Use the following to answer 1-5:

Secretin is a gastrointestinal hormone in mammals that stimulates the secretion of bicarbonate rich pancreatic juice in the small intestine. It is a small peptide that consists of 27 amino acids. Below is the nucleotide sequence (written in the 5’ ---3’ direction) of the mRNA that encodes the precursor for rat secretin, as described by Kopin et al. in 1990 (Proceedings of the National Academy of Sciences, USA 87:2299-2303). The three AUG sequences in the mRNA are in bold.

UUUAUCACACCCAGAACCCGACCAUGGAGCCUCUACUGCCCACGCCGCCGCUACUGCUGCUGCUGCUGCUGCUGCUCUCAAGUUCUUUCGUG

CUUCCUGCACCUCCCAGGACCCCAAGACACUCGGACGGGACGUUCACCAGCGAGCUCAGCCGCUUGCAGGACAGUGCCAGGCUGCAGCGCCU

GCUGCAGGGUCUGGUGGGGAAGCGCAGCGAGGAGGACACAGAAAAUAUUCCAGAGAACAGCGUGGCCCGUCCCAAGCCAUUAGAGGACCAAC

UCUGCUUGCUGUGGUCGAACACUCAGGCCCUACAGGAUUGGCUUCUGCCCAGGCUGUCCCUGGAUGGGUCCCUGUCUCUCUGGCUGCCUCCU

GGACCAAGGCCUGCUGUCGACCAUUCAGAGUGGACUGAAACAACCAGGCAGCCCAGAUGAGGGAGGAAGGGGAGUCUCCAGGAGCCUGACUG

GAGUAGGGAUUGGUUGUCCUUGGCAUCAAUAAAGAAGGAAUUUAGACCCUGGU

The amino acid sequence of functional rat secretin is:

ArgHisSerAspGlyThrPheThr SerGluLeuSerArgLeuGlnAspSerAlaArgLeuGlnArgLeuLeuGlnGlyLeuVal

The amino acid sequence of the polypeptide encoded by the rat secretin gene is:

MetGluProLeuLeuProThrProProLeduLeuLeuLeuLeuLeuLeuLeuLeuSerSerSerPheValLeuProAlaProPro

ArgThrProArgHisSerAspGlyThrPheThrSerGluLeuSerArgLeuGlnAspSerAlaArgLeuGlnArgLeuLeuGln

GlyLeuValGLylysArgSerGluGluAspThrGluAsnIleProGluAsnSerValAlaArgProLysProLeuGluAspGln

LeuCysLeuLeuTrpSerAsnThrGlnAlaLeuGlnAlaLeuGlnAspTrpLeuLeuProArgLeuSerLeuAspGlySerLeuSerLeuTrp

LeuProProGlyProArgProAlaValAspHisSerGluTrpThrGluThrThrArgGlnProArg

**1) If you read the mRNA sequence in the 5’ ----3’ direction, which of the three AUG sequences is the initiation codon?**

a) first

b) second

c) third

**2) By how many nucleotides does the sequence surrounding the initiation codon differ from the GCCGCCPuCCAUGG consensus sequence?**

a) 0

b) 1

c) 2

d) 3

e) 4

f) 5

**3) To which site in the mRNA does the small ribodomal subunit –tRNA complex initially bind?**

a) the 5’ end

b) the Shine-Dalgarno sequence seven nucleotides upstream from the initiation codon

c) the TATA box

d) the A site

e) the P site

**4) The polypeptide encoded by the rat secretin gene is much longer than functional secretin. Given the chemical properties of the first thirty two amino acids, what is the most probable function of those thirty two amino acids?**

a) They function as a signal peptide

b) They function in initiation of translation by positioning the ribosome at the Shine-Dalgarno initiation sequence

c) They function enzymatically in the processing of the quaternary structure of the functional secretin

d) They function as a segment that protects the amino acids of functional secretin from degradation.

**5) What is the sequence of the termination codon for the rat secretin gene?**

a) UAA

b) UAG

c) UGA

**6) In 1992, Jaruzelska et al. (Human Molecular Genetics 1:763-764) reported a deletion mutation of fifteen nucleotide pairs within exon 11 of the PAH gene. What should the polypeptide product of this mutant gene be when compared with functional phenylalanine hydroxylase (PAH)?**

a) It will not differ in amino acid sequence from functional PAH.

b) It will differ substantially from functional PAH because of a frameshift mutation.

c) It will contain a deletion of five amino acids when compared to functional PAH; all other amino acids will be identical.

**Use the following information to answer questions 7-9:**

In 1991, Huang et al.(Human Genetics 86:305-306) identified an A---T mutation in the third nucleotide of codon 399 (a GTA codon) in the PAH gene. (Notice that when referring to codons in DNA, we use T in place of U. Thus, a GTA codon in the sense strand of DNA corresponds to a GUA codon in the mRNA).

