Transcription Factors and Gene Expression

Introduction

The “central dogma” in biology summarizes the process of gene expression, how genetic information flows from DNA to protein. Gene expression can be influenced by many factors such as environment, other genes, and molecules called transcription factors. In this lesson, you will investigate the role of transcription factors in the production of a protein called melanin.

What To Do

Read “Natalie and Alex’s Story.” Then, answer the questions, reading the Bite when instructed.

Natalie and Alex’s Story

Natalie and her twin brother Alex are attending a concert with their parents. The two have been up all week studying for the biology midterm on protein synthesis and are fighting sleep. They have stayed after class with their teacher, Ms. Dana, made flashcards, and quizzed each other, but there is one concept they just cannot seem to understand—what is a **transcription factor**? Ms. Dana defined a transcription factor as a protein that affects the expression of many other genes. She explained that they control how much and how quickly proteins are produced, but they do not directly produce the proteins themselves. How can they do that? How can they be in charge of something, but not produce the product themselves? Natalie and Alex just don’t understand and cannot discuss it anymore, the concert is about to start.

While Natalie and Alex are not huge fans of the orchestra, they become really interested in the conductor. The twins notice that the conductor’s movements seem to match the intensity of the music. When her arms move quickly and sharply, the music is quick and choppy. When her arms wave slowly with sweeping motions, the music is slow and graceful.

Figure 1. Orchestra Conductor. The conductor (In black) controls the pace and timing of the players. *Image:* Walter Lim, Flickr

"Ah-ha!" Alex is suddenly giddy. "I get it," he says to Natalie. "A transcription factor is like a conductor! She is not making the music, but through her gestures, she is controlling the whole show. The orchestra is responding to her." Alex can see the light bulb go off in Natalie's mind.

As Natalie's eyes lit up she responded, "One conductor controls the whole show. She signals the many musicians in the orchestra, which affects the music we hear, just like a transcription factor signals many pathways and affects the proteins that are expressed!"

The twins finally understood transcription factors. They are like the conductor in an orchestra. One conductor can control the whole show.

Analysis Questions

1. Transcription and translation are two important processes that occur in cells.

a. Complete the flowchart below that models the relationship between the processes.

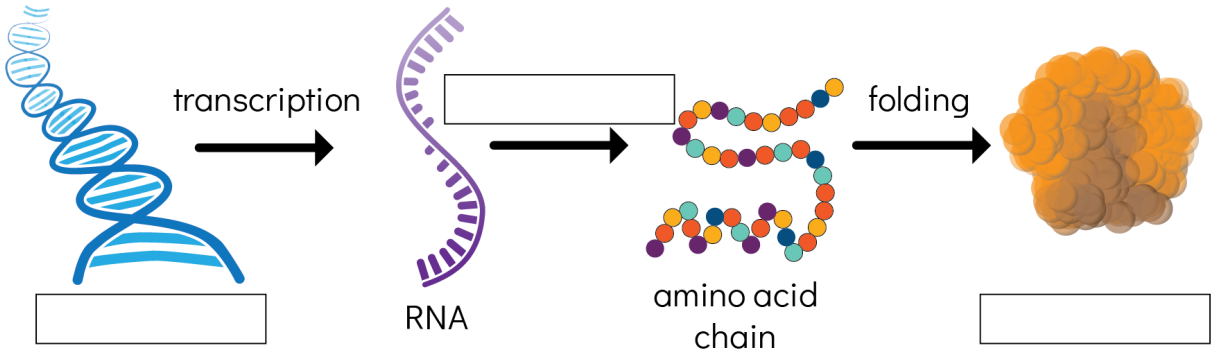

Figure 2. The Central Dogma. The inputs, outputs, and processes involved in gene expression, are collectively known as "the central dogma."

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b. Could translation occur without transcription? Justify your answer using the flowchart.

2. Having a copy of a particular gene does **not** guarantee that the gene will be expressed in an organism. For example, some genes require a special molecule, called a promoter, to be present or else it won't "show up." Describe other reasons why a trait might not show up, even if the organism has a gene for the trait.

3. In your own words, describe the function of a transcription factor.

4. The drug you read about causes the skin to tan without the sun.

a. According to the Science Bite you just read, what is the advantage of tanning?

b. If tanning has benefits, why do doctors urge people to avoid sun exposure?

c. Why are dermatologists (doctors that specialize in conditions related to the skin) so excited about the new drug?

Figure 3 below shows the death rates for skin cancer worldwide by country. The darker the orange, the higher the rate of death.

