Microarray Simulations Using Simulated Red Imported Fire Ant Venom

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ACTIVITIES AT A GLANCE

Goal: This module is designed to educate students on the basics of microarray technology and how it is used in research and as a diagnostic tool. The paper simulation will involve the analysis of an experiment employing synthetic fire ant venom and a human cell line. A second activity will introduce bioinformatics principles employing the NCBI website. A third, wet lab will involve a fictitious patient treated with an experimental drug for breast cancer.

Learning Objectives:
Upon completion of this activity, students will have acquired an introduction to molecular biology and biotechnology, learn about DNA as a research and diagnostic tool to explore cellular processes, increase their understanding of biotechnology applications, and apply the process of inquiry and discovery-based research.

Prerequisite Skills:
Reading and interpretation of scientific literature.

Teaching Time:
90 minutes (3 class periods)

National Science Education Standards Addressed:

Timeline for Teaching Microarray Simulations Using Simulated Red Imported Fire Ant Venom

Order laboratory materials
Review Computer Lab to confirm website locations, structure.
Prepare solutions for wet lab; copy material for paper simulation.
Activity 1: Paper Microarray
Activity 2: Computer Lab for Bioinformatics
Activity 3: Wet Lab Microarray

8 weeks ahead 3 days ahead Day 1 Day 2 Day 3
OVERVIEW

In this activity, students will perform a paper simulation of a microarray experiment based on actual research conducted at the University of Mississippi Medical Center. DNA microarray analysis is a form of comparative hybridization in which experiments can identify genes whose transcription changes in response to an environmental stimulus. In a basic experiment, a population of cells is subjected to a stimulus and allowed to reach a steady state of transcription. Gene expression, that is, messenger RNA levels of specific genes, in the altered cells can then be compared to those in a control population.

Cell samples, both control and test, are obtained and the messenger RNA (mRNA) is isolated from the samples. The mRNA is used to make a DNA copy, called complementary DNA (cDNA) and color-coded with fluorescent tags. The mRNA/cDNA from the control cells is dyed green; the mRNA/cDNA from the experimentally treated cells is dyed red. The DNA copy is then applied to the microarray. A microarray consists of microscopic spots of DNA oligonucleotides about 80 nucleotides in length. Each sequence is specific for a gene. Most commercial microarrays contain several thousand spots corresponding to several thousand specific genes. The cDNA binds to complementary base pairs in spots on the array. This process is known as hybridization. Based on how the DNA binds together, each spot will appear red (increased in the experimental sample), green (increased in the control sample), or yellow (equal in the control and experimental samples, a combination of red and green) when scanned with a laser.

The effect of the synthetic alkaloid Solenopsin B (Sol B), a component of red imported fire ant venom was tested on the human cell line U937. The control cells were treated incubated in media containing diluent (compound used to dissolve a test substance) while the test cells were treated with Sol B in diluent. After a 4 hour exposure, the cells were lysed and the RNA was isolated. Control and test RNA was converted to cDNA, labeled with the dyes Cy3 (green for the control) and Cy5 (red for the Sol B). The cDNAs were combined and hybridized to a glass microarray slide containing expressed sequence tags (EST) from 15,000 genes.

The labeled molecules bind to the sites on the array corresponding to the genes expressed in each cell. After this hybridization step is complete, a researcher will place the microarray in a "reader" or "scanner" that consists of some lasers, a special microscope, and a camera. The fluorescent tags are excited by the laser, and the microscope and camera work together to create a digital image of the array. These data are then stored in a computer, and a special program is used either to calculate the red-to-green fluorescence ratio or to subtract out background data for each microarray spot by analyzing the digital image of the array. The program then creates a table that contains the ratios of the intensity of red-to-green fluorescence for every spot on the array.

Review the following website animations:
http://learn.genetics.utah.edu/units/pharma/phmicroarray/
http://learn.genetics.utah.edu/units/biotech/microarray/

Materials:
- Red card stock
- Green card stock
- Ziplock bags
- Tape or glue sticks
- Scissors
Activity 1: Solenopsin B treatment of U937 Cells

Teacher Directions for Paper Simulation
1. Copy the mRNA sequences on the appropriate color paper.
2. Cut out the strips for each group and insert into Ziplock bags.
3. Copy one DNA Chip per group.

