



Hughes
Undergraduate
Biological
Science
Education
Initiative



Cystic Fibrosis
How Mutations Lead to Disease
Teacher instructions and answers

Note to teachers

This is an advanced activity. It assumes a basic knowledge of

- Membrane structure
- 3 dimensional protein structure
- Mutations
- Amino acids
- Regulation of protein activity
- Ion channels

This exercise would be a good exercise to use in reviewing these topics.

This topic also assumes knowledge of protein folding and chaperones (provided in this workshop)

Activity

Reread your case history and refamiliarize yourself with the symptoms of the patient described in your case history. **Make a short list of the symptoms below.**

Look at the table below showing how what CFTR protein level correlates with the symptoms you are observing (in the relationship between genotype and phenotype section). What percentage of normal CFTR function do you think the patient in your case has? **Write your answer below.**

Beth - <5%
Tom - <1%
Sandy - <1%
Bill - <1%

Find the mutation that your patient has in the table below.

Beth - R117H
Tom - Delta F508
Sandy - G551D
Bill - R553X

Write your answer in the space below.

Note that each person has two copies of the CFTR gene. Assume the individual in your case has two copies of the same mutant gene. In human populations various different combinations of mutations can occur.

Using the rules listed in the naming mutations section – **answer the following questions** about your mutation?

1. What is the position number of the amino acid that is changed in the case you were given?

R117H - 117
Delta F508 - 508
G551D - 551
R553X - 553

2. Is one amino acid substituted for another in the case you were given?

R117H – yes
Delta F508 - no
G551D - yes
R553X - no

If yes, which amino acid is found in the normal CFTR?

R117H – arginine
G551D - glycine

Which amino acid is found in the mutant CFTR?

R117H – histidine
G551D – aspartic acid

3. Is an amino acid deleted (missing) in the mutant CFTR of the individual in your case?

R117H – no
Delta F508 - yes
G551D - no
R553X - no

If yes, which amino acid is missing?

Delta F508 - phenylalanine

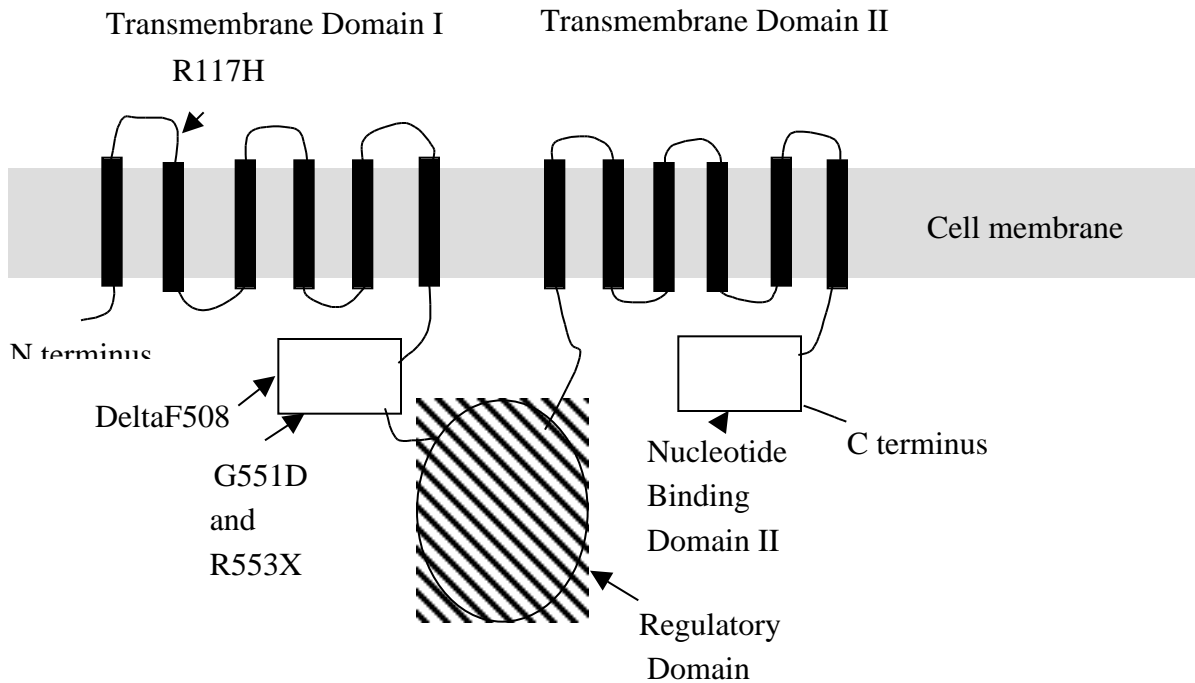
4. Does your mutation introduce a stop codon?

R117H – no
Delta F508 - no
G551D - no
R553X - yes

If yes, at which amino acid will the CFTR protein end?

R553X - 552

Now, find the location of your mutation on the map and **answer the following questions.**



5. In what area of the protein is your mutation found?

*R117H – transmembrane domain I
 Delta F508 – nucleotide binding domain I
 G551D - nucleotide binding domain I
 R553X- nucleotide binding domain I*

6. How might the function of this region be altered by your mutation?

*R117H – most likely affects ability of ion channel to allow ions to pass
 Delta F508 – most likely affects processing and transport
 G551D – most likely affects activation of channel by ATP
 R553X- since this mutation produces a truncated protein, there will be no ion channel*

7. Hypothesize as to how the mutation might lead to an alteration in the level of functional CFTR present in the cell membrane. Note this might include either the total protein level or how well the protein works or both. Be prepared to present your results to the class. Be sure to include a brief summary of your patients symptoms, the level of CFTR function you think they have, what mutation they have, where that mutation is located, and how that mutation might explain the symptoms of the patient.