Executive Summary For Teachable Unit

I. Title: Does Aflatoxin-Contaminated Peanut Butter Cause Liver Cancer?

II. Developer: Priscilla Van Wynsberghe

III. Learning goals

- *Primary* learning goals

Understand what **cancer** is
Understand the function of **p53** in the **cell cycle** and why it is commonly associated with human cancer
Gain insight into the scientific process by using the available data to decide if aflatoxin-contaminated peanut butter causes cancer
Connect the concepts of cell growth and cancer to intracellular pathways of the central dogma

- *Secondary* learning goals

Enhance understanding of the scientific method and the difference between causation and correlation
Enhance communication and group work skills

IV. Scientific teaching themes: See TU Review Rubric for guidelines.

Describe how the unit addresses the following themes:

- Scientific teaching

Active learning methods like group work, concept map generation, experimental design, and class discussions are integral parts of this lecture
Exploration of the scientific process by experimental design and data analysis

- Diversity

Reading peanut files on their own time at their own pace
Mini-lecture about the material
Pair work and discussions about questions related to mini-lectures
Group work generating concept maps
Individual write-up at the end of class

- Active learning

Small group work to design concept maps
Class discussions of small group work

- Assessment

Pre-quiz – assess prior knowledge and misconceptions
Group work & class discussions – assess understanding
Homework – assess student learning, assign grades

Teaching Plan

- Teaching Plan

Title: Does Aflatoxin-Contaminated Peanut Butter Cause Liver Cancer?

Developer: Priscilla Van Wynsberghe

Time	Topic	Activity/ Assessment	Goals
Pre-class	**Peanut Files**	*Pre-quiz, Peanut Files*	Assess student prior knowledge & misconceptions.
	Elicit/Engage: Students are directed to specific sites within the Peanut Files. Pre-quiz assesses students understanding of the reading and misconceptions. Students generate a hypothesis about the relationship between aflatoxin and liver cancer and are prepared to share their hypothesis in class.		
0-5	**Does aflatoxin-contaminated PB cause liver cancer?**	*Poll, class discussion*	Get students "hungry" to know more about cancer.
	Elicit/Engage/Explore: Ask students to share their hypotheses about the relationship between aflatoxin and liver cancer. Poll students: Do you agree or disagree with this hypothesis: aflatoxin-contaminated peanut butter causes liver cancer? What evidence is the basis for your decision? Discuss the difference between causation and correlation.		
5-25	**Liver Cancer**	*Mini lecture, Group work*	Understand what cancer is. Assess understanding, address misconceptions.
	Explain/Explore: Mini lecture about liver cancer. In small groups, students design a concept map to explain how a normal cell can become a cancerous tumor. Terms to include: normal cell, mutation(s), time, tumor, cancerous tumor.		
25-55	**Cell cycle & p53**	*Mini lecture, Group work, Class discussion*	Understand what the cell cycle is and how p53 regulates the cell cycle. Assess understanding, address misconceptions.
	Explain/Explore/Elaborate: Class discussion about what a cell needs to make to divide. Ex: protein, DNA… Mini lecture about why cell cycle control is important and that p53 regulates the cell cycle. In small groups, students design a concept map to explain how p53 is made and where p53 acts in the cell cycle. Terms to include: p53 gene, transcription, p53 mRNA, translation, p53 protein, G1, S, G2, M, DNA replication, cell division, new cell. Elaborate: What if p53 cannot function? In small groups, students will connect their two concept maps to explain how a p53 mutation could cause a cancerous tumor.		

Teaching Plan

Time	Topic	Activity/ Assessment	Goals
55-75	**Aflatoxin – putting the pieces together**	*Mini lecture, Group work*	Explain how aflatoxin-contaminated peanut butter could cause liver cancer. Assess understanding, address misconceptions.

Explain/Elaborate: Mini lecture about how the liver inactivates toxins, but sometimes by accident it activates aflatoxin (revisit bioactivation). Aflatoxin mutates the p53 gene. In small groups, students use their concept maps to explain how eating aflatoxin-contaminated peanut butter could cause cancer. Terms to include: aflatoxin, peanuts, peanut butter, mouth, liver, bioactivation. Summarize results in writing on a notecard. Revisit the question: does aflatoxin-contaminated peanut butter cause liver cancer? Alleviate fears about eating peanut butter: the USA has very stringent restrictions on aflatoxin contamination in peanut butter.

