Tutor on Cystic Fibrosis

Background—Disease and Gene

Cystic fibrosis is an inherited chronic disease that affects the lungs and digestive system of about 30,000 children and adults in the United States (70,000 worldwide). A defective gene and its protein product cause the body to produce unusually thick, sticky mucus that:

-clogs the lungs and leads to life-threatening lung infections; and

-obstructs the pancreas and stops natural enzymes from helping the body break down and absorb food.

In the 1950s, few children with cystic fibrosis lived to attend elementary school. Today, advances in research and medical treatments have further enhanced and extended life for children and adults with CF. Many people with the disease can now expect to live into their 30s, 40s and beyond.

Statistics

- About 1,000 new cases of cystic fibrosis are diagnosed each year.
- More than 70% of patients are diagnosed by age two.
- More than 40% of the CF patient population is age 18 or older.
- In 2006, the predicted median age of survival was 37 years.[1]

Much has been learned since then about the function of the gene's protein, named CFTR (for CF transmembrane conductance regulator). It appears to work like a two-way pump, channeling vital compounds in and out of a cell. When it functions normally, the protein helps regulate the transfer of sodium across cell membranes and serves as a chloride channel. But in CF this process fails,and the chloride channel stays closed. The sodium, which does not move freely, builds up in the lungs and disables a natural antibiotic that would otherwise guard against a wide range of lung infections. Bacteria then thrive in the thick, sticky mucus.[2]

1. Cystic Fibrosis is…
    1. A chronic genetic disease that affects the respiratory and digestive systems
    2. A sexually transmitted disease that can be cured with medication
    3. A sports injury
    4. An illness due to lack of fiber in a diet
2. What does the CFTR protein regulate?
    1. Where fat is deposited in the body
    2. Whether or not someone can see color
    3. The transfer of sodium across the cell membrane
    4. The transmittance of impulses through nerves

Background—Mutation/Insertion/Deletion

Cystic fibrosis (CF) is a relatively common genetic disease caused by mutations in a gene located on chromosome 7. Every cell in the body (except sperm in men and egg cells, oocytes, in females) has 46 chromosomes, or 23 pairs of chromosomes, one half inherited from the mother and the other half from the father. Genes on each of these chromosomes form the body's blueprint for producing proteins that control body functions. A gene on chromosome 7 is responsible for the normal production of a protein called cystic fibrosis transmembrane regulator (CFTR). Mutations (defects at the DNA level) in this gene lead to absent or defective CFTR production, causing CF. More than 1,000 different CF mutations have been identified, although some are much more common than others.[3]

There are a few main changes in a DNA sequence that occur that can cause major or minor changes in the protein that that particular gene sequence codes for. These are mutations. A mutation is when one base pair, A, T, C, or G, (or a few) is replaced by a different base pair. This may or may not cause a change in the amino acid the affected base pair codes for. And if it does, the damage to the protein may be minimal. Insertions and Deletions are two types of mutations. An insertion is an addition of extra base pairs to the gene sequence. The opposite of an insertion, a deletion, is where a single or a number of base pairs are taken out of the gene sequence. These two may change the entire line of amino acids down the entire gene.

Symptoms of Cystic Fibrosis

People with CF can have a variety of symptoms, including:

- very salty-tasting skin;
- persistent coughing, at times with phlegm;
- frequent lung infections;
- wheezing or shortness of breath;
- poor growth/weight gain in spite of a good appetite; and
- frequent greasy, bulky stools or difficulty in bowel movements.[4]

Statistics by mutation type:[5]

Mutation Type	Count	Frequency %
Missense	654	41.71
Frame shift	246	15.69
Splicing	201	12.82
Nonsense	151	9.63
In frame in/del	32	2.04
Large in/del	45	2.87
Promoter	8	0.51
Sequence variation	229	14.60

1. The gene that codes for Cystic Fibrosis is located:
    1. On chromosome 5
    2. On chromosome 32
    3. On chromosome 7
    4. On chromosome 61
2. Which one of these is NOT a symptom of CF?
    1. Excessive weight gain in spite of poor appetite
    2. Poor weight gain in spite of good appetite
    3. Frequent lung infections
    4. Salty-tasting skin
3. Which is the most common mutation type coding for CF?

