</p> <hr/> <hr/> <hr/> <hr/> <hr/>
--	---

see the back for some thoughts about what amino acid changes can do

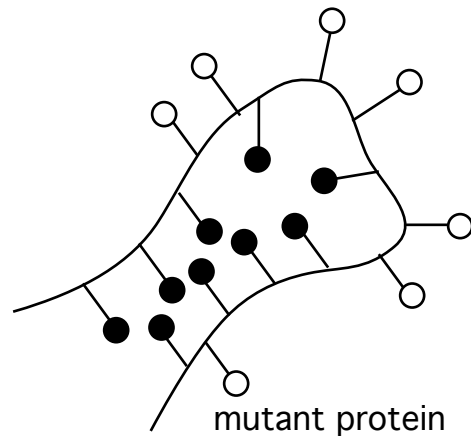
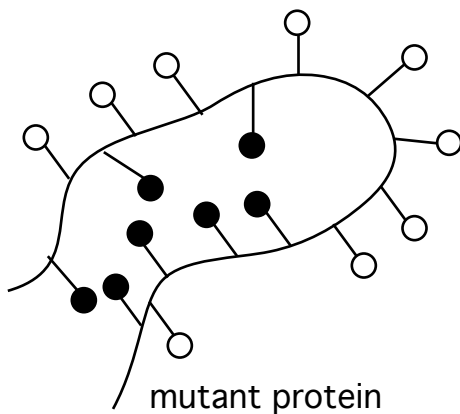
Amino acid changes can do nothing, or something, depending on what changes occur and where they are.

hydrophobic amino acid: ●

hydrophilic amino acid: ○



Mutations that change hydrophobic amino acids for other hydrophobic amino acids often have no effect. But changing a hydrophobic amino acid for a hydrophilic one can have a big effect:



Changes in shape may cause changes in function. Usually, such changes make the protein worse. Sometimes, they make it better.

There are many other kinds of changes that can alter protein function; these are just a couple of things we can picture easily.