

advances in forensic science, and improvements in agriculture.

## 17.5 Genomics and Proteomics

Proteomics is the study of the entire set of proteins expressed by a given type of cell under certain environmental conditions. In a multicellular organism, different cell types will have different proteomes, and these will vary with changes in the environment. Unlike a genome, a proteome is dynamic and in constant flux, which makes it both more complicated and more useful than the knowledge of genomes alone.

Proteomics approaches rely on protein analysis; these techniques are constantly being upgraded. Proteomics has been used to study different types of cancer. Different biomarkers and protein signatures are being used to analyze each type of cancer. The future goal is to have a personalized treatment plan for each individual.

## REVIEW QUESTIONS

- How are GMOs created?
  - introducing recombinant DNA into an organism by any means
  - in vitro fertilization methods
  - mutagenesis
  - plant breeding techniques
- Which technique used to manipulate genetic material results in a significant increase in DNA or RNA fragments?
  - gel electrophoresis
  - nucleic acid extraction
  - nuclear hybridization
  - polymerase chain reaction (PCR)
- What is the role of the plasmid in molecular cloning?
  - They are used to create clones.
  - They are used as vectors to insert genes into bacteria.
  - They are a functional part of binary fission.
  - They contain the circular chromosome of prokaryotic organisms.
- What is meant by a recombinant DNA molecule?
  - chimeric molecules
  - bacteria transformed into another species
  - molecules that have been through the PCR process
  - the result of crossing over during cell reproduction
- Bt toxin is considered to be what?
  - a gene for modifying insect DNA
  - an organic insecticide produced by bacteria
  - useful for humans to fight against insects
  - a recombinant protein
- What is one trait of the Flavr Savr Tomato?
  - has a better shelf life
  - is not a variety of vine-ripened tomato in the supermarket
  - was not created to have better flavor
  - undergoes soft rot
- What is the first step in isolating DNA?
  - generating genomic DNA fragments with restriction endonucleases
  - introducing recombinant DNA into an organism by any means
  - overexpressing proteins in *E. coli*
  - lysing the cells in the sample
- What is genomics?
  - Genomics is the study of entire genomes, including the complete set of genes, their nucleotide sequence and organization, and their interactions within a species and with other species.
  - Genomics is the process of finding the locations of genes on each chromosome.
  - Genomics is an illustration that lists genes and their location on a chromosome.
  - Genomics is a genetic marker, a gene or sequence on a chromosome that co-segregates (shows genetic linkage) with a specific trait.
- What is required in addition to a genetic linkage map to build a complete picture of the genome?
  - a genetic marker
  - a physical map
  - linkage analysis of chromosomes
  - plasmids
- Genetic recombination occurs by which process?

- a. crossing over
  - b. chromosome segregation
  - c. independent assortment
  - d. sister chromatids
- 11.** Individual genetic maps in a given species are \_\_\_\_.
- a. genetically similar
  - b. genetically identical
  - c. genetically dissimilar
  - d. not useful in species analysis
- 12.** Information obtained by microscopic analysis of stained chromosomes is used in what procedure?
- a. cytogenetic mapping
  - b. radiation hybrid mapping
  - c. RFLP mapping
  - d. sequence mapping
- 13.** Which of the following is true about linkage analysis?
- a. It is used to create a physical map.
  - b. It is based on the natural recombination process.
  - c. It involves the breaking and re-joining of DNA artificially.
  - d. It requires radiation hybrid mapping.
- 14.** The chain termination method of sequencing uses what?
- a. labeled ddNTPs
  - b. only dideoxynucleotides
  - c. only deoxynucleotides
  - d. labeled dNTPs
- 15.** What sequencing technique is used to identify regions of similarity between cell types or species?
- a. dideoxy chain termination
  - b. proteins, DNA, or RNA sequence alignment
  - c. shotgun sequencing
  - d. whole-exome sequencing
- 16.** Whole-genome sequencing can be used for advances in what field?
- a. bioinformatics
  - b. iron industry
  - c. multimedia
  - d. the medical field
- 17.** Sequencing an individual person's genome \_\_\_\_.
- a. is currently impossible
  - b. helps in predicting faulty genes in diseases
  - c. will not lead to legal issues regarding discrimination and privacy
  - d. will not help make informed choices about medical treatment
- 18.** Genomics can be used in agriculture to do what?
- a. generate new hybrid strains
  - b. improve disease resistance
  - c. improve yield
  - d. improve yield and resistance and generate hybrids
- 19.** What are the uses of metagenomics?
- a. identification of biofuels
  - b. testing for multiple drug susceptibility in a population
  - c. use in increasing agricultural yields
  - d. identifying new species more rapidly and analyzing the effect of pollutants on the environment
- 20.** Genomics can be used on a personal level to do what?
- a. determine the risks of genetic diseases for an individual's children
  - b. increase transplant rejection
  - c. predict protein profile of a person
  - d. produce antibodies for an antigen
- 21.** What is the percentage of single gene defects causing disease in developed countries?
- a. 0.05
  - b. 0.1
  - c. 0.2
  - d. 0.4
- 22.** The rapid identification of new species and the analysis of the effect of pollutants on the environment is a function of what?
- a. metagenomics
  - b. linkage analysis
  - c. genomics
  - d. shotgun sequencing
- 23.** The risks of genetic diseases for an individual's children can be determined through \_\_\_\_.

