Name _____ Period _____ Date_____

Biology
Gene Expression and Cell Types Article and Activity

Rubric for this Assessment

AST 2.5 (NGSS HS-LS-1-1): Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins, **which carry out the essential functions of life through systems of specialized cells.**

Part 1: Background Information

Watch the first 5 minutes and 19 seconds of this video (stop when they mention ligand-gated ion channels) and answer the questions below.

1. What type of biomolecule make up cell receptors?

2. What type of biomolecule typically make up signaling molecules?

3. List the general sequence of cell signaling below.

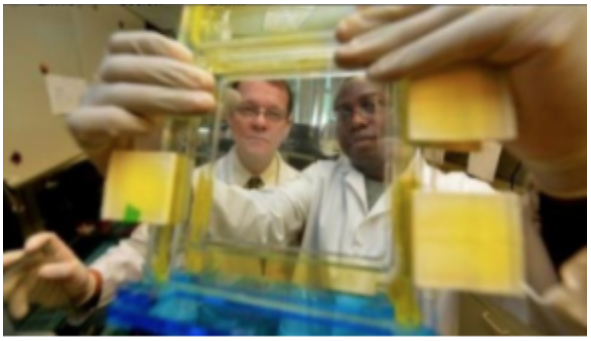
1.
2.
3.

4. Summarize the process from the steroid hormone signaling detailed in the video at 4:27. How did the general sequence of cell signaling from the question above play out?

1.
2.
3.

Part 2A: Application

In the article below, you will read about a real-life situation in which a mutation in the gene for a receptor molecule has caused health concerns for a patient. Read the article, annotating with highlighting and margin comments, and typing any questions you have in the right-hand column.



This is Dr. Lawrence C. Layman, Chief of the Section of Reproductive Endocrinology, Infertility and Genetics at the Medical College of Georgia at Georgia Regents University. *Credit: Phil Jones*

July 11, 2013 — Delayed puberty: First estrogen receptor mutation found in a young woman

A receptor mutation that essentially blocks estrogen's action has been identified for the first time in a female, researchers report.	My Questions /Notes
The 18-year-old wasn't experiencing breast development or menstruation, classic symptoms of too little estrogen, the usual cause of delayed puberty. Subsequent studies revealed instead sky-high levels of the sex hormone in her blood, said Dr. Lawrence C. Layman, Chief of the Section of Reproductive Endocrinology, Infertility and Genetics at the Medical College of Georgia at Georgia Regents University. "Her body totally ignores estrogen," Layman said. "Even at levels that are 10 to 15 times normal, it	

has no effect." In fact, in laboratory studies, 240 times the normal level was required to get a response out of the patient's receptors.

There are two confirmed estrogen receptors throughout the body, and genetic testing subsequently determined she had a mutation in the gene for estrogen receptor-α (alpha), which is essential to reproduction and bone health, researchers report in the *New England Journal of Medicine (NEJM)*. Estrogen levels in her blood were comparable to those of a mouse whose estrogen receptor-α gene has been deleted in a laboratory study.

Interestingly the first mutation in this receptor was reported nearly 20 years earlier in the *NEJM* in a 28-year old man with knock-knees and signs of insulin resistance. Studies showed his testosterone levels were normal however, his estrogen and other related hormone levels were high, leading to believe he also had essentially no response to estrogen. The research team, led by Children's Hospital Medical Center in Cincinnati, found the estrogen receptor-α defect in this male patient, concluding that estrogen is important to bone health in men as well as women.

The estrogen receptor-α mutation found in the 18-year-old female is slightly different but also results in profound estrogen resistance in women, said Layman, the new study's corresponding author. The major known impacts of estrogen in women are enabling reproduction, breast development, and bone health.

While generally healthy, the young woman sought medical help due to her lack of breast development and menstruation as well as lingering, lower-abdominal pain. Studies by Dr. Earl "Sandy" W. Stradtman Jr., a reproductive endocrinologist in Birmingham, Ala., revealed the markedly high estrogen levels as well as multiple, large ovarian cysts. It was then that Stradtman referred her to Layman, an expert in delayed puberty.

Overwhelmingly, delayed puberty results from insufficient estrogen Layman said. Estrogen production normally begins with the brain telling the ovaries to make it, so most of his patients have a problem with brain signaling. When the brain doesn't signal the ovaries to make estrogen, there is none produced therefore there is no gene expression signal to enable the body to produce breast tissue cells as well as a failure to release an egg from the ovary. This 18-year-old patient has a very large amount of estrogen built up in the blood, but the bottom line is similar for this woman because estrogen's *effect* is missing,

The receptor defect creates the slightly different problem of not being able to use the estrogen that is there, control how much is made, or control its result. For example, the woman had cystic ovaries because her body was constantly producing follicles (a cell type that produces estrogen) rather than the usual one a month needed so an egg can descend and either be fertilized or shed along with blood, cervical mucus and endometrial tissue during menstruation.

It's estrogen's binding with its receptor that activates the negative feedback system that tells the brain there is plenty of the sex hormone (estrogen) and follicles do not need to produce more. When estrogen is recognized in the body, cells will regulate gene expression so as not to make too much of the hormone. In this case, that negative feedback system didn't happen so estrogen built up in her blood, eventually dumping in her urine, said Samuel D. Quaynor, an M.D./Ph.D student at MCG and GRU and the study's first author.

