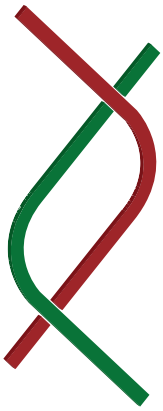
Animal Genetics

Solving Genetics Problems

Try to solve the problems from Classical Genetics. If you would have any troubles, look at the information sources in Internet:

- http://www.dnaftb.org/dnaftb/
- http://www.dnai.org/ -…

or from textbook Animal Genetics, or other sources.



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1. Classical Genetics

Cellular reproduction - mitosis and meiosis

1. A cross-shaped structure formed between nonsister homologous chromatids by crossing over that is visible during the diplonema stage of meiosis is called a _____.

2. The stage of meiosis at which synapsis occurs is called _____.

3. Four gametes result from a cell that has undergone meiosis. If the nuc1eus of the cell at pachynema had 5 picograms of DNA, the total amount of DNA in each gamete must be _____ picograms.

4. Segregation of homologous chromosomes occurs during _____ of meiosis.

5. A sunflower has a diploid chromosome number of 2n =34. How many chromatids are present in a secondary oocyte at prophase II?

6. A pair of synapsed chromosomes in the first meiotic division is called a _____.

7. The failure of a homologous chromosome pair to segregate during meiosis, therefore resulting in meiotic products with either an extra or a missing chromosome is called _____.

8. A human has 46 chromosomes in somatic (body) cells. How many chromatids are present in a secondary polar body nucleus?

9. A human cell has 46 total or 23 pairs of chromosomes. Following mitosis, the daughter cells would each have a total of _____ chromosomes. After meiosis I, the two daughter cells would have _____chromosomes, and after meiosis II _____ chromosomes.

    a) 46, 46, 46
    b) 46, 23, 23
    c) 23, 23, 23
    d) 46, 12, 12

10. Metaphase I of meiosis and mitosis differ in regard to the presence of _____.

11. For a human, the life cyc1e has the sequence

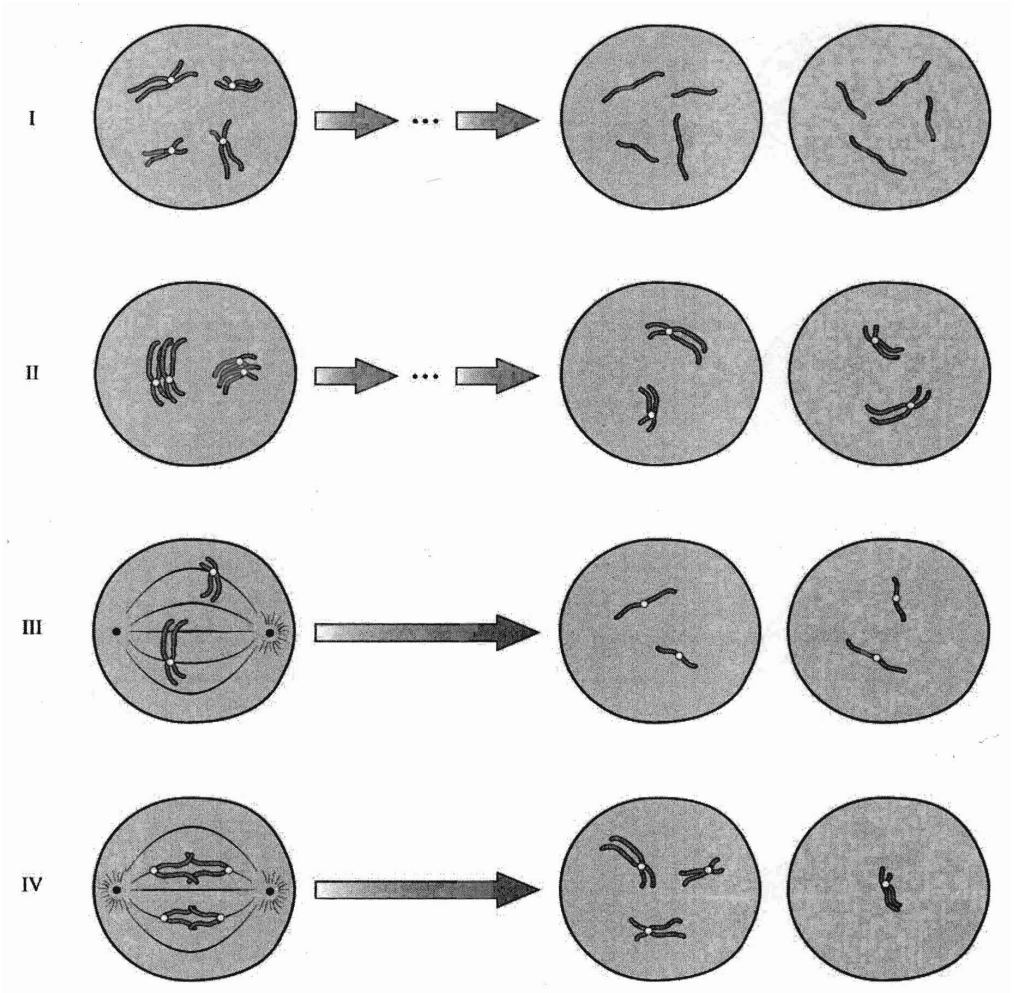
    a) 1n = 23 -> meiosis -> 2n = 46 -> fertilization -> ln = 23
    b) 2n = 46 -> meiosis -> 1n = 23 -> fertilization -> 2n = 46
    c) 1n = 23 -> mitosis -> 2n = 46 -> fertilization -> ln = 23
    d) 2n =46 -> mitosis -> 1n =23 -> fertilization -> 2n = 46

12. For each of the following stated phenomena, indicate whether it occurs in mitosis and/or meiosis and the phase or subphase at which it occurs.

    a) Chromosomes line up with their centromeres on the equatorial plate.
    b) DNA replication occurs.
    c) Homologous chromosomes undergo synapsis.
    d) Centromeres divide and sister chromosomes move to opposite poles.
    e) The cell is haploid and the chromosomes consist of one chromatid.
    f) Homologous chromosomes segregate to opposite poles.
    g) Nonsister homologous chromosomes undergo crossing over.
    h) The first appearance of haploid cells, with each chromosome consisting of two chromatids.
    i) Chromosomes are maximally condensed.
    j) Bivalents line up with their centromeres on either side of the equatorial plate.
    k) Chromatids are first visually recognized through a light microscope.

l) Two nuclei are formed, each identical to that which underwent division.
m) Independent assortment of chromosomes occurs.