Student Directions for Paper Simulation:
1. Obtain messenger RNA (mRNA) transcripts from control cells and from cells treated with solenopsin B (or any new potential chemotherapeutic agent). Each transcript represents a gene that was expressed in those cells. Some transcripts are rare and some are abundant.
2. You are going to simulate the action of the enzyme reverse transcriptase. You will make a cDNA strand from the pieces of mRNA that you have been given. Be sure to remember that cDNA contains the nitrogenous base thymine and not uracil.
3. Deprocess the mRNA by cutting it apart from the cDNA that you produced. KEEP the cDNA that you produced. Now you have a single strand of your target DNA.
4. Attach (hybridize) your cDNA to the spots on the sample microarray slide using tape. Where the target cDNA is not taped to the spot, fold it out of the way so that the other probe and target molecules in the sample have a chance to attach. Be sure that you have attached your molecules to those probes that are complementary to the probe sequences. Also remember that DNA is antiparallel.
5. For this activity we will assume that the temperature in the reaction is high enough for at least four bases in a row to be complementary to the bases in the probe DNA.
6. Discard and target cDNA that does not match any of the probes.
7. Identify which probes on the array were hybridized with RED, GREEN, OR BOTH, tagged DNA pieces.
8. Were there any cDNA transcripts that were rare? Were there any that were abundant?
   a. What does this tell you about the levels of these genes that are switched on in control cells as compared with those in treated cells? Gene expression switched on and a specific medical condition.
### Control Cell mRNA (Green label)

<table>
<thead>
<tr>
<th>mRNA Sequence (5’→3’)</th>
<th>cDNA sequence (3’→5’)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5’gcggcacgg guauggcagg</td>
<td>3’cgccgtgcc cataccgtcc</td>
</tr>
<tr>
<td>G6pd</td>
<td></td>
</tr>
<tr>
<td>5’ucaucguugg ggcgcggccag</td>
<td>3’aggtagcacc cgcgggtct</td>
</tr>
<tr>
<td>ACTB</td>
<td></td>
</tr>
<tr>
<td>5’ucaucguugg ggcgcggccag</td>
<td>3’aggtagcacc cgcgggtct</td>
</tr>
<tr>
<td>ACTB</td>
<td></td>
</tr>
<tr>
<td>5’gcggcacgg guauggcagg</td>
<td>3’cgccgtgcc cataccgtcc</td>
</tr>
<tr>
<td>G6PD</td>
<td></td>
</tr>
<tr>
<td>5’ucaucguugg ggcgcggccag</td>
<td>3’aggtgaccc cgcgggtct</td>
</tr>
<tr>
<td>ACTB</td>
<td></td>
</tr>
<tr>
<td>5’auauuguugc ugcuugggcu</td>
<td>3’ataaacaacg acgacccaga</td>
</tr>
<tr>
<td>ALODA</td>
<td></td>
</tr>
<tr>
<td>5’auauuguugc ugcuugggcu</td>
<td>3’ataaacaacg acgacccaga</td>
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<tr>
<td>ALODA</td>
<td></td>
</tr>
<tr>
<td>5’auauuguugc ugcuugggcu</td>
<td>3’ataaacaacg acgacccaga</td>
</tr>
<tr>
<td>ALODA</td>
<td></td>
</tr>
<tr>
<td>5’caggaucgg ucuggaaacu</td>
<td>3’gtccccagcc agaccttga</td>
</tr>
<tr>
<td>TNFRSF19</td>
<td></td>
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</table>
## Sol B Treated Cell mRNA (Green label)

<table>
<thead>
<tr>
<th>mRNA</th>
<th>cDNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>5’acgaacaucccgauuaugg</td>
<td>3’tgttgtgtagagctaatc</td>
</tr>
<tr>
<td>ACIN1</td>
<td></td>
</tr>
<tr>
<td>5’caggacccag gagaggaag</td>
<td>3’gtctggtgctctctct</td>
</tr>
<tr>
<td>CASPASE 4</td>
<td></td>
</tr>
<tr>
<td>5’caggacccag gagaggaag</td>
<td>3’gtctggtgctctctct</td>
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<tr>
<td>CASPASE 4</td>
<td></td>
</tr>
<tr>
<td>5’cccagucgc ucugagagg</td>
<td>3’gggtagcgcacactctcc</td>
</tr>
<tr>
<td>AXIN1</td>
<td></td>
</tr>
<tr>
<td>5’auuugacaaaaauggaaaaaa</td>
<td>3’taaactgtttactttttt</td>
</tr>
<tr>
<td>CASPASE 8</td>
<td></td>
</tr>
<tr>
<td>5’auuugacaaaaauggaaaaaa</td>
<td>3’taaactgtttactttttt</td>
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<tr>
<td>CASPASE 8</td>
<td></td>
</tr>
<tr>
<td>5’ucggccccgc gcgaagccccc</td>
<td>3’agccggggcccttccgg</td>
</tr>
<tr>
<td>DAP</td>
<td></td>
</tr>
<tr>
<td>5’cagggauccg ucugaaacu</td>
<td>3’gtccctagccagacctttt</td>
</tr>
<tr>
<td>TNFRSF19</td>
<td></td>
</tr>
<tr>
<td>5’cgccggcccg cgcugccagc</td>
<td>3’gcgggggagcgacgggtc</td>
</tr>
<tr>
<td>SIAH2</td>
<td></td>
</tr>
<tr>
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<td>3’gcgggtgccacctccgu</td>
</tr>
<tr>
<td>G6PD</td>
<td></td>
</tr>
</tbody>
</table>
Simulated Microarray