- a. metagenomics
  - b. linkage analysis
  - c. genomics
  - d. shotgun sequencing
- 24.** What is a biomarker?
- a. the color coding of different genes
  - b. a protein uniquely produced in a diseased state
  - c. a molecule in the genome or proteome
  - d. a marker that is genetically inherited
- 25.** What is a metabolome?
- a. a provisional listing of the genome of a species
  - b. a unique metabolite used to identify an individual
  - c. a method used for protein analysis
  - d. the complete set of metabolites related to the genetic makeup of an organism
- 26.** How would you describe a set of proteins with altered expression levels?
- a. a group of biomarkers
  - b. a protein signature
  - c. the result of a defect in mRNA transcription
  - d. the results of crossing over during cell replication
- 27.** What is a protein signature?
- a. a protein expressed on the cell surface
  - b. a unique set of proteins present in a diseased state
  - c. the path followed by a protein after it is synthesized in the nucleus
  - d. the path followed by a protein in the cytoplasm
- 28.** What describes a protein that is uniquely produced in a diseased state?
- a. a genomic protein
  - b. a genetic defect
  - c. a chimeric molecule
  - d. a biomarker
- 29.** The metabolites that results from the anabolic and catabolic reactions of an organisms is called what?
- a. genetic metabolic profile
  - b. metabolic signature
  - c. metabolome
  - d. metagenomics

## CRITICAL THINKING QUESTIONS

- 30.** Describe the process of Southern blotting.
- a. Southern Blotting is used to find DNA sequences. Fragments are separated on gel, incubated with probes to check for the sequence of interest, and transferred to a nylon membrane.
  - b. Southern blotting is used to find DNA sequences. Fragments are separated on gel, transferred to a nylon membrane, and incubated with probes to check for the sequence of interest.
  - c. When RNA is used, the process is called Northern blotting.
  - d. Southern blotting is used to find RNA sequences. Fragments are separated on gel, incubated with probes to check for the sequence of interest, and transferred to a nylon membrane.
- 31.** A researcher wants to study cancer cells from a patient with breast cancer. Is cloning the cancer cells an option?
- a. The cancer cells should be cloned along with a biomarker for better detection and study.
  - b. The cells should be screened first in order to assure their carcinogenic nature.
  - c. The cancer cells, being clones of each other already, should directly be grown in a culture media and then studied.
  - d. The cancer cells should be extracted using the specific antibodies.
- 32.** Discuss the uses of genome mapping.
- a. Genome mapping is useful in identifying human disease-causing genes, developing microbes to clean up pollutants, and increasing crop yield.
  - b. Genome mapping is directly required to produce recombinants, in FISH detection, and detecting the methylated parts of genetic material.
  - c. Genome mapping is useful for knowing the pedigree of diseases in humans and tracing the movement of transposons in plants.
  - d. Genome mapping identifies human disease-causing genes only.

**33.** If you had a chance to get your genome sequenced, what are some questions you might be able to have answered about yourself?

- a. One can determine the drugs that can rectify a disease, symptoms of the disease and its severity.
- b. One can determine the ancestry and genetic origin of diseases and their susceptibility to drugs.
- c. One can predict the symptoms of a disease, the vectors to be used in gene therapy and the causal organism of the disease.
- d. One can determine the pedigree of a disease, produce recombinants and detect the presence of extracellular genes using FISH.