1. Nonsense
2. Sequence variation
3. Frame shift
4. Missense

4. **A deletion is:**
    1. **an addition of base pairs**
    2. **when one base pair is changed to another**
    3. **when base pairs are removed**
    4. **when you hit the del. button on the keyboard**

Exon 10—How to find it

Exon 10 is located from base pairs 1525-1716. Each letter in the following sequence is equal to one base pair: A, T, C, or G. The numbers to the top and to the left of the list will guide you in finding exon 10. To find this gene on the NCBI database[6] search OMIM using the accession number 602421.

ENTRY 90421312 #Type genetic

TITLE 90421312 6132 bases, NULL checksum.

SEQUENCE

5 10 15 20 25 30

1 A A T T G G A A G C A A A T G A C A T C A C A G C A G G T C

31 A G A G A A A A A G G G T T G A G C G G C A G G C A C C C A

61 G A G T A G T A G G T C T T T G G C A T T A G G A G C T T G

91 A G C C C A G A C G G C C C T A G C A G G G A C C C C A G C

121 G C C C G A G A G A C C A T G C A G A G G T C G C C T C T G

151 G A A A A G G C C A G C G T T G T C T C C A A A C T T T T T

181 T T C A G C T G G A C C A G A C C A A T T T T G A G G A A A

211 G G A T A C A G A C A G C G C C T G G A A T T G T C A G A C

241 A T A T A C C A A A T C C C T T C T G T T G A T T C T G C T

271 G A C A A T C T A T C T G A A A A A T T G G A A A G A G A A

301 T G G G A T A G A G A G C T G G C T T C A A A G A A A A A T

331 C C T A A A C T C A T T A A T G C C C T T C G G C G A T G T

361 T T T T T C T G G A G A T T T A T G T T C T A T G G A A T C

391 T T T T T A T A T T T A G G G G A A G T C A C C A A A G C A

421 G T A C A G C C T C T C T T A C T G G G A A G A A T C A T A

451 G C T T C C T A T G A C C C G G A T A A C A A G G A G G A A

481 C G C T C T A T C G C G A T T T A T C T A G G C A T A G G C

511 T T A T G C C T T C T C T T T A T T G T G A G G A C A C T G

541 C T C C T A C A C C C A G C C A T T T T T G G C C T T C A T

571 C A C A T T G G A A T G C A G A T G A G A A T A G C T A T G

601 T T T A G T T T G A T T T A T A A G A A G A C T T T A A A G

631 C T G T C A A G C C G T G T T C T A G A T A A A A T A A G T

661 A T T G G A C A A C T T G T T A G T C T C C T T T C C A A C

691 A A C C T G A A C A A A T T T G A T G A A G G A C T T G C A

721 T T G G C A C A T T T C G T G T G G A T C G C T C C T T T G

751 C A A G T G G C A C T C C T C A T G G G G C T A A T C T G G

781 G A G T T G T T A C A G G C G T C T G C C T T C T G T G G A

811 C T T G G T T T C C T G A T A G T C C T T G C C C T T T T T

841 C A G G C T G G G C T A G G G A G A A T G A T G A T G A A G

871 T A C A G A G A T C A G A G A G C T G G G A A G A T C A G T

901 G A A A G A C T T G T G A T T A C C T C A G A A A T G A T T

931 G A A A A T A T C C A A T C T G T T A A G G C A T A C T G C

961 T G G G A A G A A G C A A T G G A A A A A A A T G A T T G A A

991 A A C T T A A G A C A A A C A G A A C T G A A A C T G A C T

1021 C G G A A G G C A G C C T A T G T G A G A T A C T T C A A T

1051 A G C T C A G C C T T C T T C T T C T C A G G G T T C T T T

1081 G T G G T G T T T T T A T C T G T G C T T C C C T A T G C A

1111 C T A A T C A A A G G A A T C A T C C T C C G G A A A A T A

1141 T T C A C C A C C A T C T C A T T C T G C A T T G T T C T G

1171 C G C A T G G C G G T C A C T C G G C A A T T T C C C T G G

1201 G C T G T A C A A A C A T G G T A T G A C T C T C T T G G A

1231 G C A A T A A A C A A A A T A C A G G A T T T C T T A C A A

1261 A A G C A A G A A T A T A A G A C A T T G G A A T A T A A C

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1381 A A C A A T A G A A A A A C T T C T A A T G G T G A T G A C