13. Cells from a diploid organism (2n = 4) are shown undergoing division in the diagrams, (I), (II), (III), and (IV), shown below:



a) For each of the diagrams, state whether the division shown is mitosis, meiosis I, or meiosis II?

Division I: _____ Division III: _____

Division II: _____ Division IV: _____

b) Which diagrams show synapsed chromosomes?
c) Which of the above diagrams starts with a haploid cell?
d) In which diagram did segregation of both chromosome pairs occur?
e) What is the term that best describes the phenomenon that occurred in the division of diagram IV?

Thought challenging exercise

It is generally agreed that meiosis and fertilization evolved because they produce an enormous variety of new genetic combinations upon which evolutionary forces can act. Although most higher organisms have meiosis and fertilization as part of their reproductive cycle, some plants and animals skip meiosis and fertilization and reproduce parthenogenetically by the division and differentiation of a cell produced asexually by mitosis. Discuss possible reasons for the evolution of parthenogenesis from sexually reproducing populations.

Summary of key points

Cells, the basic units of all living things, are enclosed by membranes.

Chromosomes, the cellular structures that carry the genes, are composed of DNA, RNA, and protein.

In eukaryotes, chromosomes are contained within a membrane-bounded nucleus; in prokaryotes they are not.

Eukaryotic cells possess complex systems of internal membranes as well as membranous organelles such as mitochondria, chloroplasts, and endoplasmic reticulum.

Haploid eukaryotic cells possess one copy of each chromosome; diploid cells possess two copies.

Prokaryotic cells divide by fission; eukaryotic cells divide by mitosis and cytokinesis.

Eukaryotic chromosomes duplicate when a cells DNA is synthesized; this event, which precedes mitosis, is characteristic of the S phase of the cell cycle.

As a cell enters mitosis, it duplicated chromosomes condense into rod-shaped bodies (prophase).

As mitosis progresses, the chromosomes migrate to the equatorial plane of the cell (metaphase).

Later in mitosis, the centromere which holds the sister chromatids of a duplicated chromosome together splits, and the sister chromatids separate (or disjoin) from each other (anaphase).

As mitosis comes to an end, the chromosomes decondense and a nuclear membrane reforms around them (telophase).

Each daughter cell produced by mitosis and cytokinesis has the same set of chromosomes; thus, daughter cells are genetically identical.

Diploid eukaryotic cells form haploid cells by meiosis, a process involving one round of chromosome duplication followed by two cell divisions (meiosis I and meiosis II).

During meiosis I, homologous chromosomes pair (synapse), exchange material (cross over), and separate (disjoin) from each other.

During meiosis II, chromatids disjoin from each other.

In many organisms, the haploid products of meiosis develop directly into gametes.

Answers to questions and problems

1) chiasma 2) zygonema 3) 1.25 4) anaphase I 5) 34 6) bivalent 7) nondisjunction 8) 23 9) b 10) paired chromosomes (bivalents) at MI of meiosis 11) b 12) see answer in next section 13) a. mitosis, metaphase b. mitosis, prophase c. meiosis, prophase II d. mitosis, anaphase e. meiosis, anaphase I 14) a. (I) mitosis; (II) meiosis I; (III) meiosis II; (IV) meiosis I b. II, IV; c. III; d. II; e. nondisjunction.

Mendelism: The basic principle of inheritance

1. Alternative forms of genes are called _____.

2. Name the three rediscoverers of Mendel´s principles.

Monohybrid Cross Problem

Genetics is the study of heredity and variation in organisms. We begin with a study of the monohybrid cross, invented by Mendel. In a monohybrid cross, organisms differing in only one trait are crossed. Our objective is to understand the principles that govern inheritance in plants and animals, including humans, by solving problems related to the monohybrid cross.

3. In pea plants, spherical seeds (*S*) are dominant to dented seeds (*s*). In a genetic cross of two plants that are heterozygous for the seed shape trait, what fraction of the offspring should have spherical seeds?

    a) None
    b) 1/4
    c) 1/2
    d) 3/4

4. Mendel's First principle: A phenotypic ratio of 3:1 in the offspring of a mating of two organisms heterozygous for a single trait is expected when:

    a) the alleles segregate during meiosis.
    b) each allele contains two mutations.
    c) the alleles are identical.
    d) the alleles are incompletely dominant.
    e) only recessive traits are scored.

5. In Mendel's "Experiment 1," true-breeding pea plants with spherical seeds were crossed with true-breeding

plants with dented seeds. (Spherical seeds are the dominant characteristic.) Mendel collected the seeds from this cross, grew F1-generation plants, let them self-pollinate to form a second generation, and analyzed the seeds of the resulting F2 generation. The results that he obtained, and that you would predict for this experiment are:

a) 1/2 the F1 and 3/4 of the F2 generation seeds were spherical.
b) 1/2 the F1 and 1/4 of the F2 generation seeds were dented.
c) All of the F1 and F2 generation seeds were spherical.
d) 3/4 of the F1 and 9/16 of the F2 generation seeds were spherical.
e) All the F1 and 3/4 of the F2 generation seeds were spherical.

6. A cross of F1-hybrid plants: A genetic cross between two F1-hybrid pea plants for spherical seeds will yield what percent spherical-seeded plants in the F2 generation? (Recall, spherical-shaped seeds are dominant over dented seeds.)

a) 100%
b) 75%
c) 50%
d) 25%

7. The test cross: To identify the genotype of yellow-seeded pea plants as either homozygous dominant (*YY*) or heterozygous (*Yy*), you could do a test cross with plants of genotype _____.

a) *y*
b) *Y*
c) *yy*
d) *YY*

8. Predicting the results of a test cross: A test cross is used to determine if the genotype of a plant with the dominant phenotype is homozygous or heterozygous. If the unknown is homozygous, all of the offspring of the test cross have the _____ phenotype. If the unknown is heterozygous, half of the offspring will have the _____ phenotype.

a) dominant, incompletely dominant
b) recessive, dominant
c) dominant, epistatic
d) codominant, complimentary
e) dominant, recessive

9. Codominant alleles: The human AB0 markers: Human blood type is determined by codominant alleles. There are three different alleles, known as I^A, I^B, and *i*. The I^A and I^B alleles are co-dominant, and the i allele is recessive. The possible human phenotypes for blood group are type A, type B, type AB, and type O. Type A and B individuals can be either homozygous ($I^A I^A$ or $I^B I^B$, respectively), or heterozygous ($I^A i$ or $I^B i$, respectively). A woman with type A blood and a man with type B blood could potentially have offspring with which of the following blood types?

a) type A
b) type B
c) type AB
d) type 0
e) all of the above

Dihybrid Cross Problem Set

A dihybrid cross involves a study of inheritance patterns for organisms differing in two traits. Mendel invented the dihybrid cross to determine if different traits of pea plants, such as flower color and seed shape, were inherited independently. Our objective is to understand the principles that govern inheritance of different traits in a dihybrid cross that led Mendel to propose that alleles of different genes are assorted independently of one another during the formation of gametes.