ACIN1
5’acgaacatct ccgattatgg

Caspase 4 (NLRP1)
5’caggacccag gagaggaag

AXIN1
5’cccagtgcct ggtgaggagg

Caspase 8 (CARD8)
5’atttgacaaa tggaaaaaa

DAP
5’tcggccccgc ggaagccccg

TNFRSF19
5’cagggatcgg tctggaaact

SIAH2
5’cggccccctg cgctgccagc

G6PD
5’gcggcagcgg gtatggcagg

ACTB
5’tccatctgg ggcgccccag

ALDOA
5’tatggttgc tgctggtgt
<table>
<thead>
<tr>
<th>mRNA Sequence (5’→3’)</th>
<th>cDNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>5’ gcggcagcgg guauggcagg</td>
<td></td>
</tr>
<tr>
<td>5’ uccaucgugg ggccgcccag</td>
<td></td>
</tr>
<tr>
<td>5’ uccaucgugg ggccgcccag</td>
<td></td>
</tr>
<tr>
<td>5’ gcggcagcgg guauggcagg</td>
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</tr>
<tr>
<td>5’ gcggcagcgg guauggcagg</td>
<td></td>
</tr>
<tr>
<td>5’ uauuuguugc ugcugggucu</td>
<td></td>
</tr>
<tr>
<td>5’ uauuuguugc ugcugggucu</td>
<td></td>
</tr>
<tr>
<td>5’ uauuuguugc ugcugggucu</td>
<td></td>
</tr>
<tr>
<td>5’ cagggauucg ucuggaaacu</td>
<td></td>
</tr>
<tr>
<td>mRNA</td>
<td>cDNA</td>
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<td>-------------------------------------------</td>
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<tr>
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<td></td>
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<tr>
<td>5’cgcccccccgugcgcugccgcg</td>
<td></td>
</tr>
<tr>
<td>5’gcggcgagccggguuccggccgcg</td>
<td></td>
</tr>
</tbody>
</table>
Activity 2: Bioinformatics

COMPUTER SEARCH OF GENE FUNCTION AND BIOLOGICAL PROCESSES

The purpose of this activity is to determine the function of the genes from the paper microarray that have been upregulated. By determining the gene function and the biological process they are involved in, it is possible to determine what is happening to the cell.

TEACHERS ANSWER KEY

<table>
<thead>
<tr>
<th>Gene Symbol</th>
<th>Gene Name</th>
<th>Chromosome location</th>
<th>Gene Function</th>
<th>Biological Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACIN1</td>
<td>Apoptotic chromatin condensation inducer</td>
<td>Chromosome 14; location 14q11.2</td>
<td>ATPase activity</td>
<td>Apoptosis</td>
</tr>
<tr>
<td>AXIN1</td>
<td>AXIN1</td>
<td>Chromosome 16 Location 16p 13.3</td>
<td>ISMAD Binding</td>
<td>Wnt receptor signaling pathway/Apoptosis</td>
</tr>
<tr>
<td>DAP</td>
<td>Death Associated Protein</td>
<td>Chromosome 5; Location 5p15.2</td>
<td>Apoptosis</td>
<td>Apoptosis</td>
</tr>
<tr>
<td>DAP3</td>
<td>Death Associated Protein 3</td>
<td>Chromosome 1q21-q22</td>
<td>Protein binding</td>
<td>Apoptotic mitochondrial changes</td>
</tr>
<tr>
<td>SIAH2</td>
<td>Seven in absentia homolog2</td>
<td>Chromosome 3; Location 3q25</td>
<td>Ligase activity</td>
<td>Apoptosis</td>
</tr>
<tr>
<td>TNFRSF19</td>
<td>Tumor necrosis factor receptor superfamily member 19</td>
<td>Chromosome 13 Location 13q12.11-q12.3</td>
<td>Protein binding</td>
<td>JNK cascade</td>
</tr>
<tr>
<td>CASP4</td>
<td>Apoptosis related cysteine peptidase</td>
<td>Chromosome 11 Location 11q22.2q 22.3</td>
<td>Cysteine type endopeptidase activity</td>
<td>Induction of apoptosis</td>
</tr>
<tr>
<td>CASP8</td>
<td>Caspase 8 apoptosis related cysteine peptidase</td>
<td>Chromosome 2 Location 2 q33-q34</td>
<td>Cysteine type endopeptidase</td>
<td>Pro-apoptotic gene products</td>
</tr>
<tr>
<td>G6PD</td>
<td>Glucose 6 phosphate dehydrogenase</td>
<td>Chromosome X</td>
<td>NADP or NADPH binding</td>
<td>Carbohydrate metabolic process</td>
</tr>
<tr>
<td>ACTB</td>
<td>Actin, beta</td>
<td>Chromosome 7; p15-p12</td>
<td>ATP binding</td>
<td>Cell motion</td>
</tr>
<tr>
<td>ALDOA</td>
<td>Aldolase A</td>
<td>Chromosome 16; Location 16 p 11.2</td>
<td>Actin binding</td>
<td>ATP biosynthesis</td>
</tr>
</tbody>
</table>
1. The genes listed in the table above are all up regulated in human cells in response to solenopsin B. Fill in the columns of the table using the following internet resources.

