Biology Close & Critical Reading Article

Instructions: COMPLETE ALL QUESTIONS AND MARGIN NOTES using the CLOSE reading strategies practiced in class. This requires reading of the article three times.

Step 1: Skim the article using these symbols as you read:
(+) agree, (-) disagree, (*) important, (!) surprising, (?) wondering

Step 2: Number the paragraphs. **Read** the article **carefully** and **make notes in the margin.**
Notes should include:

- Comments that show that you **understand** the article. (A summary or statement of the main idea of important sections may serve this purpose.)
- Questions you have that show what you are **wondering** about as you read.
- Notes that differentiate between **fact** and **opinion.**
- Observations about how the **writer's strategies** (organization, word choice, perspective, support) and choices affect the article.

Step 3: A **final quick read** noting anything you may have missed during the first two reads.

Your **margin notes** are part of your score for this assessment. Answer the questions carefully in **complete sentences** unless otherwise instructed.

Student _____ **Class Period** _____

Inactivating AGPS Enzyme Reduces Tumor Growth, Cripples Cancer Cells

Notes on my thoughts, reactions and questions as I read:

TOPICS: Cancer Cell Biology Enzyme Health Molecular Biology UC Berkeley
AUGUST 27, 2013

Illustration of an aggressive cancer cell. Image by O'Reilly Science Art

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In a newly published study, researchers tested the effects of reducing ether lipids on human skin cancer cells and primary breast tumors, finding that inactivating an enzyme critical to the formation of ether lipids substantially reduced the aggressiveness of the cancer cells.

Berkeley — Knocking out a single enzyme dramatically cripples the ability of aggressive cancer cells to spread and grow tumors, offering a promising new target in the development of cancer treatments, according to a new study by researchers at the University of California, Berkeley.

The paper, **published in the journal Proceedings of the National Academy of Sciences**, sheds new light on the importance of lipids, a group of molecules that includes fatty acids and cholesterol, in the development of cancer.

Researchers have long known that cancer cells metabolize lipids differently than normal cells. Levels of ether lipids – a class of lipids that are harder to break down – are particularly elevated in highly malignant tumors, although the nature of that correlation has been unclear for decades.

"Cancer cells make and use a lot of fat and lipids, and that makes sense because cancer cells divide and proliferate at an accelerated rate, and to do that, they need lipids, which make up the membranes of the cell," said study principal investigator Daniel Nomura, assistant professor in UC Berkeley's Department of Nutritional Sciences and Toxicology. "Lipids have a variety of uses for cellular structure, but what we're showing with our study is that lipids can also send signals that fuel cancer growth."

In the study, Nomura and his team tested the effects of reducing ether lipids on human skin cancer cells and primary breast tumors. They targeted an enzyme, alkylglycerone phosphate synthase, or AGPS, known to be critical to the formation of ether lipids.

The researchers first confirmed that AGPS expression increased when normal cells turned cancerous. They then found that inactivating AGPS substantially reduced the aggressiveness of the cancer cells.

"The cancer cells were less able to move and invade," said Nomura.

The researchers also compared the impact of disabling the AGPS enzyme in mice that had been injected with cancer cells.

"Among the mice that had the AGPS enzyme inactivated, the tumors were nonexistent," said Nomura. "The mice that did not have this enzyme disabled rapidly developed tumors."

Notes on my thoughts, reactions and questions as I read:

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The researchers determined that inhibiting AGPS expression depleted the cancer cells of ether lipids. They also found that AGPS altered levels of other types of lipids important to the ability of the cancer cells to survive and spread, including prostaglandins and acyl phospholipids.

"The effect on other lipids was unexpected and previously unknown," said study lead author Daniel Benjamin, doctoral student in the Nomura Research Group. "Other studies have investigated specific lipid signaling pathways, but what makes AGPS stand out as a treatment target is that the enzyme seems to simultaneously regulate multiple aspects of lipid metabolism important for tumor growth and malignancy."

Future steps include the development of AGPS inhibitors for use in cancer therapy, said Nomura.

"This study sheds considerable light on the important role that AGPS plays in ether lipid metabolism in cancer cells, and it suggests that inhibitors of this enzyme could impair tumor formation," said Benjamin Cravatt, professor and chair of chemical physiology at The Scripps Research Institute, who is not part of the UC Berkeley study. Cravatt is an expert in the role enzymes play in human diseases.

Other study co-authors include Kunxin Luo, UC Berkeley professor of molecular and cell biology and faculty scientist at the Lawrence Berkeley National Laboratory.

The National Institutes of Health and the Searle Scholar Foundation helped support this research.