After class	**Homework**	*NYT article & Essay*	Assess student learning

Extend/Evaluate: Read the article: *Molecular 'Hot Spot' Hints at a Cause of Liver Cancer*, by Natalie Angier
New York Time, April 4, 1991

Write a 1 page essay that addresses the question: do you think aflatoxin-contaminated peanut butter causes liver cancer? Your answer should explain your reasoning and be based on what you learned about gene expression and aflatoxin in class and the information provided in the article. Regardless of whether you answer the above question yes or no, include all steps, down to the level of DNA, that must occur in order for aflatoxin exposure to result in cancer.

V. Instructions/materials for implementation of this unit.

A. Lecture Notes

I. Peanut Files (Elicit/Engage)

- Reading assignment

Prior to class, students are asked to visit the online website: The Peanut Files
http://scientific teaching.wisc.edu/products/PeanutFiles/index.htm
In the Cancer section of the library read about the following terms:
Cancer and Medical Topics section: cancer, liver, liver cancer, and hepatoma
Cellular Machinery and Processes section: cell cycle and p53
Dangerous Coupounds section: mycotoxin and toxin
Mycotoxin section: Aspergillus and aflatoxin
Read about any other terms of interest in the library.
In the Articles of Interest section read and bring to class the article:
Hepatoma and groundnuts in the West Nile District of Uganda.
Read any other articles of interest.

- Pre-quiz (p10-11)

The pre-quiz can be accessed from the Learn@UW site.

- Goals

Assess student prior knowledge and misconceptions. Give students the opportunity to become familiar with the class material prior to class.

II. Does aflatoxin-contaminated peanut butter cause liver cancer? (Elicit/Engage/Explore)

- Collect hypotheses
- The last pre-quiz question asked students to generate a hypothesis about the relationship between aflatoxin and liver cancer. Ask students to share their hypotheses. Expected hypothesis: aflatoxin causes liver cancer. (ppt slide 1)
- Poll

Poll students: How many agree with the hypothesis: aflatoxin-contaminated peanut butter causes liver cancer? (ppt slide 1)
Ask students who agree: What's the evidence?
Or, ask students who disagree: What evidence would you need to be convinced that aflatoxin-contaminated peanut butter causes cancer?
Show the data from the Hepatoma and groundnuts in the West Nile District of Uganda article (Peanut Files and pre-quiz question). (ppt slide 2)
Does this prove that aflatoxin-contaminated peanut butter causes cancer?

- Mini lecture on causation vs. correlation. (ppt slide 3)
- Show learning goals (ppt slide 4)
- Goals

Follow-up on scientific method ideas brought up in first aflatoxin lecture. Get students "hungry" to know more about cancer.

- Transition

Before we decide if aflatoxin contaminated peanut butter causes liver cancer let's learn about what cancer is…

III. Liver Cancer (Explain/Explore)

- Mini lecture

What is cancer. (ppt slide 5) Picture of a tumor. Over time, with the acquisition of multiple mutations cells may grow even when they shouldn't, or cells won't die when they should. A relentlessly growing mass of abnormal cells form a tumor. Tumors can be benign or harmless if the cells remain clustered in a single mass. However, if the cells start to invade the surrounding tissue, the tumor is malignant or cancerous. Benign tumors occur early in cancer. Malignant tumor cells can spread to other locations in the body, through the blood stream or lymphatic vessels, and form secondary tumors called metastases. By the time a tumor is first detected it typically contains more than 1 billion cells. Tumors are made of our cells.

What causes cancer? (ppt slide 6) Three main factors can cause cancer: environmental carcinogens, viruses, and genetics. This lecture focuses on environmental carcinogens like aflatoxin.

Cancer is: (ppt slide 7) uncontrolled cell growth and spread caused by the accumulation of multiple mutations over time. During a human lifetime, there are 10^{16} cell divisions. Spontaneous mutation occurs at a rate of 10^{-6} mutations per gene per cell division after repair processes. This results in 10^{10} mutations per gene in a human lifetime. So, why don't we get cancer? Because, more than one mutation is needed to cause cancer and not all mutations promote cancer (i.e. are in an oncogene or tumor suppressor gene). Liver cancer takes about 7 independent mutations. Show a graph of the relationship between cancer incidence and age.

Target misconceptions. (ppt slide 8) Cancer is not: you cannot catch cancer from someone like you can catch the flu. (Note that some viruses cause cancer (Hepatitis B virus, Human papilloma virus, Epstein Barr virus…). You can catch a virus from someone, but you may not develop cancer because you have the virus). Having a genetic mutation that is often found in human cancers, does not mean that you will get cancer. Cancer is not a two-sided issue. Many factors cause cancer, sometimes.

