Key for Web Exploration, Chapter 2

1. Compare each of Mary's alleles with the wild-type coding sequence. Can you identify a mutation in either or both?

   Relative to the wild-type CFTR coding sequence, Mary's allele A has a G to A mutation at position 360. Mary's allele B has a G to A mutation at position 1652.

2. Now, translate each of Mary's alleles and compare them with the wild-type amino-acid sequence. What differences can you detect?

   Mary's allele A is identical to the wild-type amino acid sequence, so the G to A mutation at position 360 must be a silent mutation (doesn't change the amino-acid sequence). Relative to the wild-type CFTR amino-acid sequence, Mary's allele B has a glycine to aspartate change at position 551 (G551D).

3. We know that Mary is a carrier of the CF allele but does not have the disease. Summarize your findings for Mary's CFTR alleles: describe the mutation(s) that have occurred, discuss how (if at all) they affect the CFTR protein and explain how your genomic data fit with what Mary already knows, including which allele she must have inherited from each of her parents.

   Mary's molecular results agree with the genetic analysis that identifies her as a carrier: she has one allele (A) that will produce a wild-type CFTR protein, even though it has a one-nucleotide substitution (silent mutation) and one allele (B) that will produce a change in the CFTR protein (G551D). It must be allele B that she inherited from her mother, since we know Mary's mother has CF and thus must have two defective CFTR alleles. Allele A must have come from Mary's father.

4. Repeat your analysis for each of Tom's two alleles. Is he a carrier of cystic fibrosis? Summarize your findings as above and discuss the risk that Tom and Mary will have a child with CF.

   Relative to the wild-type CFTR coding sequence, Tom's allele A has a three-nucleotide deletion at position 1521. Tom's allele B is identical to the wild-type allele. Translation demonstrates that relative to the wild-type CFTR amino-acid sequence, Tom's allele A has a phenylalanine (F) amino acid deleted at position 509 (ΔF509). Tom's allele B is identical to the wild-type.

   This means that Tom is also a carrier for CF: he has one normal allele and one mutant allele. Any child that Tom and Mary have has one chance in two of inheriting Tom's mutant allele and one chance in two of inheriting Mary's mutant allele. Even though they don't have the *same* mutant alleles, the child then has one chance in four of inheriting a non-functional allele from each parent and having CF.