10. Predicting combinations of alleles in gametes of plants heterozygous for two traits. A pea plant is heterozygous for both seed shape and seed color. *S* is the allele for the dominant, spherical shape characteristic; *s* is the allele for the recessive, dented shape characteristic. *Y* is the allele for the dominant, yellow color characteristic; *y* is the allele for the recessive, green color characteristic. What will be the distribution of these two alleles in this plant's gametes?

    a) 50% of gametes are *Sy*; 50% of gametes are *sY*;
    b) 25% of gametes are *SY*; 25% of gametes are *Sy*; 25% of gametes are *sY*; 25% of gametes are *sy*;
    c) 50% of gametes are *sy*; 50% of gametes are *SY;*
    d) 100% of the gametes are *SsYy*;
    e) 50% of gametes are *SsYy*; 50% of gametes are *SSYY*.

11. When does a phenotype ratio of 9:3:3:1 occur? A phenotype ratio of 9:3:3:1 in the offspring of a mating of two organisms heterozygous for two traits is expected when:

    a) the genes reside on the same chromosome
    b) each gene contains two mutations
    c) the gene pairs assort independently during meiosis
    d) only recessive traits are scored
    e) none of the above

12. A genetic cross yielding a 9:3:3:1 ratio of offspring. Which of the following genetic crosses would be predicted to give a phenotypic ratio of 9:3:3:1?

    a) *SSYY* × *ssyy*
    b) *SsYY* × *SSYy*
    c) *SsYy* × *SsYy*
    d) *SSyy* × *ssYY*
    e) *ssYY* × *ssyy*

13. Predicting gametes of an *SsYy* plant. The gametes of a plant of genotype *SsYy* should have the genotypes:

    a) *Ss* and *Yy*
    b) *SY* and *sy*
    c) *SY, Sy, sY,* and *sy*
    d) *Ss, Yy, SY* and *sy*
    e) *SS, ss, YY,* and *yy*

14. A *SsYy* × *ssyy* test cross. Which of the following genotypes would you not expect to find among the offspring of a *SsYy* × *ssyy* test cross:

    a) *ssyy*
    b) *SsYy*
    c) *Ssyy*
    d) *ssYy*
    e) *SsYY*

15. Homozygous offspring of a dihybrid cross. In a dihybrid cross, *AaBb* x *AaBb*, what fraction of the offspring will be homozygous for both recessive traits?

    a) 1/16
    b) 1/8
    c) 3/16
    d) 1/4
    e) 3/4

Summary of key points

Mendel studied the inheritance of seven different traits in garden peas, each trait being controlled by a different gene. Mendel's research led him to formulate three principles of inheritance: (1) the alleles of a gene are either dominant or recessive; (2) different alleles of a gene segregate from each other during the formation of gametes; and (3) the alleles

of different genes assort independently.

The outcome of a cross can be predicted by the systematic enumeration of the genotypes using a Punnett square.

When more than two genes are involved, the forked-line or probability method is used to predict the outcome of a cross.

Pedigrees are used to identify dominant and recessive traits in human families.

The analysis of pedigrees allows genetic counselors to assess the risk that an individual will inherit a particular trait.

Extension of Mendelism

16. The degree to which a genotype is expressed in the phenotype is called _____.

17. The multiple phenotypic effect of a gene is called _____.

18. The phenomenon occurring when a single-gene heterozygous genotype results in a phenotype intermediate to that of the two respective homozygous genotypes is called _____.

19. How many different genotypes can occur in a population for a gene that exists in 6 different allelic forms?

20. Epistasis influences:

    a) genotypic ratios
    b) segregation of alleles
    c) the kinds of gametes formed
    d) the phenotypic ratio
    e) none of the above

21. When black mice of a true-breeding (homozygous) line are crossed with mice from a truebreeding white line, all the F1s are black. The F2 generation consists of about 9 black: 3 brown: 4 white. This is an example of _____ interaction.

22. You are studying a disease in humans caused by a recessive allele and find that not all individuals who inherit two recessive alleles have the expected disease symptoms. Which genetic term is used to describe this phenomenon?

Summary of key points

Genes often have multiple alleles.

Mutant alleles may be dominant, recessive, incompletely dominant or codominant.

If a hybrid that inherited a recessive mutation from each of its parents has a mutant phenotype, then the recessive mutants are alleles of the same gene; if the hybrid has a wild phenotype, then the recessive mutations are alleles of different genes.

Most genes encode polypeptides.

ln homozygous condition, recessive mutations often abolish or diminish polypeptide activity.

Some dominant mutations produce a polypeptide that interferes with the activity of the polypeptide encoded by the wild-type allele of the gene.

Gene action is affected by biological and physical factors in the environment.

Two or more genes may determine a trait.

A mutant allele is epistatic to a mutant allele of another gene if it has an overriding effect on the phenotype.

A gene is pleiotropic if it influences many different phenotypes.

Chromosomal basic of Mendelism

23. The position a gene occupies on a chromosome is called a _____.

24. The X chromosome in mammals that is seen as a heterochromatin spot in an interphase nucleus is called a _____.

25. The person who first conclusively proved that a gene was located on a chromosome was _____.

26. A mammal with the 48 chromosomes, XXXY, would have _____ Barr bodies in somatic cell nuclei.

27. The person who discovered sex linkage in Drosophila was _____.

28. If female human has only one X chromosome, and abnormal phenotype results called _____ syndrome.

29. If a human male has two X chromosomes and a Y chromosome, an abnormal phenotype results called _____ syndrome.

30. An aberrant chromosomal condition in which a normally diploid cell has one copy of a chromosome and two copies of all others is called _____.