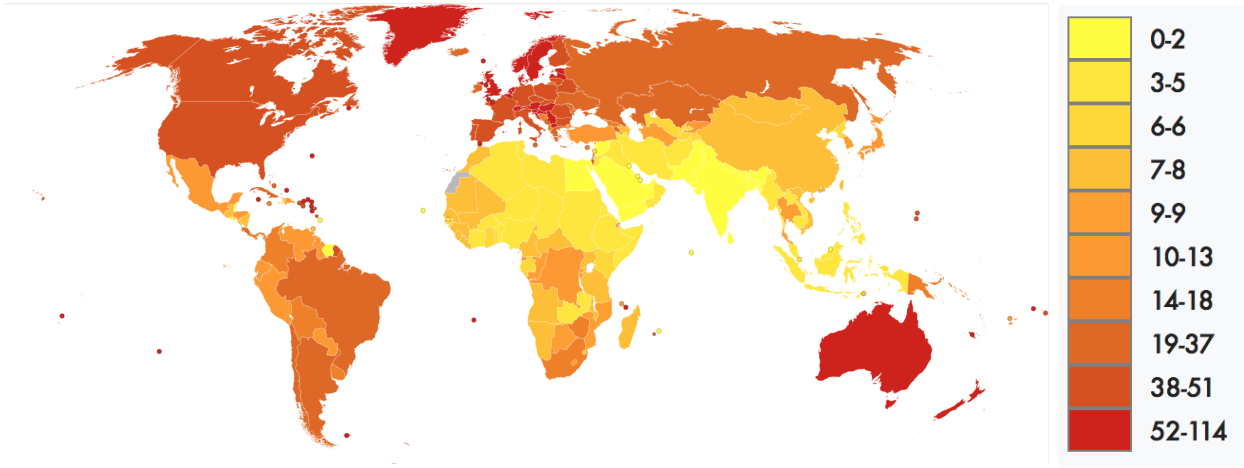

Figure 3. Global Deaths from Skin Cancer. This map, based on 2012 data from the World Health Organization, compares death rates from melanomas and other skin cancers in nations around the world. The colored scale shows deaths per one million persons.
Source: Wikimedia Commons/Chris55.

5. Make a claim about why North American and European countries have relatively high skin cancer death rates compared to African and Southeast Asian countries. Describe evidence for your claim using information from **Figure 3** Provide reasoning for your claim, citing information from the Bite.

6. Describe the relationships among inherited genes, the pigment melanin, sun exposure, and skin cancer risk.

Figure 4 below models how the new drug influences the production of melanin pigment.

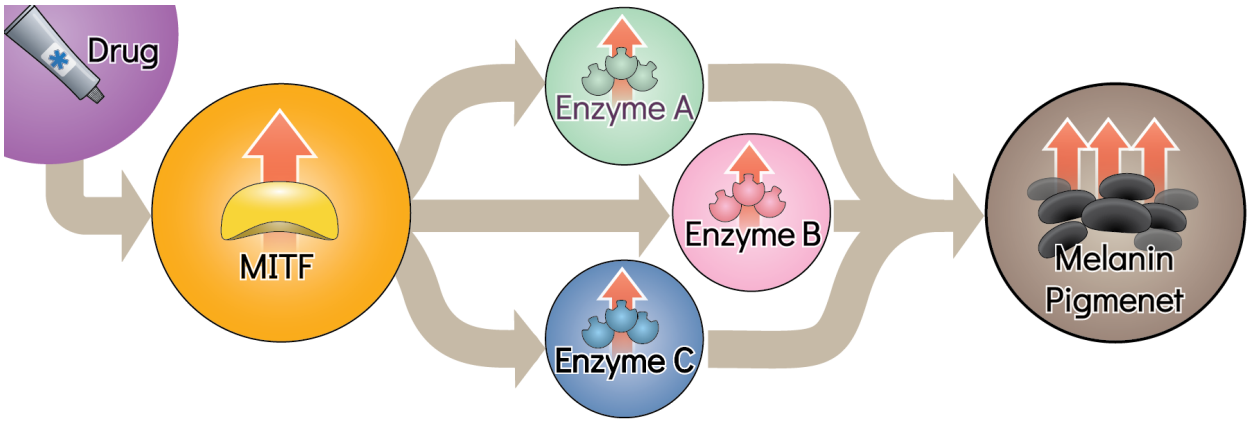

Figure 4. How the New Drug Works. The drug developed by the research team causes the production of the MITF protein to increase, which in turn increases the work of many enzymes (only three modeled here to make things simpler), which in turn increases melanin production.

7. Increasing the production of one molecule, MITF causes an increased response from enzymes A, B, and C because MITF is a transcription factor. Think back to the analogy in the introduction. In this drug pathway, the conductor is the MITF transcription factor.