**7) Which of the following terms correctly describes this mutation?**

a) transition

b) transversion

c) deletion

d) insertion

**8) Which of the following terms describes this mutation?**

a) same-sense mutation

b) missense mutation

c) nonsense mutation

d) frameshift mutation

**9) Could this mutation cause PKU?**

a) yes

b) no

**10) In 1995, Leeflang et al. (Human Molecular Genetics 4:1519-1526) examined the DNA of the HD gene (formerly called the IT15 gene) in individual sperm cells from three individuals with Huntington Disease and two normal individuals. The HD gene contains a trinucleotide CAG repeat within the coding region. The researchers found that HD genes with fifteen to eighteen repeats rarely mutated. Among 475 genes examined, in this size range, they found only three mutations, all three contraction mutations. One of the genes examined contained thirty repeats. It tended to undergo expansion mutation with a frequency of eleven percent. Genes with thirty-eight to fifty-one repeats expanded at frequencies of ninety-two to ninety-nine percent. How does the pattern these researchers observed for the HD gene compare to the pattern observed for mutations in the FMR1 gene?**

a) The pattern is very similar; larger repeats are more prone to expansion in both the HD and the FMR1 gene.

b) The pattern is only slightly similar; both genes are prone to expansion. However, the number of repeats in the HD gene influences the potential for expansion while the number of repeats in the FMR1 gene has no influence on the potential for expansion.

c) The two patterns are not similar. The HD gene tends to undergo expansion mutation, whereas the FMR1 gene does not.

**The following information pertains to questions 11-15:**

In 1997, Martin et al. (Proceedings of the National Academy of Sciences, USA 94:8907-8911) described several mutations in the Le gene in peas, the gene that governs plant height that Mendel studied. A non protein plant growth hormone called gibberillic acid (GA1) regulates the height of pea plants. When adequate GA1 is present, the plants grow to their full height. When there is inadequate GA1, the plants fail to attain their full height and are considered as dwarf plants. The Le gene encodes the enzyme 3B-hydroxylase which converts GA20 into GA1. The researchers examined several mutant versions of the Le gene and we’ll look at two of them – le and led. When compared to the nonmutant Le gene, le has a single substitution mutation that causes an Ala---Thr substitution in the 229th amino acid of the polypeptide. When compared to the nonmutant Le gene, led has the same substitution mutation as le and a deletion of a single nucleotide pair codon 125.

**11) What is the substitution mutation in the sense strand of the mutant le version of the Le gene?**

a) A---G

b) G---A

c) T---C

d) C---T

**12) What is the most probable origin of the led mutant version of the gene?**

a) It arose from a trinucleotide expansion mutation that created a gain of function mutation.

b) It arose when the mutation codon in 229 eliminated intron splicing and left a mutant gene that contains the intron in place.

c) It arose from the mutant le version of the gene when a second mutation deleted a nucleotide pair.

**13) Of the two mutant types, le and led, one causes a more severe (shorter) dwarf phenotype than the other. Given the information that you have about this gene, which of the following choices best explains the relationship between the mutations and the dwarf phenotypes?**

a) Of the two mutations, led causes a more severe dwarf phenotype frameshift mutation in the coding region of the gene.

b) Of the two mutations, led causes a more severe dwarf phenotype than le because the deletion is downstream from the substitution.

c) Of the two mutations, le causes a more severe dwarf phenotype than led because le contains a frameshift mutation in the coding region of the gene.

d) Of the two mutations, le causes a more severe dwarf phenotype than led because the deletion is downstream from the substitution.

**14) Researchers found that in mutant le plants (dwarf plants), GA1 was greatly reduced and a substance that is very similar to GA1, called GA20 was highly elevated when compared to the levels of GA1 and GA20 in tall Le plants. They further discovered that if they sprayed young le plants with GA12, the plants grew tall, but when they sprayed young le plants with GA20, the plants grew as dwarfs just as if they had not been sprayed. Which of the following describes the correct relationship between GA1 and GA20 and the enzyme 3B-hydroxylase?**

a) GA1, precedes GA20 in the biochemical pathway and GA1 is the substrate of 3B-hydroxylase.

b) GA1 precedes GA20 in the biochemical pathway and GA20 is the substrate of 3B-nydroxylase.

c) GA20 precedes GA1 in the biochemical pathway and GA1 is the substrate of 3B-hydroxylase.

d) GA20 precedes GA1 in the biochemical pathway and GA20 is the substrate of 3B-hydroxylase.

**15) In what way does the le mutation alter the chemical properties of 3B-hydroxylase?**

a) It substitutes an uncharged polar amino acid for a non polar amino acid.

b) It substitutes a negatively charged amino acid for a non polar amino acid.

c) It substitutes a positively charged amino acid for a non polar amino acid.

d) It substitutes a non polar amino acid for an uncharged polar amino acid.

e) It substitutes a negatively charged amino acid for an uncharged polar amino acid.

f) It substitutes a positively charged amino acid for an uncharged polar amino acid.