Publication: Daniel I. Benjamin, et al., "Ether lipid generating enzyme AGPS alters the balance of structural and signaling lipids to fuel cancer pathogenicity," PNAS, 2013; doi: 10.1073/pnas.1310894110

Source: Sarah Yang, UC Berkeley News

Image: O'Reilly Science Art

Notes on my thoughts, reactions and questions as I read:

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Comprehension Questions – answers may be in phrases.

1. *According to this article, what macromolecule do cancer cells use a lot of in order to grow and spread rapidly? Why does this make sense?*

2. *Based on the reading, define* **proliferate**.

3. *What is the name of the molecule they are studying the effects of (and it's abbreviation)?*

Answer each question in one or more complete sentences.

1. *What are the 2 major ways cancer cells use fats and lipids?*

2. *What does metabolism mean in this article? Does it differ from your assumed definition?*

3. *Who is Benjamin Cravatt and what is his role in this study? What is his expertise and why would he find this important/interesting?*

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In your opinion, does this article help to shed some light on the importance of enzymes on the biological processes which occur in our own bodies? Explain why or why not in a well-developed paragraph using CER.

List and define any terms you did not understand before reading this article, but have a better understanding of now (must be at least 2).

Date: Hour: Topic:

Lesson Goal: Lesson Target:

"Enzymes Review Worksheet"

* Use pgs. 49-53 in your book to help

1. Watch this video

2. What happens when chemical bonds are formed or broken? Why?

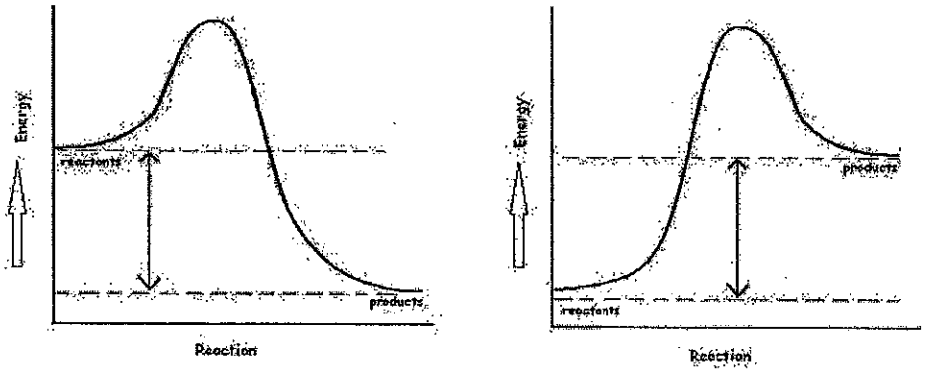
3. What do we know about Exothermic Reactions (those that release energy)?

4. What do we know about Endothermic Reactions (those that absorb energy)?

5. What is activation energy?

6. Is activation energy the same for all reactions?

7. Identify each of the following graphs a Endo- or Exothermic:

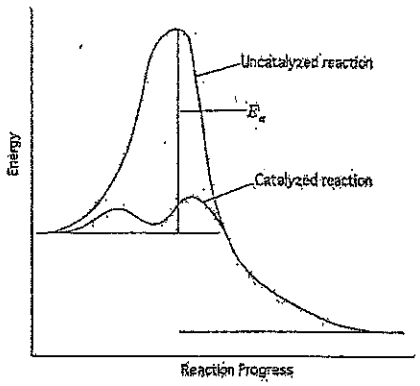


7. What is a catalyst?

8. What is an enzyme?

9. Are all catalysts enzymes?

10. Why does our body produce enzymes for reactions that would otherwise have high activation energies?



11. What effect do enzymes have on these activation energies?

12. Enzymes are often named for the job the do, for example, DNA polymerase helps to make new copies of DNA. What do you think the enzyme **lactase** does? How about **pepsin**?

13. What is a substrate?

14. What is the relationship between the active site shape and the substrate? (Think of a lock and key....)

15. What is an enzyme-substrate complex? What is released from the enzyme-substrate complex?

16. Can an enzyme do any job in our body? Explain

17. How are enzyme often controlled by our bodies?

Go to one of the the following Websites. Locate an article on Enzymes, read it, and complete the following report on that article.

- http://www.the-scientist.com/?articles.list/tagNo/2082/tags/enzymes/
- https://scitechdaily.com/tag/enzyme/

choose 1

Link to Article: (copy and paste URL or write)	
Name of Article:	
Author of Article:	
Who?: (Who's involved?)	
What?: (What's happening?)	
Where?: (Where's it happening?)	
When? (What time period is it referencing?)	
Why? (Why is it important or why is it happening?)	
How?: (How it's happening or being done)	