What does cancer look like? (ppt slide 9,10) Picture of normal liver and liver cancer.

Liver cancer statistics. (ppt slide 11) Liver cancer is the 5th most common cancer, and the 3rd most deadly cancer in the world. The 5 year survival rate for liver cancer is 7 percent because it is not easy to detect and thus is often detected at a later stage of cancer when the already difficult treatment is less effective. Liver cancer is more common in Asia and Africa than the USA. The liver's job makes it a hotspot for cancer. The liver processes and absorbs nutrients, makes clotting factors, and removes toxic chemicals. But, sometimes instead of inactivating toxic chemicals it accidentally activates them (bioactivation, discussed last week). This it what happens with aflatoxin. Show diagram of where the liver is found in the body.

- Group Work (example on p12) (ppt slide 12)

Design a concept map to explain how a normal cell can become a cancerous tumor. Terms to include: normal cell, mutation(s), time, tumor, cancerous tumor. Each group will have a large piece of paper on their desk and colored markers. Students are advised to use only a small portion of their paper.

Teacher checks students' progress, answers questions. A student from one group summarizes their concept map on the board.

- Goals

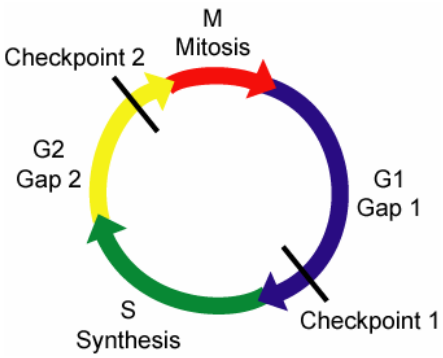
Understand what cancer is. Assess understanding. Address misconceptions.

IV. Cell cycle and p53 (Explain/Explore/Elaborate)

- Group work / Class Discussion – cell cycle (ppt slide 13)

Cancer is caused by uncontrolled cell growth. In small groups discuss: 1. What does a cell need to do, or to make in order to undergo cell division? 2. Mutations spontaneously arise during replication, can the cell stop or fix mutations? If yes, how? Solicit answers to question #1 first. Write on the board. Ex:

- Protein – always made
- Lipids – always made
- DNA – the cell needs to replicate its DNA, it does this during the S (Synthesis) phase of the cell cycle. Draw the S phase on the board
- Divide – The cell divides during the M (mitosis) phase of the cell cycle. Draw the M phase on the board.
- Growth – the cell needs to prepare for the S and M phases of the cell cycle. Before the S phase is a long G1 (gap 1) phase, during which the cell makes DNA replication machinery. Before the M phase is the G2 (gap 2) phase, during which the cell makes the cell division machinery.



An average mammalian cell divides once a day. Some cells divide faster and some cells divide slower. Liver cells divide once every 1-2 years unless stressed.

- Mini lecture – cell cycle control and p53 (ppt slide 13)

Solicit answers to question #2. Ex: DNA repair processes occur at checkpoints.

Add the concept of checkpoints to the cell cycle diagram on the board. The cell cycle has two checkpoints. The first checkpoint occurs in G1 before S phase. At this point, the cell detects if any DNA damage (because of mutation, UV light, chemical adducts, DNA breaks…) exist. If DNA damage is not present, the cycle proceeds. If DNA damage is present the cell cycle stops and repairs the damage. If the DNA damage cannot be repaired the cell kills itself (apoptosis). A second checkpoint occurs in G2 before M phase to make sure that everything is ready to enter M phase. We will focus on the first checkpoint.

p53 controls the G1 checkpoint (by binding enhancer regions to promote expression of proteins that shut down the cell cycle so that DNA damage can be repaired). p53 also promotes cell death if mutations cannot be fixed. p53 is 53 kildaltons (kilograms per mole), so they named it p53.

About 50% of human cancers have p53 mutations. The locations of the p53 gene mutation(s) differ between different cancers, and thus can be diagnostic. Most p53 mutations inhibit p53 binding to DNA and thus inhibit the G1 checkpoint. (ppt slide 14)

- Group Work (example on p12) (ppt slide 15)

In small groups, design a concept map to explain how p53 is made and where p53 acts in the cell cycle. Terms to include: p53 gene, transcription, p53 mRNA, translation, p53 protein, G1, S, G2, M, DNA replication, cell division, new cell.