**34.** Describe an example of a genomic mapping method

- a. The radiation mapping method is an example which uses radiation to break the DNA and is affected by changes in recombination frequency.
- b. Cytogenetic mapping obtains information from microscopic analysis of stained chromosomes. It can estimate the approximate distance between markers.
- c. In restriction mapping, the DNA fragments are cut by using the restriction enzymes and then stained fragments are viewed on gel.
- d. Cytogenetic mapping obtains information from microscopic analysis of stained chromosomes. It can estimate the exact base pair distance between markers.

**35.** Describe three methods of gene sequencing.

- a. Chain termination method - automated sequencers are used to generate sequences of short fragments; Shotgun sequencing method - incorporation of ddNTP during DNA replication; Next-generation sequencing - cutting DNA into random fragments, sequencing using chain termination, and assembling overlapping sequences
- b. Chain termination method - incorporation of ddNTP during DNA replication; Shotgun sequencing method - cutting DNA into random fragments, sequencing using chain termination, and assembling overlapping sequences; Next-generation sequencing - automated sequencers are used to generate sequences of short fragments
- c. Chain termination method - incorporation of ddNTP during DNA replication; Shotgun sequencing method - automated sequencers are used to generate sequences of short fragments; Next-generation sequencing - cutting DNA into random fragments, sequencing using chain termination, and assembling overlapping sequences
- d. Chain termination method - automated sequencers are used to generate sequences of short fragments; Shotgun sequencing method - cutting DNA into random fragments, sequencing using chain termination, and assembling overlapping sequences; Next-generation sequencing - incorporation of ddNTP during DNA replication

**36.** What is the greatest challenge facing genome sequencing?

- a. the lack of resources and use of chemicals for the sequencing of the DNA fragments
- b. the ethical issues such as discrimination based on person's genetics
- c. the use of chemicals during the sequencing methods that could incorporate mutations
- d. the scientific issues, like conserving the human genome sequences

**37.** How is shotgun sequencing performed?

- a. The DNA is cut into fragments, sequencing is done using the chain termination method, fragments are analyzed to see the overlapping sequences, and the entire fragment is reformed.
- b. The DNA is cut into fragments, overlapping sequences are analyzed using a computer, sequencing is done using the chain termination method, and the DNA fragment is reformed.
- c. The DNA is cut into fragments, stained with fluorescent dye, sequenced using the chain termination method, fragments are analyzed to see the overlapping sequences, and the entire DNA fragment is reformed.
- d. The DNA is cut into fragments, sequencing is done using the chain termination method, the DNA is stained with fluorescent dye, and a computer is used to analyze and reform the entire DNA fragment.

**38.** Coumadin is a drug frequently given to prevent excessive blood clotting in stroke or heart attack patients, which could lead to another stroke or heart attack. Administration of the drug also can result in an overdose in some patients, depending on the liver function of a patient. How could pharmacogenomics be used to assist these patients?

- a. Pharmacogenomics will be able to provide a counter-acting drug to decrease the effect of Coumadin.
- b. Pharmacogenomics will test every patient for their sensitivity to the drug.
- c. Pharmacogenomics will not be able to provide any help to patients highly sensitive to the drug.
- d. Pharmacogenomics will provide an overdose to each patient to test for the symptoms of the drug.

**39.** Why is so much effort being poured into genome mapping applications?

- a. Genome mapping is necessary to know the base pair difference between the markers.
- b. The mapping would help scientists understand the role of proteins in specific organelles.
- c. The mapping technique identifies the role of transposons.
- d. Genome mapping helps identify faulty alleles, which could cause diseases.

**40.** What is the reason for studying mitochondrial genomics that is most directly important for humans?

- a. Mitochondria evolved from bacteria; therefore, their genome is important to study.
- b. Mitochondria undergo rapid mutation and it is essential that this pattern be studied.
- c. Mitochondria contain DNA, and it is passed on from mother to offspring, which renders it helpful in tracing genealogy.
- d. Mitochondria are the only ATP-producing organelles of the cell, thus their genome is important.

**41.** How can proteomics complement genomics?

- a. The genes are responsible to produce proteins and this implies that proteomics complements genomics.
- b. Genomics is responsible to decide the structure of the proteins, and, thereby, the result of proteomic studies.
- c. The genome is constant but the proteome is dynamic as different tissues possess the same genes but express different genes, thereby complementing genomics.
- d. The study of genes is incomplete without the study of their respective proteins and thus they complement each other.

**42.** How could a proteomic map of the human genome help find a cure for cancer?

- a. A genetic map could help in identifying genes that could counteract the cause of cancer.
- b. Metabolomics can be used to study the genes producing metabolites during cancer.
- c. Proteomics detects biomarkers whose expression is affected by the disease process.
- d. The mapping helps in analyzing the inheritance of cancer-causing genes.