1411 A G C C T C T T C T T C A G T A A T T T C T C A C T T C T T

1441 G G T A C T C C T G T C C T G A A A G A T A T T A A T T T C

1471 A A G A T A G A A A G A G G A C A G T T G T T G G C G G T T

1501 G C T G G A T C C A C T G G A G C A G G C A A G A C T T C A

1531 C T T C T A A T G G T G A T T A T G G G A G A A A C T G G A G

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2161 G T C T C C T G G A C A G A A A C A A A A A A A A C A A T C T

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2251 T C T A T A C G A A A A T T T T C C A T T G T G C A A A A G

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5731 T A A C A A T G C T G T A T T T T A A A A G A A T G A T T A
5761 T G A A T T A C A T T T G T A T A A A A T A A T T T T T A T
5791 A T T T G A A A T A T T G A C T T T T T A T G G C A C T A G
5821 T A T T T C T A T G A A A T A T T A T G T T A A A A C T G G
5851 G A C A G G G G A G A A C C T A G G G T G A T A T T A A C C
5881 A G G G G C C A T G A A T C A C C T T T T G G T C T G G A G
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5941 C A C A G C T G T A T G A T T C C C A G C C A G C A C A G C
5971 C T C T T A G A T G C A G T T C T G A A G A A G A T G G T A
6001 C C A C C A G T C T G A C T G T T T C C A T C A A G G G T A
6031 C A C T G C C T T C T C A A C T C C A A A C T G A C T C T T
6061 A A G A A G A C T G C A T T A T A T T T A T T A C T G T A A
6091 G A A A A T A T C A C T T G T C A A T A A A A T C C A T A C
6121 A T T T G T G T G A A A
```

1. What is the sequence for Exon 10?
    1. ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAATTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTCCTATGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG
    2. GACATCTCCAAGTTTGCAGAGAAAGACAATATAGTTCTTGGAGAAGGTGGAATCACACTGAGTGGAGGTCAACGAGCAAGAATTTCTTTAGCAAG
2. What is the accession number of Exon 10 on the NCBI database?
    1. 1525
    2. 602421
    3. 1716
    4. 10

Deletion of TTT

Location: Amino Acid 508 and Base Pairs 1653-1655

This deletion mutation is the most common cause of Cystic Fibrosis. It deletes three base pairs, or a single amino acid, Phe, changing the nature of the protein.

Normal Exon 10

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAA

TTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTC

CTATGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

Deletion of TTT

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAA

TTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCGGTGTTTCCTA

TGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

6 Frame Translation

We do a SIXFRAME translation in Biology Workbench to translate the Nucleic Acid sequence into an Amino Acid sequence. The translation gives us 6 choices of which sequence is the closest match to what we want.

Normal Exon 10

Frame 1, 0 stop codons

T S L L M V I M G E L E P S E G K I K H

1 acttcacttctaatggtgattatgggagaactggagccttcagagggtaaaattaagcac 60

S G R I S F C S Q F S W I M P G T I K E

61 agtggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaa 120

N I I F G V S Y D E Y R Y R S V I K A C

121 aatatcatctttggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgc 180

Q L E E

181 caactagaagag 192

Frame 2, 3 stop codons

L H F * W * L W E N W S L Q R V K L S T

2 cttcacttctaatggtgattatgggagaactggagccttcagagggtaaaattaagcaca 61

V E E F H S V L S F P G L C L A P L K K