Teacher checks students' progress, answers questions. A student from one group summarizes their concept map on the board.

Follow up question: What if p53 cannot function because of a mutation in the p53 gene? To answer this question, suggest that students connect their two concept maps to explain how a p53 mutation could cause a cancerous tumor.

Teacher checks students' progress, answers questions. A student from one group summarizes their concept map on the board.

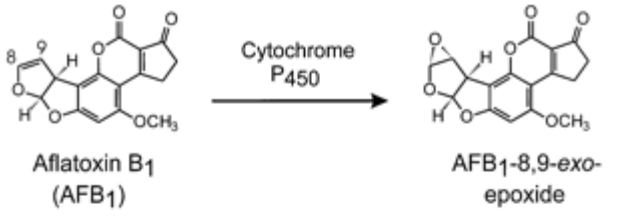
- Goals

Understand what the cell cycle is and how p53 regulates the cell cycle. Assess understanding, address misconceptions. Reinforce understanding of the central dogma (learned in previous units). Connect intracellular events (central dogma and the cell cycle) to extracellular events (tumor formation).

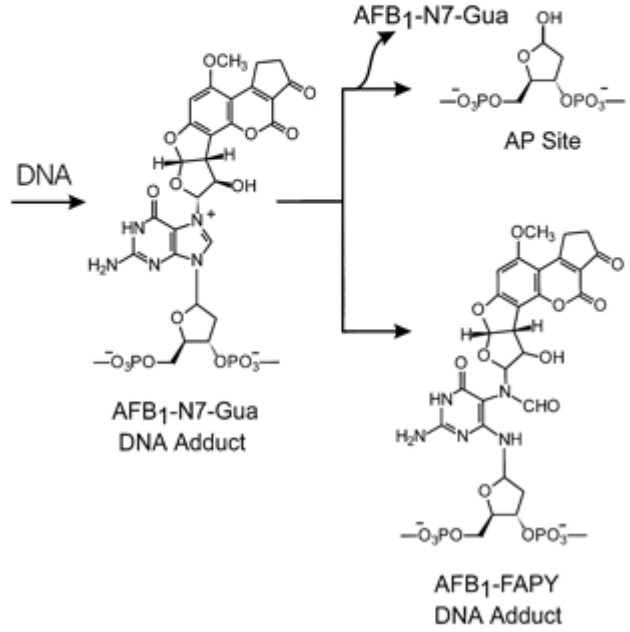
V. Aflatoxin – putting the pieces together (Explain/Elaborate)

- Mini lecture – liver function (ppt slide 16)

The liver deactivates toxins. Sometimes, by accident the liver activates aflatoxin (bioactivation). Activated aflatoxin can bind to the p53 gene. During replication, DNA polymerase doesn't recognize the nucleotide-bound aflatoxin. And repair can sometimes lead to the insertion of the wrong nucleotide, or mutation



<u>For your information.</u> Aflatoxin preferentially binds DNA at G clusters, but does not bind at all G-rich sequences. Aflatoxin preferentially binds the third nucleotide in codon 249 of the p53 gene. Stable interactions between p53 and aflatoxin in this area mediate binding.



<u>From Smela, et al. 2001.</u> Aflatoxin becomes activated by cytochromes in the liver to the 8,9-expoxide which covalently reacts with DNA to form AFB_1-N7-Gua. The positively charged imidazole ring of AFB_1-N7-Gua promotes depurination to yield an apurinic (AP) site. Or, the imidazole ring can open to form AFB_1-FAPY which is more stable. Alternatively, AFB_1 could come back off of the DNA yielding an intact guanine. dAMP is the most common base inserted opposite AP sites in *E. coli*. This would result in the GC→AT transition that is often seen in the p53 protein liver cancer patients who have been exposed to aflatoxin.

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- Group Work (example p12) (ppt slide 17)

In small groups, use concept maps to explain how eating aflatoxin-contaminated peanut butter could cause cancer. Terms to include: aflatoxin, peanuts, peanut butter, mouth, liver, bioactivation. Summarize the results in writing on a notecard (1 per person, so everyone can take one home).

Teacher checks students' progress, answers questions. A student from one group summarizes their concept map on the board.

- Revisit hypothesis: Aflatoxin-contaminated peanut butter causes liver cancer. (ppt slide 18)

Remember the disease triangle. If all factors of the disease triangle are favorable, than liver cancer caused by aflatoxin-contaminated peanut butter is likely, but not guaranteed. Why don't we know for sure? We can't do the experiment that was done with Turkey X disease. There are a lot of factors. It takes a long time to get cancer.