3. Scroll down page to “Access to GenBank”
4. Click on dbEST (Expressed Sequence Tags).
5. Type gene symbol into search box, click “GO”.

![NCBI GenBank](image-url)
6. On the nucleotide results page, click on the gene from *Homo sapiens*.

7. On the Entrez Gene page, you will find the official name of the gene.

8. Scroll down to the section “Genomic context” to find the chromosomal location of the gene.

9. Continue to scroll down the page until you reach “Gene Ontology.”

10. List the functions and processes of the gene.
Once you have completed the chart, answer the following questions.

1. What is the most likely outcome for a cell with increased expression of these genes?

2. How do cells die?

3. What is the difference between apoptosis and necrosis?

4. What role do the caspases play in the initiation of apoptosis?
Curriculum Framework Standards:

Biology and Biomedical Research

Biology I and II are laboratory-based courses that continue the study of life. The units studied will include biochemical life processes; molecular basis of heredity; natural selection and populations; behavior patterns; and advanced classification and organism studies. Critical thinking skills, projects, research, and group laboratory activities will be emphasized in each unit. Biology II teachers are also encouraged to explore additional advanced topics along with these listed competencies. The competencies are printed in bold face type.

Biology II

1. Utilize critical thinking and scientific problem solving in designing and performing biological research and experimentation. (L, P, E)
   a. Demonstrate the proper use and care for scientific equipment used in biology.
   b. Observe and practice safe procedures in the classroom and laboratory.
   c. Apply the components of scientific processes and methods in the classroom and laboratory investigations.
   d. Communicate results of scientific investigations in oral, written, and graphic form.

2. Investigate chemical processes of the cell that maintain life. (L, P)
   a. Relate chemical structure and characteristics of organic compounds to cell and organism functions.
   b. Investigate enzymatic reactions and identify factors that influence enzyme activity.

3. Explore the molecular basis of heredity. (L, P)
   b. Analyze DNA/RNA/enzyme roles in the stages of protein synthesis.

Biology I:

3. Investigate cell structures, functions, and methods of reproduction. (L)
   a. Differentiate between prokaryotic and eukaryotic cells.

5. Investigate the principles, mechanisms, and methodology of classical and molecular genetics. (L, P)
   b. Identify and illustrate how changes in DNA cause mutations and evaluate the significance of these changes.

Biomedical Research

Biomedical Research is an inquiry-based, technology-oriented, and laboratory intensive elective course that prepares students to participate in professional biomedical research activities at the university level. Major areas of study include electronic access to international biomedical literature data bases, use of the Internet to communicate with biomedical researchers and other students at remote sites, contemporary ethical considerations in the conduct and publication of research, fundamentals of molecular biology and genetics, classification and nomenclature for organic chemical reactions, and elements of cellular and human physiology.

9. Demonstrate proficiency in the application of fundamental technical procedures related to biomedical laboratory research activities. (L, P)
   a. Acquire the skills necessary to set up, operate, and interpret the results from the use of the laboratory spectrophotometer.
   b. Determine quantitatively the concentration of a solute in a solution, using the spectrophotometer.
NATIONAL SCIENCE STANDARDS

SCIENCE AS INQUIRY

Content Standard A:

As a result of activities in grades 9-12, all students should develop:

- **ABILITIES NECESSARY TO DO SCIENTIFIC INQUIRY**
  - IDENTIFY QUESTIONS AND CONCEPTS THAT GUIDE SCIENTIFIC INVESTIGATIONS. Students should formulate a testable hypothesis and demonstrate the logical connections between the scientific concepts guiding a hypothesis and the design of an experiment. They should demonstrate appropriate procedures, a knowledge base, and conceptual understanding of scientific investigations.
  - DESIGN AND CONDUCT SCIENTIFIC INVESTIGATIONS. Designing and conducting a scientific investigation requires introduction to the major concepts in the area being investigated, proper equipment, safety precautions, assistance with methodological problems, recommendations for use of technologies, clarification of ideas that guide the inquiry, and scientific knowledge obtained from sources other than the actual investigation. The investigation may also require student clarification of the question, method, controls, and variables; student organization and display of data; student revision of methods and explanations; and a public presentation of the results with a critical response from peers. Regardless of the scientific investigation performed, students must use evidence, apply logic, and construct an argument for their proposed explanations.
  - FORMULATE AND REVISE SCIENTIFIC EXPLANATIONS AND MODELS USING LOGIC AND EVIDENCE. Student inquiries should culminate in formulating an explanation or model. Models should be physical, conceptual, and mathematical. In the process of answering the questions, the students should engage in discussions and arguments that result in the revision of their explanations. These discussions should be based on scientific knowledge, the use of logic, and evidence from their investigation.
  - RECOGNIZE AND ANALYZE ALTERNATIVE EXPLANATIONS AND MODELS. This aspect of the standard emphasizes the critical abilities of analyzing an argument by reviewing current scientific understanding, weighing the evidence, and examining the logic so as to decide which explanations and models are best. In other words, although there may be several plausible explanations, they do not all have equal weight. Students should be able to use scientific criteria to find the preferred explanations.

LIFE SCIENCE

CONTENT STANDARD C:

As a result of their activities in grades 9-12, all students should develop understanding of
The cell

- Cells have particular structures that underlie their functions. Every cell is surrounded by a membrane that separates it from the outside world. Inside the cell is a concentrated mixture of thousands of different molecules which form a variety of specialized structures that carry out such cell functions as energy production, transport of molecules, waste disposal, synthesis of new molecules, and the storage of genetic material.

- Cell functions are regulated. Regulation occurs both through changes in the activity of the functions performed by proteins and through the selective expression of individual genes. This regulation allows cells to respond to their environment and to control and coordinate cell growth and division.

CONTENT STANDARD E:

As a result of activities in grades 9-12, all students should develop

- Abilities of technological design
- Understandings about science and technology

HISTORY AND NATURE OF SCIENCE

CONTENT STANDARD G:

As a result of activities in grades 9-12, all students should develop understanding of

- Science as a human endeavor
  - Individuals and teams have contributed and will continue to contribute to the scientific enterprise. Doing science or engineering can be as simple as an individual conducting field studies or as complex as hundreds of people working on a major scientific question or technological problem. Pursuing science as a career or as a hobby can be both fascinating and intellectually rewarding.

  - Scientists have ethical traditions. Scientists value peer review, truthful reporting about the methods and outcomes of investigations, and making public the results of work. Violations of such norms do occur, but scientists responsible for such violations are censured by their peers.

  - Scientists are influenced by societal, cultural, and personal beliefs and ways of viewing the world. Science is not separate from society but rather science is a part of society.

- Nature of scientific knowledge
  - Science distinguishes itself from other ways of knowing and from other bodies of knowledge through the use of empirical standards, logical arguments, and skepticism, as scientists strive for the best possible explanations about the natural world.

  - Scientific explanations must meet certain criteria. First and foremost, they must be consistent with experimental and observational evidence about nature, and must make accurate predictions, when appropriate, about systems being studied. They should also be logical, respect the rules of evidence, be open to criticism, report methods and procedures, and make knowledge public. Explanations on how the natural world changes based on
myths, personal beliefs, religious values, mystical inspiration, superstition, or authority may be personally useful and socially relevant, but they are not scientific.

- Because all scientific ideas depend on experimental and observational confirmation, all scientific knowledge is, in principle, subject to change as new evidence becomes available. The core ideas of science such as the conservation of energy or the laws of motion have been subjected to a wide variety of confirmations and are therefore unlikely to change in the areas in which they have been tested. In areas where data or understanding are incomplete, such as the details of human evolution or questions surrounding global warming, new data may well lead to changes in current ideas or resolve current conflicts. In situations where information is still fragmentary, it is normal for scientific ideas to be incomplete, but this is also where the opportunity for making advances may be greatest.
Section One: DNA and RNA

1. The term used to describe the arrangement of the individual strands in the double stranded DNA molecules is:
   a. parallel
   b. antiparallel
   c. Tangential
   d. None of these