**43.** What contributions have been made through the use of microbial genomics?

- a. Microbial genomics has provided various tools to study the psychological behaviors of organisms.
- b. Microbial genomics has been useful in producing antibiotics, enzymes, improved vaccines, disease treatments and advanced cleanup techniques.
- c. Microbial genomics has contributed resistance in other bacteria by horizontal and lateral gene transfer mechanisms.
- d. Microbial genomics has contributed to fighting global warming.

## TEST PREP FOR AP® COURSES

**44.** In separating DNA for genomic analysis, it is important to consider RNA contaminating the sample during the cell lysis step of a DNA extraction. Which is likely to cause what to occur?

- a. DNA separates into the supernatant.
- b. DNA is destroyed by the protease.
- c. DNA is unaffected by the RNA.
- d. DNA combines with the RNA.

**45.** There are many techniques for investigating human genomic disorders. Western blotting looks for protein, Eastern blotting looks for post-translational changes, Northern blotting looks at mRNA, and Southern blotting looks at DNA. If you were to look at sickle cell anemia, a disorder affecting hemoglobin produced in red blood cells, which technique would be the most useful in detecting polymorphism in a sample?

- a. Northern blotting
- b. Southern blotting
- c. Western blotting
- d. Eastern blotting

**46.** A population of insects were formally distinguished by a mix of colors on their thorax and legs. This population now appears to be split into 2 sub-groups, purple and orange-legged. Researchers hypothesize that the purple-legged group may be increasingly resistant to the Bt (*Bacillus thuringiensis*) toxin. Which idea supports this observation?

- a. transgenesis
- b. natural selection
- c. hybridization
- d. recombination

**47.** Describe the process of molecular cloning.

- a. The foreign DNA and plasmid are cut with the same restriction enzyme and DNA is inserted within the lacZ gene, whose product metabolizes lactose. The foreign DNA and vector are allowed to anneal. The vector is transferred to a bacterial host that is ampicillin sensitive and those with a disrupted lacZ gene show inability to metabolize X-gal.
- b. The foreign DNA and plasmid are denatured using high heat, and DNA is inserted within the lacZ gene, whose product metabolizes glucose. The foreign DNA and vector are allowed to anneal. The vector is transferred to a bacterial host that is ampicillin sensitive and disrupted lacZ gene will metabolize X-gal
- c. The foreign DNA and plasmid are cut with the same restriction enzyme and DNA is inserted randomly in the plasmid. The foreign DNA and vector are allowed to anneal. The vector is transferred to a bacterial host that is ampicillin sensitive and the disrupted lacZ gene shows inability to synthesize X-gal.
- d. The foreign DNA and plasmid are cut with the same restriction enzyme and DNA is inserted within the lacZ gene, whose product metabolizes lactose. The foreign DNA and vector are allowed to anneal. The vector is transformed into a viral host that is ampicillin sensitive and the disrupted lacZ gene show inability to synthesize X-gal.

**48.** There are three methods of creating maps to evaluate genomes: cytogenetic (staining chromosomes); radiation hybrid maps (fragments with x-rays); and sequence maps (comparing DNA sequences). Which of the following accurately describes the three methods?

- a. Cytogenetic mapping - stained sections of chromosomes are analyzed using microscope, the distance between genetic markers can be found; Radiation hybrid mapping - breaks DNA using radiation and is affected by recombination frequency; Sequence mapping - DNA sequencing technology used to create physical maps.
- b. Cytogenetic mapping - stained sections of chromosomes are analyzed using microscope, the approximate distance between genetic markers can be found; Radiation hybrid mapping - breaks DNA using radiation and is unaffected by recombination frequency; Sequence mapping - DNA sequencing technology used to create physical maps.
- c. Cytogenetic mapping - stained sections of chromosomes are analyzed using microscope, the distance in base pairs between genetic markers can be found; Radiation hybrid mapping - breaks DNA using radiation and is unaffected by recombination frequency; Sequence mapping - DNA sequencing technology used to create physical maps.
- d. Cytogenetic mapping - stained sections of chromosomes are analyzed using a telescope, the distance between genetic markers can be found; Radiation hybrid mapping - breaks DNA using radiation and is affected by recombination frequency; Sequence mapping - DNA sequencing technology used to create physical maps.