Aflatoxin and liver cancer in numbers. Low dose/long term aflatoxin exposure – 3x more likely to get liver cancer. Hepatitis B exposure (HBV) – 7x more likely to get liver cancer. Aflatoxin and HBV – 60x more likely to get liver cancer. HBV X protein is thought to mess with the DNA repair system thus allowing aflatoxin-induced mutations to be more permanent.

For your information: in regions of high aflatoxin exposure (Africa, regions of China…) 44% of liver cancer cases have a GC to TA substitution at codon 249 (aflatoxin exposure). In regions of low aflatoxin exposure (USA and Europe) only 1% of liver cancer cases have this mutation.

- Alleviate fears. (ppt slide 19)

The USA has very stringent restrictions on aflatoxin contamination in peanuts. So it's ok to eat peanuts and peanut butter (20ppb aflatoxin in human or animal food, 0.5ppb in milk). Commercially sold organic peanut butter has similar restrictions, but homemade doesn't. We'll talk more about this topic next week. If there's time discuss in groups: Why might aflatoxin mediated liver cancer be more prevalent in Africa than in the USA? Possible answers: no restrictions, less food choices, don't know about risk…

- Restate Learning Goals (ppt slide 20)
- Goals

Explain how aflatoxin-contaminated peanut butter could cause liver cancer. Assess understanding. Address misconceptions. Connect all of the concepts that have been discussed in this lecture. Generate a summary of these concepts for home reference.

VI. Homework (Extend/Evaluate)

- Read the article (handout)

Molecular 'Hot Spot' Hints at a Cause of Liver Cancer,
by Natalie Angier, New York Time, April 4, 1991
access at:
http://query.nytimes.com/gst/fullpage.html?res=9D0CE1D8173DF937A35757C0A967958260&sec=health&pagewanted=print

- Essay

Write a 1 page essay that addresses the question: do you think aflatoxin-contaminated peanut butter causes liver cancer? Your answer should explain your reasoning and be based on what you learned about gene expression and aflatoxin in class and the information provided in the article. Regardless of whether you answer the above

question yes or no, include all steps, down to the level of DNA, that must occur in order for aflatoxin exposure to result in cancer. Rubric is on p12-15.

- Goals

Assess student learning.
Assign grades

Required Materials:

- 2 Large piece(s) of paper per group
- Colored markers for each group
- 1 notecard (3"x5") for everyone in the class
- Homework assignment

References

1. Aflatoxin, http://www.aflatoxin.info/health.asp
2. Aguilar, F, Hussain, S, Cerutti, P. 1993. Aflatoxin B_1 induces the transversion of G→T in codon 249 of the p53 tumor suppressor gene in human hepatocytes. *Proc. Natl. Acad. Sci. USA*. 90: 8586-8590.
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4. Angier, N. 1991. Molecular 'Hot Spot' Hints at a Cause of Liver Cancer. *New York Times.* http://query.nytimes.com/gst/fullpage.html?res=9D0CE1D8173DF937A35757C0A967958260&sec=health&pagewanted=print
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16. The Peanut Files, http://scientificteaching.wisc.edu/products/PeanutFiles/index.htm

17. Smela, M, Currier, S, Bailey, E, Essigmann, J. 2001. The chemistry and biology of aflatoxin B_1: from mutational spectrometry to carcinogenesis. *Carcinogenesis*. 22: 535-545.
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B. Pre-Quiz:

Access from The Peanut Files homepage
http://scientificteaching.wisc.edu/products/PeanutFiles/index.htm

1. What is the difference between a hypothesis, a prediction and a theory? A hypothesis is a statement that tentatively explains a scientific phenomenon, and is testable by investigation. A prediction is a guess about what will happen. A theory is a hypothesis that has successfully passed scrutiny by several experiments. A theory is not a fact and can be overturned if enough evidence is collected against it.

2. What is the difference between an infectious agent and a toxin? A toxin is a protein that is poisonous, while an infectious agent is a microorganism that can cause disease.

3. True or False – The fungus *Aspergillus* can infect the human liver, thereby causing liver cancer. False. *Aspergillus* produces a toxin called aflatoxin that if ingested can become activated in the human liver. Activated aflatoxin can cause liver cancer. *Aspergillus* can infect a person but this causes Aspergillosis not cancer.