Which component of the drug pathway aligns to these parts of the analogy:

a. the members of the orchestra

b. the music

8. Why would a drug that only increases the production of enzyme A not have the same effect as the drug described in the Science Bite that increases the production of MITF? (*Hint:* Think about MITF's role as a conductor.)

Use **Figure 5** below to answer Questions 9 and 10.

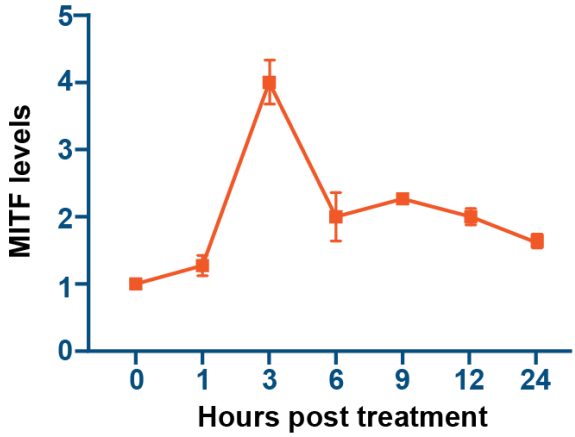

Figure 5. Experimental Levels of the MITF Transcription Factor. The drug is applied to the mice at hour 0, and levels of the MITF transcription factor are measured at different hours post-treatment.
Source: Mujahid *et al.,* 2017.

9. Using the graph above, describe the trend in MITF production. In your answer, include information about how long it takes MITF to be expressed to its highest level and how long the MITF expression stays above normal (between 1–2 on the *y*-axis).

10. Look back at **Figure 4.** The drug first increases MITF expression, which then increases the action of the pigment producing enzymes, which then increases production of the melanin pigment itself. Thus there is likely a delay in melanin production following drug treatment.

a. Draw another line on the graph in **Figure 5** to represent the pigment production following drug exposure.

b. Directions for applying sunscreen indicate that it should be applied twenty minutes prior to going out into the sun. How does that timeframe compare to the timeframe for effectiveness of the drug here?

c. How do you account for the time difference between the effectiveness of the two methods of sun protection (the new drug and traditional sun screens)?

Connect to the Big Question

11. In this study, mice act as model organisms for humans. A **model organism** is a non-human animal that is studied for the purposes of understanding a biological phenomenon. In this case, mice are used to study the process of tanning and skin pigmentation in response to this drug.

a. What are some of the reasons that mice can be used as a model for humans for this study?

b. How do scientists observe the drug's effects on the mice? How do these effects inform how the drug will be used in humans?

c. Would you volunteer to have a new drug tested on you? For each of the following, explain whether you would you be more or less likely to volunteer for:

- a drug that has worked pretty well on mice OR a drug that has worked very well on fruit flies?

- a drug with effects you can see (like, with the skin tanning drug) OR a drug with effects you cannot see (that act on an internal organ, such as the heart or lungs)?

- a drug that could cure a disease you have OR a drug that could change the way you look (by, for example, giving you thicker hair, or stronger fingernails)?

12. After testing this drug on mice, researchers created similar drugs for humans using the same considerations that you outlined in Question 11. They tested these drugs on human skin. Results are shown in **Figure 6.**

a. Rank the three drugs shown below in terms of effectiveness in triggering the tanning response.

b. What other factors are important for selecting which drug to further test in humans besides the intensity of the tan it causes?

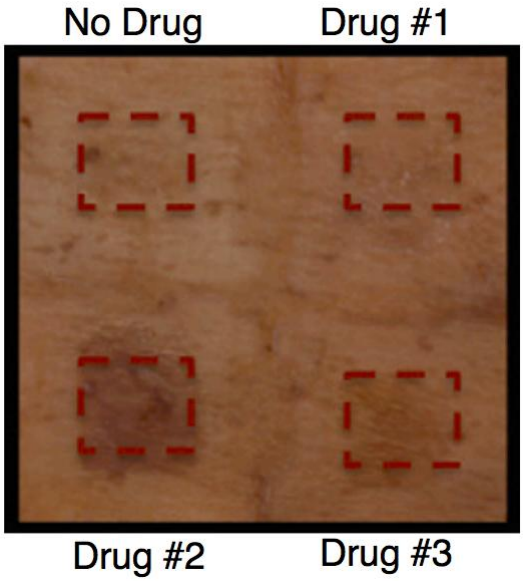

Figure 6. Drug Results. Human skin eight days after one of 4 treatments: No drug, drug #1, drug #2, or drug #3. *Source:* Mujahid *et al.,* 2017