**Mutations & Protein Synthesis**

AP Biology

1. Identify the gene involved
2. Determine the amino acid sequence of the normal and mutant alleles
3. Note the affected protein product
4. Deduce if the mutation is a point or frameshift one

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**1. Tay-Sachs** is an autosomal recessive disease caused by mutations in both alleles of a gene (*HEXA*) on chromosome 15. *HEXA* codes for the alpha subunit of the enzyme β-hexosaminidase A. This enzyme is found in lysosomes, organelles that break down large molecules for recycling by the cell. Normally, β-hexosaminidase A helps to degrade a lipid called GM2 ganglioside, but in Tay-Sachs individuals, the enzyme is absent or present only in very reduced amounts, allowing excessive accumulation of the GM2 ganglioside in neurons. The progressive neurodegeneration seen in the varied forms of Tay-Sachs depends upon the speed and degree of GM2 ganglioside accumulation, which in turn is dependent upon the level of functional β-hexosaminidase A present in the body.

Normal HEXA allele: …CGT ATA TCC TAT GCC GAC…

Mutant (one of many) Tay Sachs allele: insertion of TATC, here at the ninth nucleotide spot

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**2. Sickle cell disease** is caused by a particular mutation in the HBB gene. This mutation results in the production of an abnormal version of beta-globin called hemoglobin S or HbS. In this condition, hemoglobin S replaces both beta-globin subunits in hemoglobin. Replacing the amino acid causes the abnormal HbS subunits to stick together and form long, rigid molecules. The rigid HbS molecules bend red blood cells into a sickle (crescent) shape. The sickle-shaped cells die prematurely, which can lead to a shortage of red blood cells (anemia). The sickle-shaped cells can also block small blood vessels, causing pain and organ damage. Persons need to inherit both HbS genes to express the disease; persons inheriting one copy express Sickle Cell trait.

Normal Hemoglobin (HbB) gene: …CTG ACT CCT GAG GAG AAG TCT…

Mutant Sickle Cell (HbS) T substituted for A in the sixth amino acid (here at the 11th nucleotide)

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**3.** Mutations in the CFTR gene cause **cystic fibrosis**. The CFTR gene provides instructions for making a channel that transports negatively charged particles called chloride ions into and out of cells. Chloride is a component of sodium chloride, a common salt found in sweat. Chloride also has important functions in cells; for example, the flow of chloride ions helps control the movement of water in tissues, which is necessary for the production of thin, freely flowing mucus.

Mutations in the CFTR gene disrupt the function of the chloride channels, preventing them from regulating the flow of chloride ions and water across cell membranes. As a result, cells that line the passageways of the lungs, pancreas, and other organs produce mucus that is unusually thick and sticky. This mucus clogs the airways and various ducts, causing the characteristic signs and symptoms of cystic fibrosis.

Normal CFTR gene sequence: …ATC ATC TTT GGT GTT…

Mutant Cystic Fibrosis sequence has a deletion of position 508 amino acid, here the 6-8th nucleotides

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**4.** **Hemochromatosis** is a disorder that causes the body to absorb too much iron from the diet. The excess iron is stored in the body's tissues and organs, particularly the skin, heart, liver, pancreas, and joints. Because humans cannot increase the excretion of iron, excess iron can overload and eventually damage tissues and organs.

HFE is one of many genes that play an important role in regulating the absorption, transport, and storage of iron. The protein encoded by the HFE gene is a membrane protein. Mutation in this gene impairs the control of iron absorption during digestion and alters the distribution of iron to other parts of the body. As a result, iron accumulates in tissues and organs, which can disrupt their normal functions.

Normal HFE sequence: ….AGA TAT ACG TGC CAG GTG GAG….

Mutant has an A substitution at the 282nd (11th in this fragment) nucleotide

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References:

"Disorder Guide." *Oak Ridge National Laboratory*. N.p., 25 Feb. 2003. Web. 11 Feb. 2013. <http://www.ornl.gov/sci/techresources/Human\_Genome/posters/chromosome/diseaseindex.shtml#general>.

"Geneti Conditions." *Genetis Home Reference*. National Institutes of Halth, 4 Feb. 2013. Web. 11 Feb. 2013. <http://nih.gov>.