62 gtggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaaa 121

I S S L V F P M M N I D T E A S S K H A

122 atatcatctttggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgcc 181

N * K

182 aactagaagag 192

Frame 3, 6 stop codons

F T S N G D Y G R T G A F R G * N * A Q

3 ttcacttctaatggtgattatgggagaactggagccttcagagggtaaaattaagcacag 62

W K N F I L F S V F L D Y A W H H * R K

63 tggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaaaa 122

Y H L W C F L * * I * I Q K R H Q S M P

123 tatcatctttggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgcca 182

T R R

183 actagaagag 192

Frame 4, 5 stop codons

L F * L A C F D D A S V S I F I I G N T

-1 ctcttctagttggcatgctttgatgacgcttctgtatctatattcatcataggaaacacc -60

K D D I F F N G A R H N P G K L R T E *

-61 aaagatgatattttctttaatggtgccaggcataatccaggaaaactgagaacagaatga -120

N S S T V L N F T L * R L Q F S H N H H

-121 aattcttccactgtgcttaattttaccctctgaaggctccagttctcccataatcaccat -180

* K * S

-181 tagaagtgaagt -192

Frame 5, 2 stop codons

S S S W H A L M T L L Y L Y S S * E T P

-2 tcttctagttggcatgctttgatgacgcttctgtatctatattcatcataggaaacacca -61

K M I F S L M V P G I I Q E N * E Q N E

-62 aagatgatattttctttaatggtgccaggcataatccaggaaaactgagaacagaatgaa -121

I L P L C L I L P S E G S S S P I I T I

-122 attcttccactgtgcttaattttaccctctgaaggctccagttctcccataatcaccatt -181

R S E

-182 agaagtgaagt -192

Frame 6, 7 stop codons

L L V G M L * * R F C I Y I H H R K H Q

-3 cttctagttggcatgctttgatgacgcttctgtatctatattcatcataggaaacaccaa -62

R * Y F L * W C Q A * S R K T E N R M K

-63 agatgatattttctttaatggtgccaggcataatccaggaaaactgagaacagaatgaaa -122

F F H C A * F Y P L K A P V L P * S P L

-123 ttcttccactgtgcttaattttaccctctgaaggctccagttctcccataatcaccatta -182

E V K

-183 gaagtgaagt -192

Frame 1 [Longest ORF], 0 stop codons

- - - - M V I M G E L E P S E G K I K H

1 ------------atggtgattatgggagaactggagccttcagagggtaaaattaagcac 60

S G R I S F C S Q F S W I M P G T I K E

61 agtggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaa 120

N I I F G V S Y D E Y R Y R S V I K A C

121 aatatcatctttggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgc 180

Q L E E

181 caactagaagag 192

Deletion of TTT 6 Frame Translation

Frame 1, 0 stop codons

T S L L M V I M G E L E P S E G K I K H

1 acttcacttctaatggtgattatgggagaactggagccttcagagggtaaaattaagcac 60

S G R I S F C S Q F S W I M P G T I K E

61 agtggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaa 120

N I I G V S Y D E Y R Y R S V I K A C Q

121 aatatcatcggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgccaa 180

L E E

181 ctagaagag 189

Frame 2, 3 stop codons

L H F * W * L W E N W S L Q R V K L S T

2 cttcacttctaatggtgattatgggagaactggagccttcagagggtaaaattaagcaca 61

V E E F H S V L S F P G L C L A P L K K

62 gtggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaaa 121

I S S V F P M M N I D T E A S S K H A N

122 atatcatcggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgccaac 181

* K

182 tagaagag 189

Frame 3, 6 stop codons

F T S N G D Y G R T G A F R G * N * A Q

3 ttcacttctaatggtgattatgggagaactggagccttcagagggtaaaattaagcacag 62

W K N F I L F S V F L D Y A W H H * R K

63 tggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaaaa 122

Y H R C F L * * I * I Q K R H Q S M P T

123 tatcatcggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgccaact 182

R R

183 agaagag 189

Frame 4, 5 stop codons

L F * L A C F D D A S V S I F I I G N T

