**Cancer, Viruses, and DNA Tech Notes 2019**

**Cancer results from genetic changes that affect cell cycle control**

Cell Cycle Control:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ are cancer-causing genes.

Proto-oncogenes are genes that code for proteins that are responsible for normal cell growth. Proto-oncogenes become oncogenes when a mutation occurs that causes an increase in the product of the proto-oncogene or an increase in the activity of each protein molecule produced by the gene.

Cancer can also be caused by a mutation in a gene whose products normally inhibit cell division. These genes are called tumor-suppressor \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

An important tumor-suppressor gene is the p53 gene. The product of this gene is a protein that suppresses cancer in four ways.

1. The p53 protein can activate the p21 gene, whose product halts the cell cycle by binding to cyclin-dependent kinases. This allows time for DNA to be repaired before the resumption of cell division.

2. The p53 protein activates a group of miRNAs , Which inhibit the cell cycle.

The p53 protein turns on genes directly involved in DNA repair.

4. When DNA damage is too great to repair, the p53 protein activates “suicide” gene whose products cause cell death, a process termed apoptosis.

Collection of Mutations:

The multi-step model of cancer development is based on the idea that cancer results from the accumulation of mutations that occur throughout life. The longer we \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, the more mutations that are accumulated and the more likely that cancer might develop.

Embryonic development represents what happens when gene regulation proceeds correctly and cancer shows what can happen when gene regulation goes awry.

**Concept: A virus consists of a nucleic acid surrounded by a protein coat:**

Viruses:

A \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ consists of a nucleic acid surrounded by a protein coat.

-Smaller than ribosomes, the tiniest viruses are about 20 nm across.

-The two essential components of a virus are a protein shell or capsid that surrounds the genetic material (either double- or single- stranded DNA or double- or single- stranded RNA).

-Many viruses found in animals have membranous viral envelopes that surround the capsid and aid the viruses in infecting their hosts.

-Bacteriophages or phages, are viruses that infect bacterial cells.

**Concept: Viruses replicate only in host cells:**

Need of a host:

Viruses replicate only in \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ cells

-Viruses have a limited host range. This means they can infect only a very limited variety of hosts. Example: Human cold virus infects only cells of the upper respiratory tract.

-Viral reproduction occurs only in host cells. Two variations have been studied in bacteriophages.

-The lytic cycle ends in the death of the host cell by rupturing it (lysis). In this cycle, a bacteriophage injects its DNA into a host cell and takes over the host cell’s machinery to synthesize new copies of the viral DNA as well as protein coats. These self-assemble, and the bacterial cell is lysed, releasing multiple copies of the virus.

-In the lysogenic cycle the bacteriophage’s DNA becomes incorporated into the host cell’s DNA and is replicated along with the host cell’s genome. The viral DNA is known as a prophage. Under certain conditions, the prophage will enter the lytic cycle, described on the previous page.

Backwards:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ are RNA viruses that use the enzyme reverse transcriptase to transcribe DNA from an RNA template. The new DNA then permanently integrates into a chromosome in the nucleus of an animal cell. The host transcribes the viral DNA into RNA that may be used to synthesize viral proteins or may be released from the host cell to infect more cells. Example: HIV is a retrovirus.

Viruses have the ability to introduce genetic change into organisms as well as to undergo rapid genetic change themselves. Moving from one host to another, viruses may pick up pieces of the first host’s DNA and carry it to the next cell to be infected. This is very common in bacteria infected by viruses where the process is called \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Mutations and Prions:

RNA viruses lack replication \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_-checking mechanisms and thus have higher rates of mutation. Mutations may accumulate rapidly and give rise to diverse clones of the virus within one organism, as occurs in humans with AIDS, or result in new genetic strains that may cause disease. This rapid mutation of viruses explains why there is no vaccine against the common cold.

**Concept: Prions are formidable pathogens:**

­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ are misfolded, infectious proteins that cause the misfolding of normal proteins in the brains of various animal species. Their damage to the brain accumulates over time and eventually leads to death. Examples of diseases caused by prions include mad cow disease and, in humans, Creutzfeldt-Jakob disease.

**Concept: DNA Sequencing and Cloning are valuable tools in genetic engineering and biological inquiry**

The key to unlocking the concepts of biotechnology is to understand the terms. Know the following commonly used terms:

 -Genetic engineering is the process of manipulating genes and genomes.

 -Biotechnology is the process of manipulating organism or their components for the purpose of making useful products.