Summary of key points

Individual chromosomes become visible during cell division; between divisions they form in a diffuse network of fibers called chromatin.

Diploid somatic cells have twice as many chromosomes as haploid gametes.

The cells of males and females may have different numbers of X and Y sex chromosomes; however, the number of autosomes in these cells is the same.

Genes are located on chromosomes.

The disjunction of chromosomes during meiosis is responsible for the segregation and independent assortment of genes.

Nondisjunction during meiosis leads to abnormal numbers of chromosomes in gametes, and ultimately, in zygotes.

Linkage and crossing over

31. The linkage phase in which the dominant alleles of two genes are on one homologous chromosome and the two respective recessive alleles are on the other homolog is called _____.

32. The phenomenon of a crossover at one point inhibiting the formation of another crossover in an adjacent region is called _____.

33. The term describing genes located on the same chromosome is _____.

34. The linkage phase in which a dominate allele of one gene and a recessive allele of a second gene are found on one homolog and the respective recessive and dominant alleles are on the other homolog is called _____.

35. If in the hybrid, *Ef/eF*, crossing over occurs 40% of the time, then the frequency of the *E F* gamete will be _____.

36. A dihybrid plant, *Cc Dd*, is self-fertilized and the double recessive, *cc dd*, phenotype occurs in 4% of the progeny.

    a) What is the expected frequency of the *c D* gamete?
    b) What is the linkage phase of this dihybrid plant?

37. A mouse has a chromosome number 2n = 40. How many linkage groups does the mouse have?

Summary of key points

Linkage between two genes is detected as a deviation from expectations based on Mendel's Principle of Independent Assortment.

The frequency of recombination measures the intensity of linkage. In the absence of linkage, this frequency is 50 percent; for very tight linkage, it is close to zero.

Recombination is caused by the physical exchange between paired homologous chromosomes early in the prophase of the first meiotic division.

At any one point along a chromosome, the process of exchange (crossing over) involves only two of the four chromatids in a meiotic tetrad.

Late in prophase I, crossovers become visible as chiasmata.

The genetic maps of chromosomes are based on the average number of crossovers that occur during meiosis.

Genetic map distances are estimated by calculating the frequency of recombination between genes in experimental crosses.

Recombination frequencies less than 20 percent estimate map distance directly; however, recombination frequencies greater than 20 percent underestimate map distance because multiple crossover events do not always produce recombinant chromosomes.

An average of one chiasma during meiosis is equivalent to 50 centiMorgans of genetic map distance.

Recombination can bring favorable mutations together.

Chromosomal rearrangements, especially inversions, can suppress recombination.

Recombination is under genetic control.

Answers to questions and problems

1) alleles 2) dominance 3) d 4) a 5) e 6) d 7) c 8) e 9) e 10) b 11) c 12) c 13)c 14) e 15) a 16) expressivity 17) pleiotropy 18) partial or incomplete dominance 19) 21 20) d 21) recessive epistasis 22) reduced penetrance 23) locus 24) Barr body 25) Calvin Bridges 26) 2 27) Morgan 28) Turner 29) Klinefelter 30) trisomic 31) coupling/cis 32) interference 33) linkage 34) repulsion/trans 35) 10 36) a) The homozygous recessive phenotype (*cc dd*) occurred in a frequency of 4% or 0.04. Since the *cc dd* genotype results from the fusion of two *cd* gametes, the frequency of the *cd* gamete must be 0.2 , (02 x 0.2 = 0.04). This frequency is less than 0.25 and thus *cd* is a recombinant. The other recombinant gamete *CD* also should occur in a frequency of 0.2. This leaves 0.6 of the gametes as nonrecombinants. *cD* is one of the two nonrecombinant types. Its frequency is 0.3. b) From the calculations and reasoning involved in part a), we can assign the linkage phase of the dihybrid parent as *c D/C d*. This is the repulsed or trans linkage phase. 37) The number of linkage groups is determined by the number of different chromosomes. The mouse has (2n = 40; 1n= 20) 20 different chromosomes or 20 linkage groups.

2 Molecular Genetics

DNA and the Molecular Structure of Chromosomes

1. The basic building block of a nucleic acid is called a _____.

2. The proteins that are rich in basic amino acids and function in the initial packaging of DNA in eukaryotes are called _____.

3. The 11 nm by 6 nm particle that consists of an octomer of histones around which is coiled a 146-basepair-long sequence of DNA is called a _____.

4. If a double-stranded DNA molecule contains 15% guanine, it must contain _____ % thymine.

5. An enzyme that catalyzes the destruction of a DNA molecule by breaking phosphodiester bonds is called _____.

6. The two pyrimidines found in DNA are _____ and _____.

7. The purines found in DNA are _____ and _____.

8. If a double-stranded DNA molecule contains 12% cytosine, then it must contain _____ % guanine.

9. The pyrimidines found in RNA are _____ and _____.

10. A segment of DNA has the base-pair sequence

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ATGGCA
TACGGT
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How many hydrogen bonds occur in this six base-pair sequence?

11. A nucleic acid with the base composition of 45% adenine, 45% cytosine, 5% thymine and 5% guanine is:

    a) double-stranded DNA
    b) double-stranded RNA
    c) single-stranded DNA
    d) single-stranded RNA

12. A nucleic acid with the base composition of 30% adenine, 20% cytosine, 30% thymine and 20% guanine is:

    a) double-stranded DNA
    b) double-stranded RNA
    c) single-stranded DNA
    d) single-stranded RNA

13. A nucleic acid with a base composition of 22% adenine, 20% cytosine, 30% uracil and 28% guanine is:

    a) double-stranded DNA
    b) double-stranded RNA
    c) single-stranded DNA
    d) single-stranded RNA

14. The interphase chromatin consists of:

    a) supercoiled DNA molecules free of histones
    b) 30-nm fibers
    c) 10 nm-fibers and a scaffold of nonhistone proteins
    d) 10 nm-fibers consisting of DNA and histones

15. One strand of a DNA molecule has the following sequence 5'- ACGTATGA- 3'.

The complementary strand must be:

a) 5'-TGCATACT-3'
b) 5'-TCATACGT-3'
c) 5'-UCAUACGT-3'
d) 5'-ACGTATGA-3'

Summary of key points

The genetic material must perform three essential functions: the genotypic function-replication, the phenotypic function-gene expression, and the evolutionary function-mutation.