-1 ctcttctagttggcatgctttgatgacgcttctgtatctatattcatcataggaaacacc -60

D D I F F N G A R H N P G K L R T E * N

-61 gatgatattttctttaatggtgccaggcataatccaggaaaactgagaacagaatgaaat -120

S S T V L N F T L * R L Q F S H N H H *

-121 tcttccactgtgcttaattttaccctctgaaggctccagttctcccataatcaccattag -180

K * S

-181 aagtgaagt -189

Frame 5, 2 stop codons

S S S W H A L M T L L Y L Y S S * E T P

-2 tcttctagttggcatgctttgatgacgcttctgtatctatattcatcataggaaacaccg -61

M I F S L M V P G I I Q E N * E Q N E I

-62 atgatattttctttaatggtgccaggcataatccaggaaaactgagaacagaatgaaatt -121

L P L C L I L P S E G S S S P I I T I R

-122 cttccactgtgcttaattttaccctctgaaggctccagttctcccataatcaccattaga -181

S E

-182 agtgaagt -189

Frame 6, 7 stop codons

L L V G M L * * R F C I Y I H H R K H R

-3 cttctagttggcatgctttgatgacgcttctgtatctatattcatcataggaaacaccga -62

* Y F L * W C Q A * S R K T E N R M K F

-63 tgatattttctttaatggtgccaggcataatccaggaaaactgagaacagaatgaaattc -122

F H C A * F Y P L K A P V L P * S P L E

-123 ttccactgtgcttaattttaccctctgaaggctccagttctcccataatcaccattagaa -182

V K

-183 gtgaagt -189

Frame 1 [Longest ORF], 0 stop codons

- - - - M V I M G E L E P S E G K I K H

1 ------------atggtgattatgggagaactggagccttcagagggtaaaattaagcac 60

S G R I S F C S Q F S W I M P G T I K E

61 agtggaagaatttcattctgttctcagttttcctggattatgcctggcaccattaaagaa 120

N I I G V S Y D E Y R Y R S V I K A C Q

121 aatatcatcggtgtttcctatgatgaatatagatacagaagcgtcatcaaagcatgccaa 180

L E E

181 ctagaagag 189

Since the sequence we chose (both normal and mutated) to translate is not at the beginning, nor at the end, of the entire sequence of the cystic fibrosis gene, the optimal Frame to choose would be Frame 1 since it has zero stop codons. We do not want to choose Frame 1 [Longest ORF] because it takes our Frame 1 and chops off amino acids at the beginning of it until it finds the amino acid that could code for the start of translation (M).

Alignment of Normal and Deletion of Phe

Normal TSLLMVIMGE LEPSEGKIKH SGRISFCSQF SWIMPGTIKE NIIFGVSYDE YRYRSVIKAC QLEE

Mutate TSLLMVIMGE LEPSEGKIKH SGRISFCSQF SWIMPGTIKE NII-GVSYDE YRYRSVIKAC QLEE

As you can see, we have aligned the normal and mutated sequences according to the amino acid sequence. The – in the bottom sequence indicates where the deletion happened, while in the normal sequence on the top you find the F.

Deletion of Phe Amino Acid Sequence

1. Which frame of the normal Exon 10 has the highest number of stop codons?
    1. Frame 1
    2. Frame 6
    3. Frame 3

4. Frame 1 [Longest ORF]

2. Which frame of the mutated Exon 10 is the closest match to our sequence?

    1. Frame 1
    2. Frame 6
    3. Frame 3
    4. Frame 1 [Longest ORF]

Mutations on Exons 10 & 11

Sequence Variation A to G (different)

Location: Amino Acid 513 and Base Pairs 1670

This mutation replaces one amino acid with an amino acid with very different properties, therefore the protein translated will not be effective.

Normal Exon 10

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAATTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTCCTATGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

Sequence Variation (different)

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAA

TTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTC

CTATGGTGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

6 Frame Translation→

Alignment