4. Is cancer contagious? Why or why not? Cancer is not contagious. Cancer occurs when our cells grow in an uncontrolled manner. Uncontrolled cell growth is often caused by mutations in our genes that regulate cell division. Mutated genes can be inherited or caused by environmental factors (like certain chemicals) or some viruses. Viruses are contagious but acquisition of a virus that could cause cancer does not mean that you will get cancer.

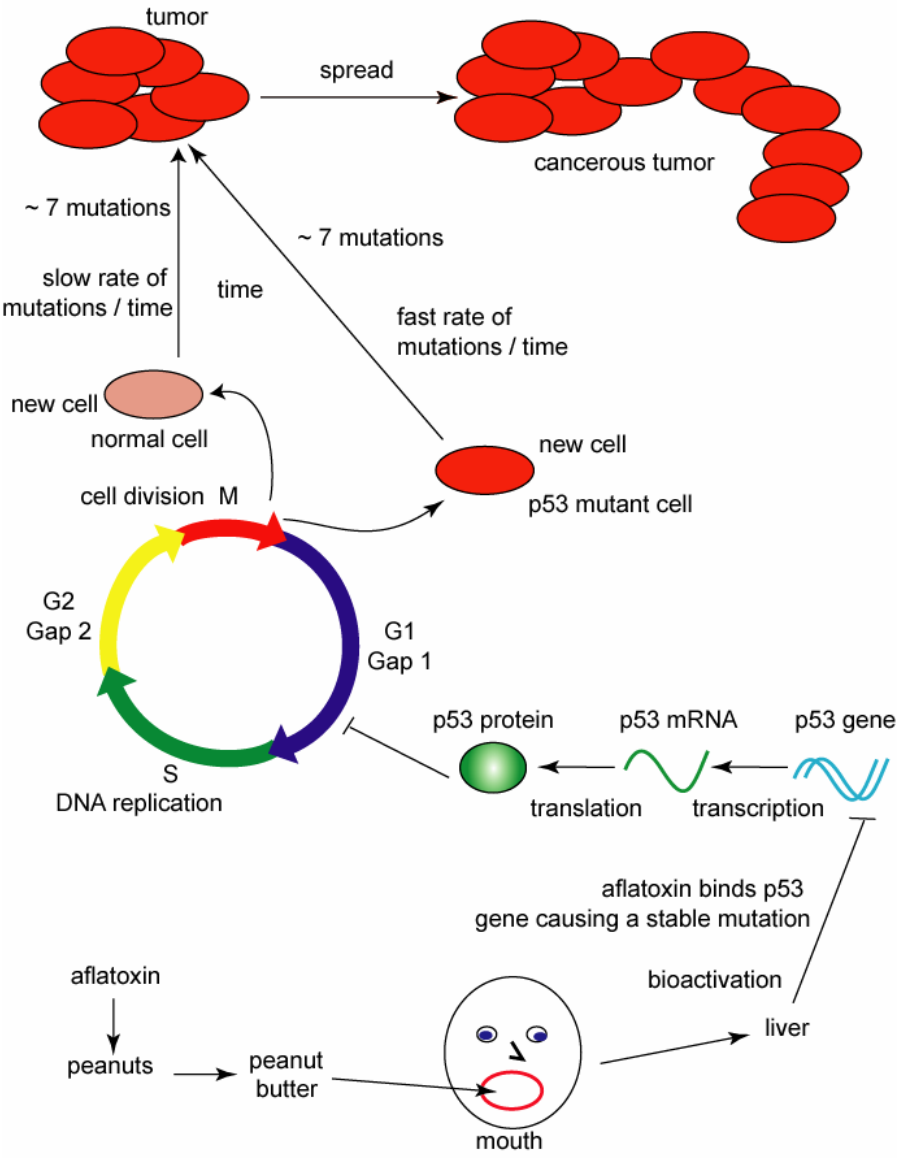
5. Why is the liver more susceptible to cancer? One of the main roles of the liver is to deactivate toxins so that they can be safely excreted from the body. But, sometimes the liver actually activates toxins (this is called bioactivation). Activated toxins can mutate liver cells. If too many mutations occur or if mutations occur in genes that regulate the cell cycle than liver cancer can occur.