The genetic information of most living organisms is stored in deoxyribonucleic acid (DNA).

In some viruses, the genetic information is present in ribonucleic acid (RNA) - for example HIV viruses.

Viroids and prions are infectious naked molecules of RNA and protein, respectively.

DNA usually exists a s a double helix, with the two strands held together by hydrogen bonds between the complementary bases: adenine paired with thymine and guanine paired with cytosine.

The complementarity of the strands of a double helix makes DNA uniquely suited to store and transmit genetic information.

The two strands of a DNA double helix ha ve opposite chemical polarity.

RNA usually exists as a single-stranded molecule containing uracil instead of thymine.

The functional DNA molecules in cells are negatively supercoiled.

The DNA molecules in prokaryotic and viral chromosomes are organized into negatively supercoiled domains.

Bacterial chromosomes contain circular molecules of DNA segregated into about 50 domains.

Each eukaryotic chromosome contains one giant molecule of DNA packaged into 10-nm ellipsoidal beads called nucleosomes.

The condensed chromosomes that are present in mitosis and meiosis are composed of 30-nm chromatin fibers.

At metaphase, the 30-nm fibers are segregated in to domains by scaffolds composed of nonhistone chromosomal proteins.

The centromeres (spindle-fiber-attachment regions) and telomeres (termini) of chromosomes have unique structures that facilitate their functions.

Eukaryotic genomes contain repeated DNA sequences, with some sequences present a million times or more.

The DNA sequences in eukaryotic genomes are commonly· grouped into three classes: (1) unique or single-copy sequences present in one to a few copies per genome, (2) moderately repetitive sequences present in 10 to 105 copies, and (3) highly repetitive sequences present in over 105 copies per genome.

Two families of moderately repetitive transposable elements make up 10 percent of the human genome and play an important role in its evolution.

cleotide 2) histones 3) nucleosome 4) 35 5) nuclease 6) thymine and cytosine 7) adenine and guanine 8) 12 9) uracil and cytosine 10) There are two hydrogen bonds between adenine and thymine, and three hydrogen bonds between guanine and cytosine. Therefore, fifteen hydrogen bonds occur in the six base-pair sequence containing three A:T base pairs and three G:C base pairs. 11) c; In a double-stranded DNA molecule the number of purines (A + G) must equal the number of pyrimidines (C + T) and A= T and G = C. In this DNA there is 45% adenine and 5% thymine. Since A ≠ T, the DNA must be single-stranded. 12) a 13) d; This nucleic acid contains uracil instead of thymine; therefore, it must be RNA. Since A ≠ U, and C ≠ G, this RNA is single-stranded. 14) d 15) b; The strands of a DNA are held together by complementary base-pairs. The strands are also of opposite polarity. Therefore, the strand complementary to 5'-ACGTATGA-3' must be 3'-TGCATACT-5'.

Replication of DNA

1. The enzyme that catalyzes the formation of a covalent bond between the 5' and 3' ends of newly synthesized single strands of DNA during DNA replication is called _____.

2. The enzyme that replicates most of the DNA in *E. coli* that also has a proofreading function is _____.

3. During DNA replication of *E. coli*, the enzyme that removes RNA primers and replaces them with DNA is called _____.

4. The relatively short, single-stranded DNA fragments that are synthesized during discontinuous DNA

replication and joined together to forma continuous strand are called _____.

5. The enzyme that uncoils DNA into single strands prior to DNA replication is called _____.

6. The synthesis of the leading strand of DNA proceeds from ____ → ____ direction and the lagging strand is synthesized in the ____ → ____ direction.

7. Short RNA primers are synthesized during DNA replication by an enzyme called _____.

8. The enzyme that forms a phosphodiester bond between adjacent nucleotides, but does not extend the strand is called _____.

9. During DNA synthesis, the extended single strands of DNA are maintained by _____.

10. In eukaryotes, the DNA polymerase complex that also has primase activity, but is otherwise most similar to DNA polymerase III of prokaryotes is called _____.

11. In eukaryotes, the DNA polymerase that apparently catalyzes the replication of the leading strand is called _____.

Summary of key points

DNA replicates by a semiconservative mechanism: as the two complementary strands of a parental double helix unwind and separate, each serves as a template for the synthesis of a new complementary strand.

The hydrogen-bonding potentials of the bases in the template strands specify complementary base sequences in the nascent strands.

Replication is initiated at unique origins and usually proceeds bidirectionally from each origin.

DNA synthesis is catalyzed by enzymes called DNA polymerases.

All DNA polymerases. require a primer strand, which is extended, and a template strand, which is copied.

All DNA polymerases have an absolute requirement for a free 3'-0H on the primer strand, and all DNA synthesis occurs in the 5' to 3' direction.

The 3' → 5' exonuclease activities of DNA polymerases proofread nascent strands as they are synthesized, removing any mispaired nucleotides at the 3' termini of primer strands.

DNA replication is complex, requiring the participation of a large number of proteins.

DNA synthesis is continuous on the progeny strand that is being extended in the overall 5' → 3' direction, but is discontinuous on the strand growing in the overall 3' → 5' direction.

New DNA chains are initiated by short RNA primers synthesized by DNA primase.

The enzymes and DNA-binding proteins involved in replication assemble into a replisome at each replication fork and act in concert as the fork moves along the parental DNA molecule.

The large DNA molecules in eukaryotic chromosomes replicate bidirectionally from multiple origins.

Two or three DNA polymerases, (a, , and/ or €) are present at each replication fork in eukaryotes.

Telomeres, the unique sequences at the ends of chromosomes, are added to chromosomes by a unique enzyme called telomerase.

Answers to questions and problems

1) DNA ligase 2) DNA polymerase III 3) DNA polymerase I 4) Okazaki fragments 5) DNA helicase 6) 5' → 3'; 5' → 3' 7) DNA primase 8) DNA ligase 9) single-stranded DNA-binding proteins 10) DNA polymerase a 11) topoisomerases 12) DNA polymerase

Transcription and RNA processing

1. Noncoding intervening sequences in eukaryotic genes that interrupt the coding sequences are called _____.

2. A specific DNA sequence to which the RNA polymerase binds to start transcription is called a _____.

3. The molecule that transmits information, stored in the DNA of the nucleus, to the ribosomes in the cytoplasm where it is read is called _____.