Normal ----MVIMGE LEPSEGKIKH SGRISFCSQF SWIMPGTIKE NIIFGVSYGE YRYRSVIKAC QLEE

Exon10 TSLLMVIMGE LEPSE-KIKH SGRISFCSQF SWIMPGTIKE NIIFGVSYDE YRYRSVIKAC QLE-

---

Sequence Variation G to T (similar)

Location: Amino Acid 480 and Base Pair 1570

This mutation replaces an amino acid with one that is similar in properties. The protein that gets coded from this sequence may function properly.

Normal Exon 10

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAATTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTCCTATGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

Sequence Variation (similar)

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGTTAAAATTAAGCACAGTGGAAGAA

TTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTC

CTATGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

6 Frame Translation→

Alignment

Normal TSLLMVIMGE LEPSEGKIKH SGRISFCSQF SWIMPGTIKE NIIFGVSYDE YRYRSVIKAC QLEE

Mutate TSLLMVIMGE LEPSEVKIKH SGRISFCSQF SWIMPGTIKE NIIFGVSYDE YRYRSVIKAC QLEE

Sequence Variation G to A

Location: Amino Acid 551 and Base Pairs 1784

Normal Exon 11

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAATTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTCCTATGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

Sequence Variation

GACATCTCCAAGTTTGCAGAGAAAGACAATATAGTTCTTGGAGAAGGTGGAATCACACTGAGTGGAGATC

AACGAGCAAGAATTTCTTTAGCAAG

6 Frame Translation→

Alignment

Normal DISKFAEKDN IVLGEGGITL SGDQRARISL A

Mutate DISKFAEKDN IVLGEGGITL SGGQRARISL A

Missense Variation C to T (stop)

Location: Amino Acid 553 and Base Pair 1789

A missense mutation creates a stop codon, which basically cuts off the rest of the gene sequence following the mutation. Therefore, the protein is not complete.

Normal Exon 11

ACTTCACTTCTAATGGTGATTATGGGAGAACTGGAGCCTTCAGAGGGTAAAATTAAGCACAGTGGAAGAATTTCATTCTGTTCTCAGTTTTCCTGGATTATGCCTGGCACCATTAAAGAAAATATCATCTTTGGTGTTTCCTATGATGAATATAGATACAGAAGCGTCATCAAAGCATGCCAACTAGAAGAG

Sequence Variation (stop)

GACATCTCCAAGTTTGCAGAGAAAGACAATATAGTTCTTGGAGAAGGTGGAATCACACTGAGTGGAGGTC

AATGAGCAAGAATTTCTTTAGCAAG

6 Frame Translation→

Alignment

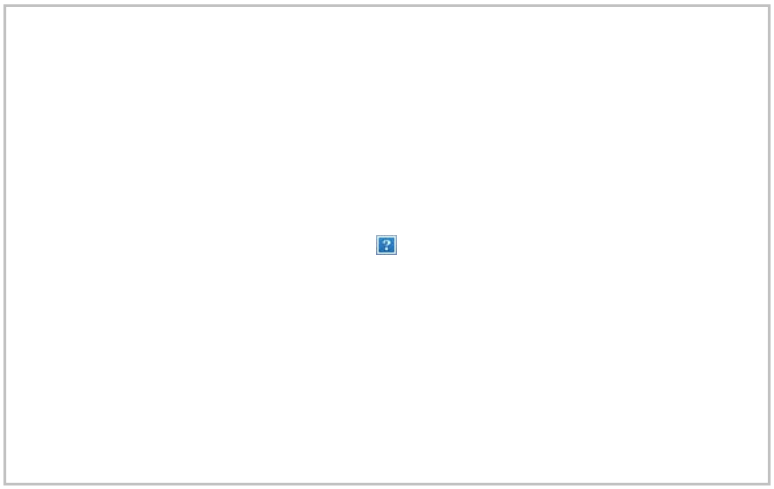
Mutate DISKFAEKDN IVLGEGGITL SGGQ------ -

Normal DISKFAEKDN IVLGEGGITL SGGQRARISL A

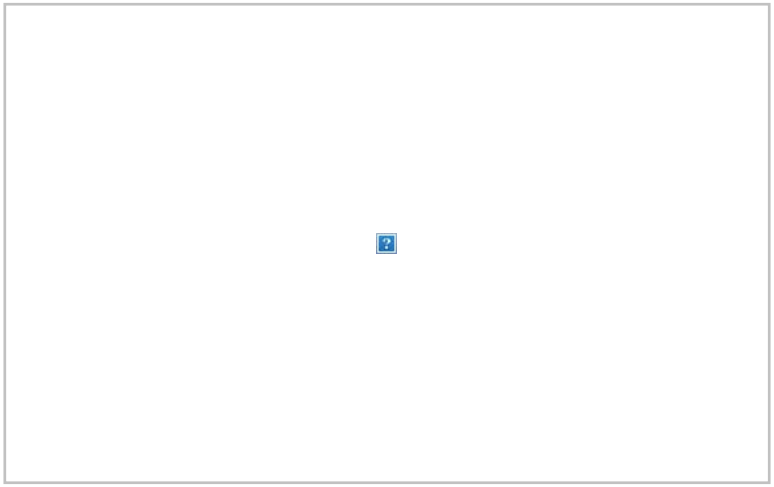
1. What does a missense mutation cause?
    1. One A.A. to be replaced by another
    2. A stop codon
    3. A mutation that doesn’t make sense
    4. A start codon
2. Replacing an A.A. with a very different A.A. causes:
    1. The protein to function normally and without change in shape
    2. The protein to have another function

3. A change in shape of the protein, but it still functions
4. The protein to be unusable

3D Protein Structure



This is the protein structure of a non-mutated gene sequence for the CFTR protein.



This is the protein translated from the mutated gene sequence. The mutation is our most common Cystic Fibrosis mutation at amino acid 508—the deletion of there base pairs, TTT, or in other words, the deletion of the amino acid Phe.

Summary

Questionnaire

Evaluation

1 *http://www.cff.org/AboutCF/*

2 *http://www.hhmi.org/genetictrail/a130.html*

3 *http://www.labtestsonline.org/understanding/conditions/cystic_fibrosis.html*

4 *http://www.cff.org/AboutCF/*

5 *http://www.genet.sickkids.on.ca/cftr/StatisticsPage.html*

6 http://www.ncbi.nlm.nih.gov/sites/entrez?db=omim