6. What is the cell cycle? What are the steps of the cell cycle? What is the role of p53 in the cell cycle? The cell cycle is an ordered set of events, starting with one cell, and culminating with division into two daughter cells. The cell cycle is divided into four stages: Gap 1 (G1) where the cell prepares for DNA replication; Synthesis (G2) where DNA replication occurs; Gap 2 (G2) where the cell prepares for cell division; and Mitosis (M) where the chromosomes separate and cell division occurs. p53 mainly acts at the checkpoint in the G1 stage of the cell cycle. If DNA is damaged, p53 is activated and halts

the cell cycle so that repair processes can occur. If there is too much DNA damage, p53 induces cell death.

7. After reading the Peanut Files article of interest, Hepatoma and groundnuts in the West Nile District of Uganda, generate a hypothesis about the relationship between aflatoxin and liver cancer. Be prepared to discuss your hypothesis in class. There are many possible hypotheses. One is: Aflatoxin causes liver cancer. Another hypothesis is: Aflatoxin does not cause liver cancer.

Concept Map Example



Aspergillus can grow on peanuts in the soil. *Aspergillus* produces aflatoxin. Peanut butter can contain aflatoxin if it's made from peanuts that are contaminated with aflatoxin. If we eat peanut butter contaminated with aflatoxin, our liver could activate the aflatoxin by bioactivation. Activated aflatoxin can bind the p53 gene and cause a mutation in the p53 gene. This mutation causes p53 protein to be nonfunctional. Nonfunctional p53 protein won't stop the cell cycle to repair DNA damage in. This can cause multiple mutations to accumulate in a cell.

Over time, with the addition of multiple independent mutations a normal cell can be changed into a mutant cell that replicates when it shouldn't and doesn't die when it should. This can form a tumor. A cell with a mutant p53 gene is more prone to mutations (has a faster rate of mutation acquisition over time) and is thus more likely to initiate tumor formation. If the tumor cells spread than it becomes a cancerous tumor. So, aflatoxin-contaminated peanut butter can cause liver cancer. Since p53 becomes activated and mutates the p53 gene in liver cells, aflatoxin-contaminated peanut butter can contribute to liver cancer.

Rubric for Take-home Essay

Does aflatoxin-contaminated peanut butter cause liver cancer?

- 1. Read the article (handout)

Molecular 'Hot Spot' Hints at a Cause of Liver Cancer,
by Natalie Angier, New York Time, April 4, 1991
access at:
http://query.nytimes.com/gst/fullpage.html?res=9D0CE1D8173DF937A35757C0A967958260&sec=health&pagewanted=print

- 2. Essay

Write a 1 page essay that addresses the question: do you think aflatoxin-contaminated peanut butter causes liver cancer? Your answer should explain your reasoning and be based on what you learned about gene expression and aflatoxin in class and the information provided in the article. Regardless of whether you answer the above question yes or no, include all steps, down to the level of DNA, that must occur in order for aflatoxin exposure to result in cancer.

Example:

Aflatoxin-contaminated peanut butter can cause liver cancer, but it doesn't have to. If you eat peanut butter contaminated with aflatoxin, then your liver will try to deactivate aflatoxin so that it can be safely excreted from the body. This is because one of the jobs of the liver is to deactivate toxins. However, in the process of trying to deactivate aflatoxin, the liver actually activates aflatoxin. This is called bioactivation. Activated aflatoxin binds to the p53 gene and causes a mutation in the p53 gene. During transcription the mutation in the p53 gene gets incorporated in the p53 mRNA. Then, during translation the mutation in the p53 mRNA causes a mutation in the p53 protein. In normal cells p53 stops the cell cycle, in response to DNA damage, in the Gap 1 (G1) stage so that the DNA can be repaired. If DNA damage can't be repaired, then p53 induces cell death.

The cell cycle is an ordered set of events, starting with one cell, and culminating with division into two daughter cells. The cell cycle is divided into four stages: Gap 1 (G1) where the cell prepares for DNA replication; Synthesis (G2) where DNA replication occurs; Gap 2 (G2) where the cell prepares for cell division; and Mitosis (M) where the chromosomes separate and cell division occurs.

When the p53 protein is mutated by aflatoxin it can't do these functions. So cells with DNA damage will grow and replicate when they shouldn't and they won't die when

they should. This is a hallmark of cancer. Cancer is characterized by uncontrolled cell growth. Cancer occurs because of the acquisition of multiple mutations over time. So when the p53 protein is mutated by aflatoxin, cells are more likely to get more mutations (because DNA damage isn't repaired) and they won't die when they should. Since aflatoxin is activated in liver cells, p53 becomes mutated in liver cells. Thus aflatoxin-contaminated peanut butter can cause liver cancer.