4. The 3' end of a pre-mRNA is modified by the addition of a _____ tail.

5. In eukaryotes, the population of primary transcripts is called _____.

6. The conserved part of a promoter of eukaryotic genes that is centered at about thirty bases upstream of the transcription initiation site is called the _____.

7. The conserved part of the promoter of a eukaryotic gene that is located about eighty bases upstream of the transcription initiation site is called the _____.

8. The sequences of eukaryotic genes that code for amino acid sequences or RNA sequences of the processed gene product are called _____.

9. The eukaryotic enzyme complex that catalyzes the transcription of protein-coding genes is called _____.

10. The following is a partial sequence of a gene in humans with some of the upstream sequences:

    5′- TATAAAACGTGCATCGACGTACGATATCGCCGTACCGCTGCAC-3′

    3′- ATATTTTGCACGTAGCTGCATGCTATAGCGGCATGGCGACGTG-5′

    Indicate the RNA that is transcribed by RNA polymerase II from the portion of the gene shown.

Summary of key points

Metabolism occurs by sequences of enzyme-catalyzed reactions, with each enzyme specified by one or more genes.

The central dogma of molecular biology is that genetic information flows from DNA to DNA during chromosome replication, from DNA to RNA during transcription, and from RNA to protein during translation.

Transcription involves the synthesis of an RNA transcript complementary to one strand of DNA of a gene.

Translation is the conversion of information stored in the sequence of nucleotides in the RNA transcript into the sequence of amino acids in the polypeptide gene product, according to the specifications of the genetic code.

In eukaryotes, genes are present in the nucleus, whereas polypeptides are synthesized in the cytoplasm.

Messenger RNA molecules function as intermediaries that carry genetic information from DNA to the ribosomes, where proteins are synthesized.

RNA synthesis, catalyzed by RNA polymerases, is similar to DNA synthesis in plany respects.

RNA synthesis occurs within a localized region of strand separation, and only one strand of DNA functions as a template for RNA synthesis.

RNA synthesis occurs in three stages: (1) initiation, (2) elongation, and (3) termination.

RNA polymerases - the enzymes that catalyze transcription-are complex, multimeric proteins.

The covalent extension of RNA chains occurs within locally unwound segments of DNA.

Chain elongation stops when RNA polymerase encounters a transcription-termination signal.

Three different RNA polymerases are present in eukaryotes, and each polymerase transcribes a distinct set of genes.

Eukaryotic gene transcripts usually undergo three major modifications: (1) the addition of 7-methyl guanosine caps to the 5' termini, (2) the addition of poly(A) tails to the 3' ends, and (3) the excision of intron sequences.

The information content of some eukaryotic transcripts is altered by RNA editing, which changes the nucleotide sequences of transcripts prior to their translation.

Most, but not all, eukaryotic genes are split into coding sequences called exons and noncoding sequences called introns.

Some genes contain very large introns; others harbor large numbers of small introns.

The biological significance of introns is still open to debate.

Noncoding intron sequences are excised from RNA transcripts in the nucleus prior to their transport to the cytoplasm.

Introns in tRNA precursors are removed by the concerted action of a splicing endonuclease and ligase, whereas introns

in some rRNA precursors are spliced out autocatalytically - with no protein involved.

The introns in nuclear pre-mRNAs are excised on complex ribonucleoprotein structures called spliceosomes.

The intron excision process must be precise, with accuracy to the nucleotide level, to assure that codons in exons distal to introns are read correctly during translation.

Answers to questions and problems

1) introns 2) promoter 3) messenger RNA (mRNA) 4) poly (A) 5) heterogeneous nuclear RNA (hnRNA) 6) TATA box, Hogness box 7) CAAT box 8) exons 9) RNApolymerase II

10) The TATA box in eukaryotes is centered about 30 bp upstream of the point of transcription initiation. By analyzing the sequence of nucleotides in the portion of the gene indicated, the TATA box and the start point of transcription are found and indicated in hold face.

5'-**TATAAA**ACGTGCATCGACGTACGATATCGCCGT**A**CCGCTGCAC-3'

3'-ATATTTTGCACGTAGCTGCATGCTATAGCGGCA**T**GGCGACGTG-5'

5'-**A**CCGGUGCAC-3'

The base sequence of the mRNA transcribed from the DNA is shown complementary to the sense strand of the DNA double-helix.

Translation and the Genetic Code

Triplet nucleotide sequence of mRNA codons

UUU Phe	UCU Ser	UAU Tyr	UGU Cys
UUC Phe	UCC Ser	UAC Tyr	UGC Cys
UUA Leu	UCA Ser	UAA *Stop*	UGA *Stop*
UUG Leu	UCG Ser	UAG *Stop*	UGG Trp
CUU Leu	CCU Pro	CAU His	CGU Arg
CUC Leu	CCC Pro	CAC His	CGC Arg
CUA Leu	CCA Pro	CAA Gln	CGA Arg
CUG Leu	CCG Pro	CAG Gln	CGG Arg
AUU Ileu	ACU Thr	AAU Asn	AGU Ser
AUC Ileu	ACC Thr	AAC Asn	AGC Ser
AUA Ileu	ACA Thr	AAA Lys	AGA Arg
AUG Met/*I*	ACG Thr	AAG Lys	AGG Arg
GUU Val	GCU Ala	GAU Asp	GGU Gly
GUC Val	GCC Ala	GAC Asp	GGC Gly
GUA Val	GCA Ala	GAA Glu	GGA Gly
GUG Val	GCG Ala	GAG Glu	GGG Gly

1. A triplet of nucleotides in a tRNA that recognizes, by complementary base pairing, the triplets of nucleotides in the mRNA is called an _____.

2. A single base-pair change in a gene that results in a single amino acid substitution in the corresponding protein is called a _____ mutation.

3. A complex structure composed of protein and RNA molecules that functions as the site of amino acid polymerization is called a _____.

4. Which end (5' or 3') of an mRNA is synthesized first?

5. Which end of a polypeptide is the oldest (amino terminal or carboxyl terminal)?

6. If the anticodon in a tRNA is 3' - CCU - 5', what is the complementary sequence in the gene coding for this tRNA?

7. Which group of an amino acid covalently bonds to the tRNA?

8. A protein was sequenced in several mutant individuals. It was found that these mutants resulted in single amino acid substitutions at position number eight from the amino terminal end of the polypeptide. Arrows indicate the sequence in which the mutants were recovered. Assuming single nucleotide changes, indicate the most likely codon for each of the amino acids shown below.