 -Recombinant DNA is DNA that has been artificially made, using DNA from different sources-and often different species. An example is the introduction of a human gene into an E. coli bacterium.

 -Gene \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ is the process by which scientists can produce multiple copies of specific segments of DNA that they can then work with in the lab. Many bacteria have DNA outside the main circular chromosome in plasmids. A plasmid is a small, circular extra-chromosomal loop of DNA. Plasmids are often used in biotechnology.

 -Restriction enzymes are used to cut strands of DNA at specific locations (called restriction sites). They are mostly derived from bacteria where they serve the important function of protection against invading viruses.

 --When a DNA molecule is cut by restriction enzymes, the result will always be a set of restriction fragments, which may have at least one single-stranded end, called a sticky \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. Sticky ends can form hydrogen bonds with complementary single-stranded pieces of DNA. These unions can be sealed with the enzyme DNA ligase.

 -PCR (Polymerase chain reaction) is a method used to amplify a particular piece of DNA without the use of cells. PCR is used to amplify DNA when the source is impure or scanty (like a crime scene).

 -The basic steps of PCR include:

 1. Denaturation: \_\_\_\_\_\_\_\_\_\_\_\_ briefly to separate DNA strands.

 2. Annealing: Cool to allow primers to form hydrogen bonds with ends of target sequence.

 3. Extension: DNA polymerase adds nucleotides to the 3’ end of each primer

 4. Cycle: Heat up and cool several times. Each repetition causes those DNA fragments to copy.

 -Gel electrophoresis is a lab technique used to separate macromolecules, primarily DNA and proteins. The principles of this separation of DNA include:

 1. An electric current is applied to the field. DNA is negatively charged and migrates to the positive electrode.

 2. A gel made of a polymer is used as a matrix to separate molecules by size. The gel allows smaller molecules to move more easily than larger fragments of DNA.

 3. The DNA must be stained or tagged for visualization.

 -Restriction fragment length polymorphisms (\_\_\_\_\_\_\_\_\_\_\_\_) result from small differences in DNA sequences and can be detected by electrophoresis. The difference in banding patterns after electrophoresis allows for diagnosis of disease or is used to answer paternity and identity questions.

 -The process just described leads to a genomic \_\_\_\_\_\_\_\_\_\_\_\_\_\_. A genomic library is a set of thousands of recombinant plasmid clones, each of which has a piece of the original genome being studied. A cDNA library is made up of complementary DNA made from mRNA transcribed by reverse transcriptase. This technique rids the gene of introns but may not contain every gene in the organism.

**Concept: Biologists use DNA technology to study gene expression and function:**

 -Genome-wide studies of gene expression are made possible by the use of DNA microarray \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. DNA microarray chips work as follows:

 1. Small amounts of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_-stranded DNA (ssDNA) fragments representing different genes are fixed to a glass slide in a tight grid, termed a DNA chip.

 2. The mRNA molecules from the cells being tested are isolated and used to make cDNA using reverse transcriptase, then tagged with a fluorescent dye.

 3. The cDNA bonds to the ssDNA on the chip, indicating which genes are “on” in the cell (actively producing mRNA). This enables researchers, for example, to see differences in gene expression between breast cancer tumors and noncancerous breast tissue.

**Concept: Cloned organisms and stem cells are useful for basic research and other applications:**

In animal cloning the nucleus of an egg is \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ and replaced with the diploid nucleus of a body cell, a process termed nuclear transplantation. The ability of a body cell to successfully form a clone decreases with embryonic development and cell differentiation.

The major goal of most animal cloning is reproduction, but not for humans. In humans, the major goal is the production of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ cells. A stem cell can both reproduce itself indefinitely and, under the proper conditions, produce other specialized cells. Stem cells have enormous potential for medical applications.

Embryonic stem cells are pluripotent, which means “capable of differentiating into many different cell types.” The ultimate aim is to use them for the repair of damaged or diseased organs, such as insulin-producing pancreatic cells for people with diabetes or certain kinds of brain cells for people with Parkinson’s disease.

**Concept: The practical application of DNA technology affect our lives in many ways:**

There are many different uses for DNA technology, some of which are as follows:

 -Diagnosis of disease: A number of diseases can be detected by RFLP analysis (for example, cystic fibrosis, sickle-cell disease) or though amplification of blood samples to test for viruses (for example, HIV).