2. A nucleotide consists of:
   a. Phosphate and a base
   b. Phosphate, and a sugar
   c. A base and an amino acid
   d. A phosphate, a sugar, and a base

3. Adenine, thymine, guanine, and cytosine are what components of DNA?
   a. Hydrogen bonds
   b. Sugar moieties
   c. Phosphodiester groups
   d. Nitrogen bases

4. Which of the following IS NOT found in DNA?
   a. Adenine
   b. Guanine
   c. Cytosine
   d. Thymine
   e. Uracil

5. Which DNA sequence is homologous to 5’GATTCTCAAAGGACT3’?
   a. 5’GATTCTCAAAGGACT3’
   b. 3’GATTCTCAAAGGACT5’
   c. 3’CTAAGAGTTTCCTGA5’
   d. 5’CTAAGAGTTTCCTGA3’

6. One DNA strand binds to the other strand through:
   a. Peptide bonds
   b. Disulfide bonds
   c. Hydrogen bonds
   d. Phosphodiester bonds
7. The sugar in RNA _____, the sugar in DNA is ____
   a. Deoxyribose, Ribose
   b. Ribose, Deoxyribose
   c. Ribose, Phosphate
   d. Ribose, Uracil

8. In transcription, name the starting material, the ending material, and the major enzyme that catalyzes the process?
   a. DNA, mRNA, DNA polymerase
   b. tRNA, protein, peptidyl transferase
   c. mRNA, DNA, reverse transcriptase
   d. DNA, mRNA, RNA polymerase

9. After transcription, which of the following is NOT necessary for protein synthesis to occur?
   a. tRNA
   b. Ribosomes
   c. mRNA
   d. DNA

10. Which of the following IS NOT found in RNA?
    a. Adenine
    b. Guanine
    c. Cytosine
    d. Uracil
    e. Thymine

11. Messenger RNA (mRNA) is different from other types of RNA because mRNA has:
    a. A 3’ poly(A) tail
    b. Introns and Exons
    c. A 3’ methylated cap
    d. A cruciform structure

Section Two: DNA Microarrays

12. A stretch of chromosome that codes for a trait can be called a(n):
    a. Chromatid
    b. Replication Fork
    c. Gene
    d. Base Pair

13. A gene can control:
    a. Cell growth
    b. Cell division
    c. Cell death
    d. All of the above
14. How many genes does a human have?
   a. 200
   b. 2,000
   c. 20,000
   d. 200,000

15. A DNA microarray is a tool used in Genomics (the study of many genes at once), it is used to:
   a. Locate all the differences in gene expression for various cell types
   b. Locate the cause of problems in multiple genes
   c. Identify the exact location of different genes
   d. None of the above

16. In a DNA microarray, each of the spots contains multiple copies of _____ that represent one _____:
   a. mRNA, DNA
   b. DNA, Gene
   c. DNA, Chromosome
   d. Chromosome, mRNA

17. In a DNA microarray, mRNA ultimately forms:
   a. Proteins
   b. cDNA
   c. Daughter strands of DNA
   d. mRNA

18. Normally, DNA produces RNA; however, RNA can produce DNA using an enzyme called:
   a. Ligase
   b. DNA polymerase
   c. Restriction enzymes
   d. Reverse transcriptase

19. When two separate, single stranded complementary (i.e., having matching base pairs in the correct order and orientation) sequences of DNA are allowed to react, they will reform the double stranded structure by:
   a. Hybridization
   b. Denaturation
   c. Cleavage
   d. Digestion

20. Where do the two complementary sequences of DNA come from in a DNA microarray?
   a. Both from the mRNA
   b. One from each sample (ie. Healthy and Cancer)
   c. One from the mRNA and one from the actual DNA microarray
   d. None of the above

21. On a DNA microarray, a gene is considered “on” if:
   a. It binds to its complementary sequence
b. It successfully synthesizes a protein  
c. It does not have a poly(A) tail  
d. It is being expressed as mRNA