Important points that should be addressed in homework:

1. State position, text should support their position.

2. Why liver cancer? – one of the liver's jobs is to deactivate toxins. But the liver actually activates aflatoxin (bioactivation) Because this occurs in the liver. Aflatoxin can cause liver cancer.

3. What does aflatoxin do? – aflatoxin causes a mutation in the p53 gene which results, after transcription and translation, in a mutation in the p53 protein.

4. What does p53 do? – p53 controls checkpoint 1 of the cell cycle. DNA damage activates p53. p53 stalls the cell cycle in G1 until the mutation is repaired. If the mutation can't be repaired, p53 induces cell death.

5. What is the cell cycle? – The cell cycle is an ordered set of events, starting with one cell, and culminating with division into two daughter cells. The cell cycle is divided into four stages: Gap 1 (G1) where the cell prepares for DNA replication; Synthesis (G2) where DNA replication occurs; Gap 2 (G2) where the cell prepares for cell division; and Mitosis (M) where the chromosomes separate and cell division occurs.

6. What happens if p53 is mutated? – If p53 is mutated then cells with DNA damage won't be stopped in the G1 phase of the cell cycle or destroyed. So cells can accumulate more and more mutations.

7. What is cancer? – cancer is uncontrolled cell growth. i.e. cells grow when they shouldn't and don't die when they should.

8. Why can p53 mutations lead to cancer? – If p53 can't halt cells for DNA damage repair to occur or induce cells with too many mutations to die, then cells will grow when they shouldn't and don't die when they should. And these cells are more likely to accumulate more mutations. This is a hallmark of cancer.

These criteria are summarized in the following rubric.

Rubric for Grading Aflatoxin week 2 homework.

Criteria for Teacher	Levels of Completion		
	Comprehensive (receives all points)	**Proficient (-2 to -3pts / part)**	**Needs Improvement (lose all pts / part)**
Position & Scientific Thinking (20pts)	▪ Position is clear ▪ Text supports position ▪ Concepts connect aflatoxin-contaminated PB to liver cancer	▪ Position is clear ▪ Reasoning supports position ▪ Most concepts are connected	▪ No position **(-3pts**) ▪ Reasoning does not support position ▪ Concepts are not connected or missing
Liver (20pts)	▪ Liver's role in deactivating toxins is correctly defined or bioactivation of aflatoxin in liver is mentioned ▪ Put pieces together: since aflatoxin is activated in the liver it can cause liver cancer	▪ Liver's role in deactivating toxins is incorrect or unmentioned & Bioactivation defn is incorrect or absent **(-3pts)** ▪ Pieces unconnected	▪ Liver is not discussed
Aflatoxin (15pts)	▪ Acquistion of aflatoxin is clear – eat it in PB ▪ Aflatoxin effect on p53 gene is clear ▪ central dogma: p53 gene mutation -> mRNA -> ptn	▪ Acquisition of aflatoxin and effect of aflatoxin on p53 gene is unclear **(-3pts)** ▪ Central dogma incorrect **(-3pts)**	▪ Acquisition of aflatoxin and effect of aflatoxin on p53 gene is very unclear or is absent
p53 (25pts)	▪ p53's role in cell cycle is clear (controls G1 checkpoint, DNA damage repaired or cells killed) ▪ If p53 mutated, cells don't stop in G1 and repair DNA damage & cells don't die if too much damage -> cells get lots of mutations ▪ This can cause cancer	▪ Role of p53 in the cell cycle is unclear **(-3pts)** ▪ Result of p53 mutation incorrect or unclear **(-3pts)** ▪ Link between p53 mutation and cancer not made	▪ Role of p53 in the cell cycle is very unclear or absent ▪ Result of p53 mutation incorrect ▪ Link between p53 mutation and cancer not made
Cancer (10pts)	▪ Correct definition – uncontrolled cell growth ▪ Path from normal cell to tumor is clear (many mutations + time, cells don't die when should & grow when shouldn't (defn.)) ▪ Because bioactivation in liver, liver cancer results	▪ Definition incorrect **(-3pts)** ▪ Normal cell to cancerous tumor unclear: many mutations **(-3pts)**, defn **(-3pts)** ▪ Liver cancer connection unclear **(-3pts)**	▪ Definition incorrect ▪ Path from a normal cell to a cancerous tumor is very unclear or absent ▪ Liver cancer connection unclear or absent