 -Gene therapy: This is the alteration of an afflicted individual’s genes. Gene therapy holds great potential for treating disorders traceable to a single defective gene, such as cystic fibrosis.

The production of pharmaceuticals: Gene splicing and cloning can be used to produce large amounts of particular proteins in the lab (for example, human insulin and growth hormone).

-\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ animals are created when eggs are fertilized in vitro and then a desired gene is cloned and inserted into the nucleus of the embryo. If successful, the transgenic animal will express the ”foreign” gene, which might be for a human protein that can be produced in large quantities, for example, goats are used to express human antithrombin in milk.

-Forensic application: DNA samples taken from the blood, skin cells, or hair of alleged criminals suspects can be compared to DNA collected from the crime scene. Genetic profiles can be compared and used to identify persons at that crime scene.

-Environmental \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_: scientists engineer metabolic capabilities into microorganisms, which are then used to treat environmental problems, such as removing heavy metals from toxic mining sites.

-Agricultural applications: Certain genes that produce desirable traits have been inserted into crop plants to increase their productivity or efficiency. An organism that has acquired by artificial means one or more genes from another species or variety is termed a genetically modified (GM) organism. Currently, a debate is in progress over the safety of GM organisms.

**Concept: Scientists use bioinformatics to analyze genomes and their functions:**

-Bioinformatics is the use of computers, software, and mathematical \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ to process and integrate the incredible volume of data from sequencing projects such as the Human Genome Project. In addition to DNA sequences, protein interactions are analyzed in an approach called proteomics.

-Systems biology aims to model the behavior of entire biological systems and is enhanced by bioinformatics. This has many applications, including medical ones-for example, in the understanding and treatment of cancers.

**Concept: Genomes vary in size, number of genes, and gene density:**

More than 3,700 genomes (about 3,500 of them prokaryotes) have now been sequenced with thousands more in progress. In general, bacteria and archaea have fewer genes than eukaryotes, and the number of genes in eukaryotic genomes is less than was expected.

-There does not seem to be any correlation between the complexity of an organism and its number of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. The 1 mm nematode *C. elegans* and humans both have between 20,000 and 21,000 genes! The human genome is able to function with relatively few genes by utilizing alternative splicing of RNA transcripts. Recall that this process results in more than one functional protein from a single gene.

**Concept: Multicellular eukaryotes have much noncoding DNA and many multigene families:**

-Only a tiny part of the human genome-1.5%- codes for proteins or is transcribed into rRNAs or tRNAs. Much of the rest is \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ DNA, sequences that are present in multiple copies in the genome.

-Transposable elements make up much of the repetitive DNA. These are stretches of DNA that can move from one location to another in the genome with the aid of an enzyme, transposase.

-Transposons can interrupt normal gene function if inserted in the middle of a functional gene, or alter gene expression if inserted into a regulatory element. Although these effects may be harmful or lethal, over many generations some may have small beneficial effects.

-Transposons can account for multiple copies of genes and the resulting genetic diversity provides raw material for natural selection.

-Multigene families are collections or two or more identical or very similar \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. A classic example is the human alpha-globin and beta-globin gene families. Here, the genes for different human globins are on different chromosomes. This allows for different forms of the beta-globin gene to function at different times in the human life cycle. For example, the embryonic and fetal forms of hemoglobin have a higher affinity for oxygen that the adult forms, ensuring the efficient transfer of oxygen from mother to fetus.

**Concept: Duplication, rearrangement, and mutation of DNA contribute to genome evolution:**

How might genes with novel functions evolve? Duplication event can lead to the evolution of genes with related functions, such as those of the alpha-globin and beta-globin gene families. Mutations and transpositions can occur, and nonfunctional pseudogenes may be found in the clusters. Ultimately, new genes with new functions may occur.

**Concept: Comparing genome sequences provide clues to evolution and development:**

-Determining which genes have remained similar, that is, are highly conserved in distantly related species can help clarify evolutionary relationships among species that diverged from each other long ago.

-Evo-devo is a field of biology that compares developmental processes to understand how they may have evolved and how changes can modify existing organismal features or lead to new ones.

-Homeotic genes are master regulatory genes that control placement and spatial organization of body parts by controlling the developmental fate of groups of cells.

-A \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ is a widely conserved 180-nucleotide sequence found within homeotic genes. When we say that a sequence is widely conserved, this means that it is found in many groups (for example, fungi, animals, and plants) with very few differences. This hints at the related ness and common evolution of all life-forms.