22. A down regulated gene means that:  
   a. A gene is over expressed in one sample as compared to the other  
   b. A gene is not expressed at all  
   c. A gene is not as expressed in one sample as compared to the other  
   d. All genes are expressed
<p>| <strong>GLOSSARY</strong> |
|-------------------|---------------------------------|
| <strong>Alkaloid</strong>       | Any of various organic compounds that have basic chemical properties and that usually contain at least one nitrogen atom. |
| <strong>Amenable</strong>       | Capable of being tested. |
| <strong>Anaphylaxis</strong>    | An exaggerated allergic reaction to a foreign protein resulting from previous exposure to it. |
| <strong>Apoptosis</strong>      | Programmed cell death is a form of cell death in which a programmed sequence of events leads to the destruction of cells without releasing harmful substances into the surrounding area. Apoptosis plays an important role in health by eliminating aged cells, unnecessary cells, and unhealthy cells. A protein called bcl-2 prevents apoptosis in normal healthy cells. However, many cancer cells, which would normally be destroyed by apoptosis because they proliferate too quickly, produce high levels of bcl-2 in order to evade destruction. |
| <strong>Aptly</strong>          | Able to learn quickly and easily |
| <strong>Asymmetry</strong>      | A lack of balance or symmetry |
| <strong>Biphasic</strong>       | Having two phases |
| <strong>Blebbing</strong>       | An irregular bulge in the plasma membrane of a cell undergoing apoptosis. |
| <strong>Cancer</strong>         | Any malignant growth or tumor caused by abnormal and uncontrolled cell division; it may spread to other parts of the body through the lymphatic system or the blood stream. |
| <strong>Causality</strong>      | The relationship between cause and effect |
| <strong>Chromatin</strong>      | The substance in the nucleus of a cell that is made up of DNA and proteins. During mitosis it condenses into chromosomes. |
| <strong>Cytotoxic</strong>      | A substance that has a toxic effect on certain cells. |
| <strong>Dermal cells</strong>   | Cells that make up a layer of the skin |
| <strong>Dysregulation</strong>  | The impairment of the normal functioning of the regulatory mechanism in living organisms |
| <strong>Edema</strong>          | A presence of abnormally large amounts of fluid in the spaces between cells of the body. |
| <strong>En masse</strong>       | All together |
| <strong>Epidermal</strong>      | Describing the outermost layer of the skin. |
| <strong>Equilibrium</strong>    | A state of rest or balance |
| <strong>Eradicate</strong>      | To destroy completely. |
| <strong>Erythema</strong>       | A redness of the skin caused by dilatation and congestion of the capillaries, often a sign of inflammation or infection. |
| <strong>Eukaryotes</strong>     | Cell or organism with membrane-bound, structurally discrete nucleus and other well-developed subcellular compartments; eukaryotes include all organisms except viruses, bacteria, and blue-green algae. Organisms possessing a nuclear envelope. |
| <strong>Fragmentation</strong>  | The process of breaking down into smaller parts |
| <strong>Hemolytic</strong>      | The breaking down of red blood cells. |
| <strong>Homeostasis</strong>    | The ability or tendency of an organism or cell to maintain internal equilibrium by adjusting its physiological processes |
| <strong>Homologous</strong>     | In evolutionary biology, any similarity between characters that is due to their shared ancestry. |</p>
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrolytic</td>
<td>Tending to remove or eliminate water</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Overly sensitive</td>
</tr>
<tr>
<td>Hypotrophy</td>
<td>A process in which a tissue or organ deteriorates due to the loss of cells.</td>
</tr>
<tr>
<td>Immunoglobulin E</td>
<td>A class of antibodies that cause allergic reactions and help remove intestinal parasites.</td>
</tr>
<tr>
<td>Inadvertently</td>
<td>Unintentional</td>
</tr>
<tr>
<td>Incapacitated</td>
<td>Unable to act or respond</td>
</tr>
<tr>
<td>Interferon</td>
<td>Proteins that prevent a virus from reproducing within the infected cells and induce resistance to the virus in other cells.</td>
</tr>
<tr>
<td>Invalid</td>
<td>Weak; unable to care for oneself</td>
</tr>
<tr>
<td>Ionizing</td>
<td>To separate into ions</td>
</tr>
<tr>
<td>Ischemic</td>
<td>A decrease in the blood supply to a bodily organ, tissue, or part caused by constriction or obstruction of the blood vessels.</td>
</tr>
<tr>
<td>Foraging</td>
<td>The gathering of food</td>
</tr>
<tr>
<td>Mandibles</td>
<td>A jaw-like mouthpart in an ant used for piercing.</td>
</tr>
<tr>
<td>Mitosis</td>
<td>The usual method of cell division, characterized typically by the resolving of the chromatin of the nucleus into a threadlike form, which condenses into chromosomes, each of which separates longitudinally into two parts, one part of each chromosome being retained in each of two new cells resulting from the original cell.</td>
</tr>
<tr>
<td>Morphology</td>
<td>The form and structure of an organism considered as a whole</td>
</tr>
<tr>
<td>Necrotic</td>
<td>Descriptive of cell death</td>
</tr>
<tr>
<td>Nematode</td>
<td>Unsegmented worms with elongated rounded body pointed at both ends</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Relating to the nervous system</td>
</tr>
<tr>
<td>Orchestrate</td>
<td>To arrange or control</td>
</tr>
<tr>
<td>Papillomaviruses</td>
<td>Any of several viruses of the family Papovaviridae, containing circular DNA, causing tumors of the skin that are not dangerous.</td>
</tr>
<tr>
<td>Phagocytosed</td>
<td>Having been surrounded and engulfed by another cell, forming a vacuole.</td>
</tr>
<tr>
<td>Phenomenon</td>
<td>A fact, occurrence, or circumstance observed or observable</td>
</tr>
<tr>
<td>Pheromones</td>
<td>A chemical substance released by an animal that serves to influence the behavior of other members of the same species.</td>
</tr>
<tr>
<td>Pivotal</td>
<td>Of vital or critical importance</td>
</tr>
<tr>
<td>Progeny</td>
<td>Descendents or offspring</td>
</tr>
<tr>
<td>Proliferation</td>
<td>a rapid and often excessive spread or increase</td>
</tr>
<tr>
<td>Pruritis</td>
<td>An intense chronic itching.</td>
</tr>
<tr>
<td>Pustule</td>
<td>A swollen section of the skin that is filled with pus.</td>
</tr>
<tr>
<td>Radiation</td>
<td>The process in which energy is emitted as particles or waves.</td>
</tr>
<tr>
<td>Resilient</td>
<td>Able to readily recover</td>
</tr>
<tr>
<td>Saccharomyces</td>
<td>The scientific name for a species of budding yeast</td>
</tr>
<tr>
<td>cerevisiae</td>
<td></td>
</tr>
<tr>
<td>Solenopsis invicta</td>
<td>The scientific name for red fire ant</td>
</tr>
<tr>
<td>Tumor</td>
<td>An uncontrolled and abnormal growth of cells</td>
</tr>
<tr>
<td>Turbid</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Vesicles</td>
<td>A small sac containing liquid.</td>
</tr>
<tr>
<td>Weal</td>
<td>A raised mark on the skin.</td>
</tr>
</tbody>
</table>
**Microarray Simulation:**