Wild-type		mutant 1		mutant 2		mutant 3		mutant 4
Thr ____	→	Ala ____	→	Val ____	→	Met ____	→	Leu ____

9. A fragment of a polypeptide, Met-Leu-Ala-Gly, is encoded by the following sequence of DNA:

Strand A `-GTTACAACCGGCCA-`

Strand B `-CAATGTTGGCCGGT-`

   a) Which strand is the template strand?
   b) Indicate the 3' and 5' ends of the template strand of the DNA.
   c) Which polypeptide bond in the above polypeptide was formed first?
   d) Which amino acid is at the amino terminal end of the polypeptide?

10. The amino acid sequence of a protein encoded by two mutant alleles was compared to the amino acid sequence of the protein encoded by the normal gene.

	1	2	3	4	5	6	7	8
Normal	Met	Lys	Tyr	Ser	Glu	Trp	Val	Val
Mutant 1	Met	Lys	Tyr					
Mutant 2	Met	Lys	Tyr	Arg	Ser	Gly	Trp	

   a) Indicate the type of change at the mRNA level that resulted from mutant number 1 and the specific codon affected.
   b) Indicate the type of change at the mRNA level that resulted from mutant number 2, the initial codon affected, and which possible codons were utilized for each amino acid of the normal protein.

11. The following is a sequence of nucleotides in a DNA double helix that codes for a short polypeptide. The messenger RNA encoded by this DNA has both translational initiation and termination codons.

Strand A `AAATCAATAGTTAGAACCCATCTTG`

Strand B `TTTAGTTATCAATCTTGGGTAGAAC`

   a) Which strand is the template strand?
   b) What is the polarity of the strands of the DNA double helix?
   c) What is the base sequence of the mRNA coded by this DNA?
   d) What is the amino acid sequence of the polypeptide encoded by this mRNA?

Summary of key points

Most genes exert their effect(s) on the phenotype of an organism through proteins, which are large macromolecules composed of polypeptides.

Each polypeptide is a chain-like polymer assembled from different amino acids.

The amino acid sequence of each polypeptide is specified by the nucleotide sequence of a gene.

The vast functional diversity of proteins results in part from their complex three-dimensional structures.

Genetic information carried in the sequence of nucleotides in mRNA molecules is translated into sequences of amino acids in polypeptide gene products by intricate macromolecular machines called ribosomes.

The translation process is complex, requiring the participation of many different RNA and protein molecules.

Transfer RNA molecules serve as adaptors, mediating the interaction between amino acids and codons in mRNA.

The process of translation involves the initiation, elongation, and termination of polypeptide chains and is govemed by the specifications of the genetic code.

Each of the 20 amino acids in proteins is specified by one or more nucleotide triplets in mRNA.

Of the 64 possible triplets, given the four bases in mRNA, 61 specify amino acids and 3 signal chain termination.

The code is nonoverlapping, with each nucleotide part of a single codon, degenerate, with most amino acids specified by two or four codons, and ordered, with similar amino acids specified by related codons.

The genetic code is nearly universal; with minor exceptions, the 64 triplets have the same meaning in all organisms.

The wobble hypothesis explains how a single tRNA can respond to two or more degenerate codons.

Some suppressor mutations alter the anticodons of tRNAs so that the mutant tRNAs recognize chain termination codons and insert amino acids in response to their presence in mRNA molecules.

Comparisons of the nucleotide sequences of genes with the amino acid sequences of their polypeptide products have verified the codon assignments deduced from *in vitro* studies.

Answers to questions and problems

1) ATP 2) missense 3) ribosome 4) 5’ 5) amino terminal 6) 5’ GGA 3’ 7) carboxyl 8) ACG, GCG, GUG, AUG, UUG or CUG 9) a) strand A; b) 3’- GTTACAACCGGCCA- 5’; c) Met-Leu; d) Met

10) a) When you look at the product of mutant I, it is noticed that it is only a partial polypeptide. This suggests that a nonsense mutation may account for it. A single base substitution in the DNA could change a codon for serine to a nonsense codon, i.e., UCA → UGA, UCA → UAA, or UCG → UAG.

b) Mutant II has the first three amino acids in its polypeptide identical to that of the normal. The rest of the amino acids are different, suggesting that a single addition or deletion of a base has affected the reading frame. To determine what has happened and to deduce as much as possible about the codons utilized to produce the normal, start by inserting possible codons for the amino acids of the normal and mutant protein. When this is done we don’ t have to designate any changes in the first three codons. The mutant and normal differ, starting at the fourth position. A deletion of the U base of the serine codon UCG or the U/C base of the tyrosine codon shifts the reading frame one base to the right, so that the next codon is CGG for Arg.

Normal	Met	Lys	Tyr	Ser	Glu	Trp	Val	Val
	AUG	AAG	UAU	UCA	GAA	UGG	GUG	GU_
		A	C	G	G			
	AUG	AAG	UAU	CG G	AGU	GGG	UGG	
		A	C					
Mutant II	Met	Lys	Tyr	Arg	Ser	Gly	Trp	

The next codon is either AAU or AGU. Since the next amino acid in the mutant protein is serine, the codon must be AGU. The next codon is GGG for glycine, followed by UGG for tryptophan. The assignments of the frameshifted codons in many cases dictate the codons used for the normal protein. The codon assignments for the normal mRNA are Met (AUG) - Lys (AAG or AAA) - Tyr (UAU or UAC)- Ser (UCG)- Glu (GAA)- Trp (UGG)- Val (GUG)- Val (GUU, GUC, GUA, or GUC).

11) a) strand A; b) Strand A, 5’→ 3’; Strand B, 3’ → 5’; c) 5’-AUGGGUUCUAACUAUUGAUUU-3’; d) fMet-Gly-Ser-Asn-Tyr.

Mutation DNA

1. A single base pair change in a gene that results in a single amino acid substitution in the corresponding protein is called a _____ mutation.

2. Nitrous acid is mutagenic because it deaminates _____ to _____, and _____ to _____.

3. Which type of mutation may result if a single base pair is inserted or deleted in the DNA double helix?

4. A point mutation that results in premature termination of translation of the corresponding mRNA is called a _____ mutation.