49. How many cells with different genetic variations are possible after a single round of meiosis?

- a. two
- b. three
- c. four
- d. eight

## SCIENCE PRACTICE CHALLENGE QUESTIONS

50. Prokaryotes have an adaptive strategy to identify and respond to viral infections. This strategy uses segments of the cyclic DNA called CRISPRs and genes encoding CRISPR-associated (cas) proteins. When a virus enters the cell, a strand of viral DNA is excised by a cas protein and inserted into the bacterial DNA in a CRISPR region. When the same viral DNA is encountered subsequently, this foreign DNA is targeted by cas proteins that carry RNA markers transcribed from the inserted segment. The cas proteins cleave the viral DNA. The bacteria “remember” the infectious agent, providing a form of immunity.

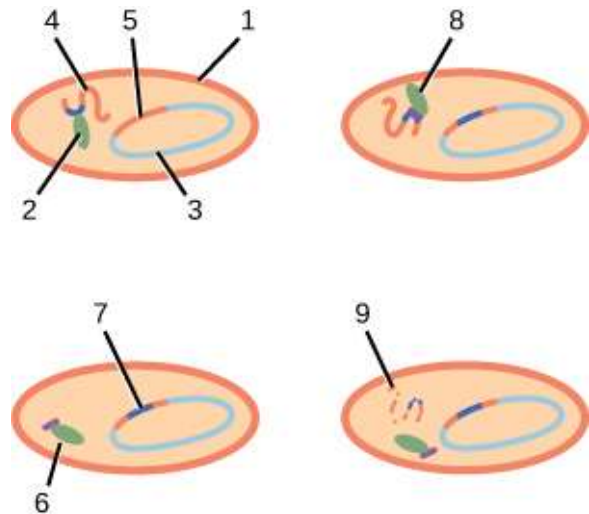


Figure 17.17

A. Use the diagram above to identify the components of a transcript-based response of bacteria to the presence of

viral DNA by placing the corresponding number next to each feature of the diagram:

\_\_\_ viral DNA \_\_\_ degraded viral DNA \_\_\_ cell membrane

\_\_\_ cellular DNA \_\_\_ cas protein \_\_\_ stored viral DNA template

\_\_\_ excised viral DNA \_\_\_ cas protein-RNA complex

\_\_\_ cas protein-RNA-viral DNA complex

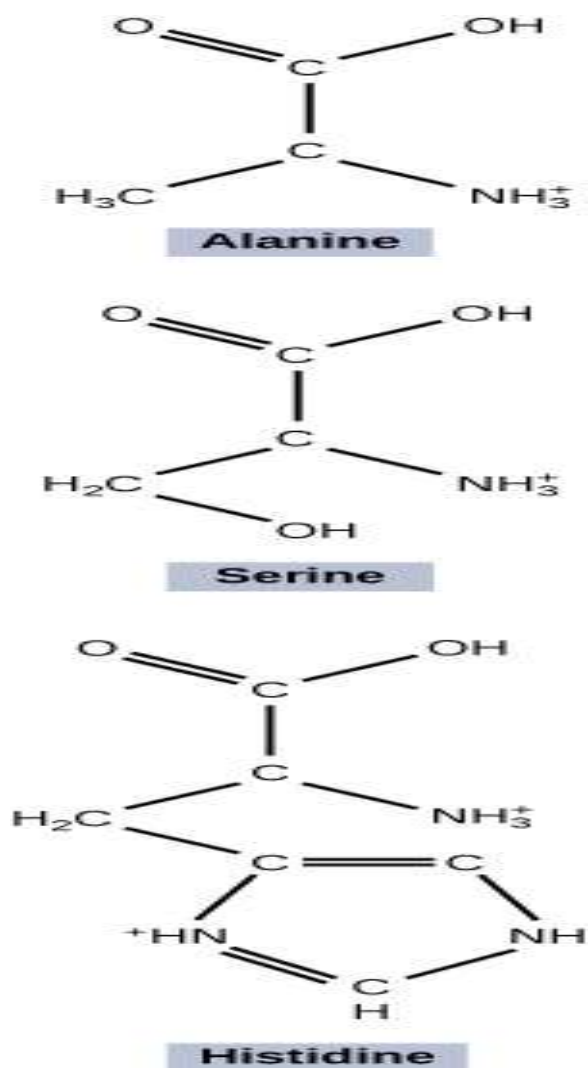
The CRISPR system was discovered in cultures of yogurt in 2002. Subsequently, researchers developed a technology based on the manipulation of this system. The code for the prokaryotic CRISPR/cas system is highly conserved and is found in the human genome. DNA sequences are known to encode proteins responsible for many heritable diseases. CRISPR/cas is a technology that allows DNA to be cleaved at the boundaries of a nucleotide sequence, making the protein dysfunctional. The break in the strand is then recognized and replaced with the code for the functional protein. If the editing is done with zygote-forming cells, the change is inherited. Not only the patient, but all progeny of the patient, are cured. This technology is the first to easily make genomic modifications of a germ line. In the words of a prominent molecular biologist, this technology, which was recognized as the *Breakthrough of 2015* in the journal *Science*, “democratizes genetic engineering.” Just as PCR became a standard, widely used tool, any molecular biology lab is now able to apply this technology.