<table>
<thead>
<tr>
<th>Term</th>
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<tbody>
<tr>
<td>Catalyzed</td>
<td>To initiate</td>
</tr>
<tr>
<td>Complement</td>
<td>The complement of a nucleic acid sequence replaces each base by its complementary base: adenine (A) by thymidine (T), cytosine (C) by guanine (G), and vice versa. In RNA, adenine is paired not with thymidine but with uracil (U). By convention, DNA and RNA molecules have a consistent orientation (5' to 3') which is used in writing their sequences. To preserve this orientation, the complement of a sequence is written backwards compared to the original. For example, an RNA sequence ACGGUACU has the DNA complement AGTACCGT.</td>
</tr>
<tr>
<td>Complementary DNA (cDNA)</td>
<td>A DNA sequence which was produced from mRNA by reverse transcription. A cDNA is so-called because its sequence is the complement of the original mRNA sequence. However, when double-stranded cDNA is synthesized, it contains both the original sequence and its complement.</td>
</tr>
<tr>
<td>Fluorescent Tag</td>
<td>Chemical markers that aid in the detection of the molecule to which it has been attached.</td>
</tr>
<tr>
<td>Hybridize</td>
<td>To bind complementary pairs of DNA molecules. A DNA molecule has a very strong preference for its sequence complement, so just mixing complementary sequences is enough to induce them to hybridize. Hybridization is temperature dependent, so DNA's that hybridize strongly at low temperature can be temporarily separated (denatured) by heating.</td>
</tr>
<tr>
<td>Messenger RNA (mRNA)</td>
<td>The type of RNA which codes for protein, as opposed to ribosomal RNA (rRNA) and transfer RNA (tRNA). mRNA is translated to protein by a cell’s ribosomes.</td>
</tr>
<tr>
<td>Microarray</td>
<td>A tool that permits the identification of DNA samples and examination of gene expression in individual tissues and different conditions.</td>
</tr>
<tr>
<td>Probe</td>
<td>In a microarray experiment, the solution of labeled DNA that is hybridized with the array. For comparative transcription studies, two cDNA probes are prepared from the total mRNA of two different kinds of cells and labeled with two different reporters.</td>
</tr>
<tr>
<td>Reverse transcription</td>
<td>The copying of an RNA molecule back into its DNA complement. The enzymes that perform this function are called reverse transcriptases. Reverse transcription is used naturally by retroviruses to insert themselves into an organism's genome. Artificially-induced reverse transcription is a useful technique for translating unstable mRNA molecules into stable cDNA.</td>
</tr>
<tr>
<td>Transcription</td>
<td>Production of mRNA from DNA genetic information.</td>
</tr>
</tbody>
</table>