5. A mutation of a DNA strand in which a purine replaces a pyrimidine and vice versa is called a _____.

6. A mutation of a DNA strand in which a different purine replaces a purine, and a pyrimidine replaces a pyrimidine is called a _____.

7. The base-pair sequence in a region of a gene coding for a polypeptide is:

   Strand A 3′–TTTACCACCCCTACCAGAACACTT–5′

   Strand B 5′–AAATGGTGGGGATGGTCTTGTGAA–3′

   a) If this gene codes for a polypeptide that contains three tryptophans, which strand is transcribed?
   b) What is the nucleotide sequence of the mRNA transcribed from this DNA?
   c) What is the polypeptide sequence of the protein translated from this mRNA?
   d) Hydroxylamine affects the bold-faced base pair and causes a mutation during DNA replication. What is the amino acid sequence of the polypeptide coded by the mutant gene?

8. The following is an eight amino acid sequence from the amino terminal end of a wild-type enzyme of *E. coli*.

   fMet - Trp - Cys- Trp - Gln -Leu - Asn - Trp - (aa)n

After treatment of the bacteria culture with an acridine, a mutant is isolated that lacks the enzyme activity. Only a partial polypeptide consisting of five amino acids is detected as the gene product in the mutant strain. The amino acid sequence is:

fMet- Gly - Ala - Gly - Asn

A culture of the mutant bacteria is grown in the presence of an acridine and a revertant with partial enzyme activity is recovered. The mutant had a normal sized polypeptide chain, differing from the wild-type in that it had different amino acids at positions two, three, four and five. The amino acid sequence of the partial revertent was:

fMet- Gly - Ala - Gly - Asn - Leu - Asn - Trp - (aa)n

Determine, as much as possible, the nucleotide sequence of the mRNA coding for the polypeptide of the wild-type, mutant and partial revertent strains.

Summary of key points

Mutations are heritable changes in the genetic material that provide the raw material for evolution.

Mutations occur in both germ-line and somatic cells, but only germ-line mutations are transmitted to progeny.

Mutations can occur spontaneously or be induced by mutagenic agents in the environment.

Mutation usually is a nonadaptive process in which an environmental stress simply selects organisms with preexisting, randomly occurring mutations.

Restoration of the wild-type phenotype in a mutant organism can result from either back mutation or a suppressor mutation.

The effects of mutations on the phenotypes of living organisms range from undetectable to lethal changes.

Most mutations exert their effects on phenotype by altering the amino acid sequences of polypeptides, the primary gene products.

The mutant polypeptides, in turn, cause blocks in metabolic pathways.

Mutations are induced by chemicals, ionizing irradiation, ultraviolet light, and endogenous transposable genetic elements.

Point mutations are of three types: (1) transitions - purine for purine and pyrimidine for pyrimidine substitutions; (2) transversions - purine for pyrimidine and pyrimidine for purine substitutions; and (3) frameshift mutations - additions or deletions of one or two nucleotide pairs, which alter the reading frame of the gene distal to the site of the mutation.

Multiple DNA repair systems have evolved to safeguard the integrity of genetic information in living organisms.

Each repair pathway corrects a certain type of damage in DNA.

Answers to questions and problems

1) missense 2) adenine to hypoxanthine and cytosine to uracil 3) frameshift 4) nonsense 5) transversion 6) transition

7) a) To solve this problem, first pick the DNA strand that has three triplets, ACC, that are complementary to the tryptophan codon, UGG. That is strand A.

b) Next transcribe strand A of the DNA to obtain the mRNA sequence:

5′-AAAUGGUGGGGAUGGUCUUGUGAA-3′

c) Translate this mRNA in the reading frame that results in three tryptophans in the resulting polypeptide

5’-AAA|UGG|UGG|GGA|UGG|UCU|UGU|GAA-3’

Lys Trp Trp Gly Trp Ser Cys Glu

d) Hydroxylamine reacts specifically with cytosine to form hydroxlyaminocytosine, which in turn pairs with adenine during DNA replication to cause CG→TA transitions. Therefore, if the boldfaced base pair is affected, the **C** will be substituted with **T** in the mutant.

G **A**

This will result in the following nucleotide sequence of the affected mRNA with just a single base change indicated by bold-facing: 5’- AAAUGGUGG**AGA**UGGUCUUGUGAA- 3’

The new codon AGA, resulting from the single base change, codes for Arg. Therefore, the amino acid sequence coded by the mutant gene is Lys Trp Trp **Arg** Trp Ser Cys Glu.

8) The key to solving this problem is knowing that acridines cause single base-pair additions or deletions in the DNA double helix. When these occur in the coding region of a gene they result in frameshift mutations. The next step is to indicate all possible codons for the amino acids of the wild type protein as follows:

fMet -	Trp -	Cys-	Trp -	Gln -	Leu -	Asn -	Trp -	(aa)n
AUG	UGG	UGU	UGG	CAA	UUA	AAU	UGG	
		UGC		CAG	UUG	AAC		
					CU_			

Compare the amino acid sequence of the mutant with that of the wild-type. Find the first amino acid at which they vary and see whether it is a single base addition or deletion that has caused the change in amino acid sequence.

The deletion of the U in the first Trp codon in the mRNA changes the reading frame to generate the codon GGU for Gly.

fMet- Gly - Ala - Gly - Asn
AUGUGGUGC

The codons for the amino acids of the mutant are determined by comparing to the possible wild-type codons and realizing that the reading frame has been shifted one base to the right. The nucleotide sequence of the mutant mRNA is therefore determined to be:

fMet- Gly - Ala - Gly - Asn
AUGUGGU GCU GGC AAU UGA AUUGG
C A C

The nonsense codon generated downstream from the initial point of the frameshift causes premature termination of translation of the mutant mRNA and only a polypeptide that is five amino acids long. The nucleotide sequence of the wild-type mRNA is:

fMet - Trp - Cys- Trp - Gln - Leu - Asn - Trp - (aa)n
AUG UGG UGC UGG CAA UUA AAU UGG
C G C

Only amino acids two through five differ between the partial reverent and the wild-type protein. The mutation that partially restored enzymatic activity was induced by an acridine. An addition of a base pair (AT in this case) in the gene and a U in the mRNA restored the correct reading frame.

fMet- **Gly**- **Ala**- **Gly**- **Asn** - Leu - Asn - Trp - (aa)n
AUG GGU GCU GGC AAU UUA AAU UGG
C G C