Without estrogen, insulin levels also typically increase, putting the patient at risk for diabetes. Estrogen receptor-α is linked to the cell signaling necessary to allow insulin to let glucose into the cell to be digested and metabolized. Without estrogen receptor-α, more insulin is necessary for the metabolism of glucose making it more difficult to get energy to your cells from your food.

While the woman's glucose and insulin levels were normal, she did have an unusual response to an oral glucose test that indicated glucose and insulin problems could be in her future, Researchers also noted that the male's elevated levels might be related to obesity.

To fully understand the impact of the receptor mutation, they'd like to do large-scale screening to see if other substances bind to its altered state. Since the young woman is adopted, her biological family history was unavailable, but she was just over five feet tall and had lower than expected bone mass for her age, although she was still growing. Abnormally high bone turnover was indicated as well. Estrogen has been linked to bone health, as a low amount of estrogen is one of the major causes of postmenopausal osteoporosis. Estrogen receptors are largely responsible for the regulation of bone metabolism (the building and recycling of bone cells) and can be found on bone and bone marrow cells throughout the body. (Streicher) Estrogen receptor-α was cloned in 1986 and estrogen receptor-β was cloned 10 years later. Eliminating estrogen receptor-β doesn't cause any significant problems in mice and eliminating estrogen receptor-α had the most impact in female mice.	

Article Source: Medical College of Georgia at Georgia Regents University. (2013, July 11). Delayed puberty: First estrogen receptor mutation found in a young woman. *ScienceDaily*. Retrieved June 24, 2018 from www.sciencedaily.com/releases/2013/07/130711113426.htm

Streicher, Carmen, et al. "Estrogen Regulates Bone Turnover by Targeting RANKL Expression in Bone Lining Cells." *Nature News*, Nature Publishing Group, 25 July 2017, www.nature.com/articles/s41598-017-06614-0.

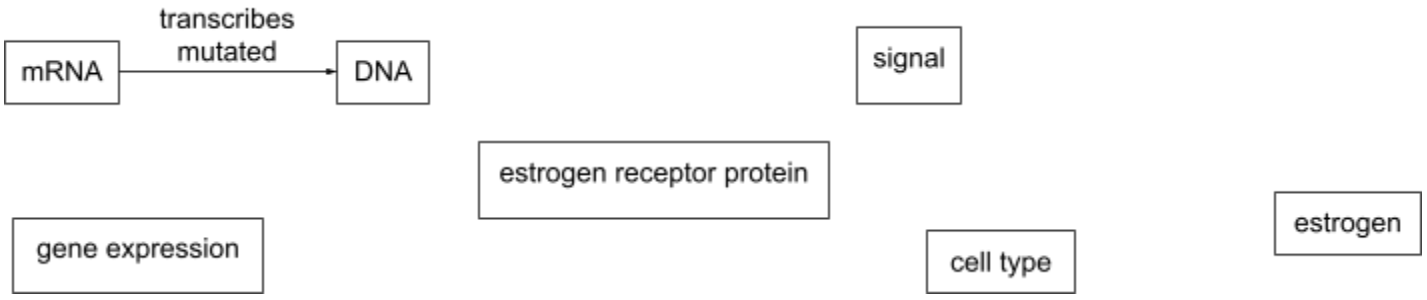
Original Research Cited: Samuel D. Quaynor, Earl W. Stradtman, Hyung-Goo Kim, Yiping Shen, Lynn P. Chorich, Derek A. Schreihofer, Lawrence C. Layman. **Delayed Puberty and Estrogen Resistance in a Woman with Estrogen Receptor α Variant**. *New England Journal of Medicine*, 2013; 369 (2): 164 DOI: 10.1056/NEJMoa130361

Part 2B: Reflection & CER

Rubric for this Assessment

5. Use information from the article to explain the importance of estrogen in female development/puberty.
_____ is important in _____ because...

6. Use Google Drawing to draw a concept map showing the cause and effect that occurred in this patient. **The words have been put into the Google Drawing for you, including one linked example. Your job is to organize them with arrows and linking words to connect them in a way that describes their relationships.**



7. This patient's cells did not receive the estrogen signal because of her mutated estrogen receptors. As a result, she had a decrease in function with certain types of cells in her body. Using evidence from the text, describe what happened to at least 2 cell types that were either (1) never formed or (2) changed by the lack of response to the estrogen signal.

Word bank

transcription	DNA	mutation	signaling	response

translation	protein	trait	gene	

Rubric for this Assessment

Choose from the sentence frames provided, or write your own.

Claim

Make a claim about at least two cell types that were either (1) never formed or (2) changed by the lack of response to the estrogen signal.

According to ____, ___ suggests that ___.

The relationship between ___ and ___ is ___.

Evidence

Provide evidence from the text to support your claim. *Remember evidence can be numbers, text, or images.*

The evidence for this is ...

This claim is supported by ...

___ shows that ___.

Reasoning

Provide scientific reasoning using the concepts of proteins, protein synthesis, and the effects of mutations as to why the normal or healthy cells were missing in this patient.

This data is supported by the idea that ___ because …

___ suggests that ___ because …

___ can be explained by ___ because …

This evidence makes sense because ___.

___ supports this position because …