ANSWER KEY

THE EUKARYOTIC CELL CYCLE AND CANCER

ABOUT THIS WORKSHEET

This worksheet complements the Click and Learn "The Eukaryotic Cell Cycle and Cancer" developed in conjunction with the 2013 Holiday Lectures on Science, "Medicine in the Genomic Era" (http://www.hhmi.org/biointeractive/eukaryotic-cell-cycle-and-cancer).

PROCEDURE

Follow the instructions as you proceed through the Click and Learn and answer the questions in the spaces below.

Click on the "Background" tab on the right side.

1. Compare and contrast the reasons cell division is important for unicellular and multicellular organisms.

   - reproduce organism
   - repair dead/damaged cells
   - development/growth

2. Provide an example of why cell division remains important to an adult organism even after it is fully developed.

   replace cells that are dead/damaged, tissues w high turnover

3. What is the role of growth factors? – molecular signals
   cause cells to divide

4. Cells divide, differentiate, or die. What is differentiation?

   specialize in structure + function

5. What is apoptosis? Explain its purpose.

   Programmed cell death. Eliminates unnecessary cells + kills abnormal/damaged cells

6. Organisms maintain the right number of cells by regulating the cell cycle. What are "cell cycle regulators"?

   molecular signals that stimulate or halt division

7. *Watch the video clip of cell division in the small intestine.* Name the general location along the villus where the following processes occur:

   Cell Division: outside villi

   Cell Differentiation: crypt → lumen

   Apoptosis: top of villi

8. Name one harmless result of too little cell division.
hair loss

9. Name one harmless result of too much cell division.
warts

Click on "Cell Cycle Phases" in the center purple circle on the right and use the "Overview" information in the window on the left to answer the questions below.

10. List, in order, the four events we collectively call the "cell cycle." Next to each event, write the correlating cell cycle phase name.
    a. G1 - first gap phase
    b. S - synthesis phase
    c. G2 - second gap phase
    d. M - mitosis

11. In general, what is the purpose of a checkpoint in the cell cycle?
check to see if previous phase went OK

12. What is one potential outcome when errors occur in this highly regulated cell cycle process?
cancer

Click on "Cell Cycle Regulators and Cancer" in the center purple circle on the right. Use the information under "Regulators Overview" in the window on the left to answer the questions below.

13. What type of protein that regulates the cell cycle is encoded by proto-oncogenes?
stimulating protein

14. What type of protein that regulates the cell cycle is encoded by tumor suppressor genes?
inhibitory protein

15. The most important cell cycle regulators are the CDKs (cyclin-dependent kinases)

16. What is a kinase, and what does it do?
enzymes that add a phosphate to other proteins

17. When are cyclin-dependent kinases (CDKs) present inside the cell during the cell cycle?
When they are bound to cyclins (proteins)

18. When are cyclins present inside the cell during the cell cycle?

cycles up + down depending on the phase

19. CDKs form molecular complexes with cyclins. What do activated CDK-cyclin complexes do?

stimulate the cell cycle → division

Using the cell cycle diagram on the right and both links in the center purple circle, complete the table below for each phase. Use bullet points and focus on major events that occur during each phase, checkpoint, and regulatory process. Complete the entire row before moving on to the next phase.

PHASE	PHASE EVENTS	CHECKPOINT EVENTS	REGULATORY PROCESSES
G1	-right after cytokinesis -cell increases in size + preps for DNA replication	-No DNA damage -sufficient resources	▶ CDK-cyclins phosphorylate proteins → S phase ■ Tumor Suppressor genes prevent tumors
S	-cell replicates its DNA -2 complete sets of chrom.	No errors during DNA replication	▶ Growth factors stimulate ↑ cyclin conc. ■ Proteins must repair mistakes to DNA during replication
G2	-cell keeps growing -preps for division	-No DNA damage -Chromosome set complete -enough cell components	▶ One damaged repaired, CDK-cyclins activated → M ■ p53 will stop cell until DNA repaired
M (mitosis)	-cell stops growing -divides into 2 identical daughter cells	-all chromosomes attached to Mitotic spindle	▶ APC/C proteins initiate destruction of centromere ■ MAD proteins halt anaphase until spindle is attached at all centromeres

APC/C - anaphase-promoting complex/cyclosome
MAD - mitotic arrest deficient protein

20. *Go to "Cell Cycle Phases" and click on "Interphase."* The interphase alternates with mitosis. What happens during interphase and which phases does it include?

cell grows + replicates DNA : $G_1 \rightarrow S \rightarrow G_2$

21. *Go to "Cell Cycle Phases" and click on "Go."* The Go phase is a resting or nondividing stage. What three factors determine whether a cell enters Go?

differentiation : stage in development, type, resources

22. Provide an example of a fully differentiated cell that is (a) permanently in Go and (b) one that can leave Go to progress through the cell cycle and divide again.

a. neuron

b. liver

Click on "Cell Cycle Regulators and Cancer" in the center purple circle on the right. Then click on the "Cancer Overview" tab in the window to the left (right tab).

23. Cancer is the result of an improperly regulated cell cycle. Name two reasons why cells can form tumors.

- passing through cell cycle unchecked
- programmed cell death

24. What causes uncontrolled cell division at the genetic level?

- mutations affecting proteins that normally regulate the cell cycle

25. *Watch the video clip.* At the cellular level in this example, explain what occurs if the APC gene is mutated.

- trouble differentiating, keep growing → tumor

26. Normally, proto-oncogenes stimulate the cell cycle. What do mutated proto-oncogenes (i.e., oncogenes) cause?

increase the speed of cell division
↳ putting the foot on accelerator

27. Normally, tumor suppressor genes inhibit the cell cycle. What do mutated tumor suppressor genes cause?

loss of the ability to inhibit cell cycle

28. To cause cancer, proto-oncogenes require (1 or 2) *(circle one)* allele(s) to be mutated and are therefore considered (dominant / recessive) *(circle one)*. This results in gain of function.

29. To cause cancer, tumor suppressor genes require (1 or (2) *(circle one)* allele(s) to be mutated and are therefore considered (dominant / (recessive) *(circle one)*. This results in loss of function.

30. *Watch the video clip.*
    a. Using the gas pedal analogy, explain the impact on the cell cycle of a proto-oncogene versus an oncogene.

gas pedal (normal) oncogene → go, go, go
always dividing (proto-oncogene)

    b. Using the brake pedal analogy, explain the impact on the cell cycle of *one* mutated tumor suppressor gene allele versus *two* mutated tumor suppressor gene alleles.

breaks (normal) ts gene (inhibit cell growth)
one mutation – cell cycle ok
two mutations – proceeds too quickly

RB- retinoblastoma

ADVANCED EXTENSION QUESTIONS (OPTIONAL)

Now that you have finished the Click and Learn, use your knowledge to answer the following questions.

31. *p53* is a tumor suppressor gene, and some scientists refer to it as "the guardian of the genome."

    a. Explain its normal role and why scientists would regard it as the "guardian of the genome."

    p53 is a tumor suppressor gene that stops tumor formation. It binds to DNA + can prevent advancement to the next phase of division

    b. Explain what happens to the cell cycle if both *p53* alleles are mutated.

    cells divide uncontrollably + form tumors

32. Explain why people who inherit one mutated allele of the *BRCA1* gene have a higher likelihood of developing cancer.

    → helps repair damaged DN

33. Predict a potential outcome of a mutated MAD protein.

    Could result in cells with abnormal chromosome numbers.

34. Use the model illustrated in the figure below to answer the accompanying questions.