**B. Pose three questions**—whose pursuit would require an understanding of genetics—regarding the ethical and social issues that accompany the use of this medical technology.

**C. Explain** the value of genetic variation within a population. **Predict** a possible effect that this technology could have, if unregulated, on human genetic variation.

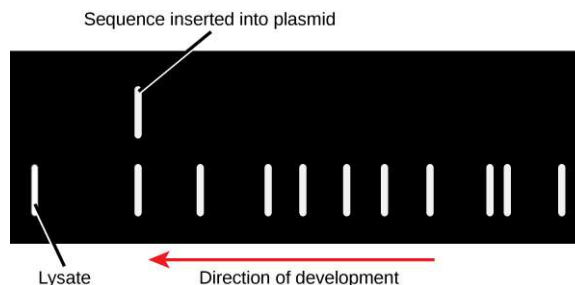
**51.** Gel electrophoresis of polymers and polymer fragments is an important element in many investigations. Samples of a solution are pipetted into the wells of a gel. The gel is placed in a solution that maintains a constant pH, and an electric field is applied over the length of the gel. Separated components are transferred to a substrate where they can be visualized and identified by comparison with samples of standards. Application of this method to DNA is called a Southern blot, named for the inventor of the technology. The method’s application to RNA is called a northern blot, another demonstration that biologist have fun (there are also western, eastern, and far-eastern blots, but these techniques are *not* named for their inventors).

A. Consider the three amino acids shown below and **explain** how, when pipetted into a gel and subjected to an electric field, the amino acids move; how the amino acids are separated as they move; and which amino acid moves furthest.



**Figure 17.18**

B. A biologist wants to determine whether a new protocol is successful in constructing and amplifying a molecular clone of a segment of DNA introduced as a plasmid. After the procedure is complete, the bacterial cells containing the plasmid with the inserted segment are lysed, and a gel is run into which samples of the lysate and the sequences to be cloned have been pipetted. Use the data displayed in the developed gel shown below to **evaluate the question** of whether the protocol was successful.



**Figure 17.19**



C. **Design a plan** to answer the question of whether the new DNA has been incorporated into the DNA of the host organism.

52. Genetic engineering can be applied to heritable information to produce what is referred to as a “knockdown organism.” Biotechnology also can be applied to produce nonheritable changes in a “knockdown gene.” Post-transcriptional strategies target the mRNA product of a gene. One such strategy uses the conserved genes that encode RNA interference (RNAi) proteins for the regulation of levels of mRNA transcription.

Some viral RNA is double stranded (dsRNA). A cell responds to the presence of double-stranded RNA by the attachment of the enzyme DICER, which cuts dsRNA into short fragments. One strand of the fragment is transferred to the RNA-induced silencing complex (RISC), which searches for an mRNA with a sequence matching that of the fragment strand. When detected, this mRNA is degraded.

A. Common in cancer cells is a mutation of the gene that encodes the protein p53, whose role is to detect and repair

errors in DNA; if repairs cannot be made, p53 initiates apoptosis. **Create a visual representation** to **explain** how the DICER-RISC system within the cell can be used to suppress the translation of a mutated form of the gene encoding p53, potentially destroying a tumor.

B. Whole-genome sequences provide a library of potentially expressed proteins, but they do not provide information on the functions of each protein. In an approach called reverse genetics, investigations attempt to determine the function of the gene, often by silencing the gene using RNAi technology. Assume that you have the ability to synthesize dsRNA from a DNA segment taken from an organism whose whole genome has been determined. **Design a plan** for collecting data that could be used to assign a function to the protein encoded by this sequence. (Hint: Don't worry about the number of experiments that might need to be conducted to implement your plan. An automated technique called high-throughput screening robotically supports thousands of simultaneous experiments.)