Name: _____

Albinism: From genotype to phenotype

***Phenotype**: What does a person with albinism **look** like?*

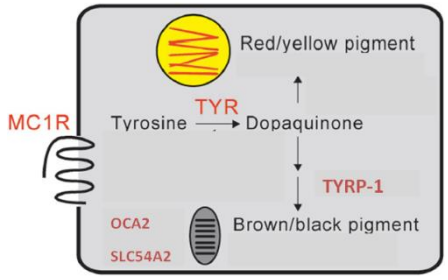
Oculocutaneous albinism is a group of conditions that affect coloring (pigmentation) of the skin, hair, and eyes. Approximately 1 in 20,000 exhibit this disorder and affected individuals typically have very fair skin and white or light-colored hair. Long-term sun exposure greatly increases the risk of skin damage and skin cancers, including an aggressive form of skin cancer called melanoma. Albinism also reduces pigmentation of the colored part of the eye known as the iris and the light-sensitive tissue at the back of the eye called the retina. People with this condition usually have vision problems such as reduced sharpness, rapid, involuntary eye movements (nystagmus), and increased sensitivity to light (photophobia). Melanin is an extremely important molecule in humans for many reasons, one being its ability to protect the DNA in the cell's nucleus from damage by UV light from the sun. This is one reason the skin darkens after being exposed to sunlight and people living closer to the equator have darker skin for this extended protection.

Albinism is not only seen in humans, as it is actually found across all major animal groups since nearly all produce melanin. It has been observed in countless species of mammals, birds, reptiles, amphibians, fish and even invertebrates. This is not surprising since the gene for melanin production, the protein responsible for producing pigment in skin, hair and eyes, is similar among these species. All it takes is one small change to result in a change in this protein's shape to make it non-functional.

In humans, the four types of oculocutaneous albinism are designated as type 1 (OCA1) through type 4 (OCA4). Oculocutaneous albinism type 1 is characterized by white hair, very pale skin, and light-colored irises. Type 2 is typically less severe than type 1; the skin is usually a creamy white color and hair may be light yellow, blond, or light brown. Type 3 includes a form of albinism called rufous oculocutaneous albinism, which usually affects dark-skinned people. Affected individuals have reddish-brown skin, ginger or red hair, and hazel or brown irises. Type 3 is often associated with milder vision abnormalities than the other forms of oculocutaneous albinism. Type 4 has signs and symptoms similar to those seen with type 2. Because their features overlap, the four types of oculocutaneous albinism are most accurately distinguished by their genetic cause (NCBI; www.ncbi.nlm.nih.gov)

***Genotype**: Which **gene**(s) are affected that cause the disorder?*

The four types of oculocutaneous albinism each result from mutations in single genes: *TYR*, *OCA2*, *TYRP1*, or *SLC45A2*. Changes in the *TYR* gene cause type 1; mutations in the *OCA2* gene are responsible for type 2; *TYRP1* mutations cause type 3; and changes in the *SLC45A2* gene result in type 4. These genes are involved in producing the pigment melanin. In the retina, melanin also plays a role in normal vision. Mutations in any of these genes disrupt the ability of cells to make melanin, which reduces pigmentation in the skin, hair, and eyes.



Alterations in the *MC1R* gene can change the appearance of people with oculocutaneous albinism type 2. This gene helps regulate melanin production and is responsible for some normal variation in pigmentation. People with genetic changes in both the *OCA2* and *MC1R* genes have many of the usual features of oculocutaneous albinism type 2, including light-colored eyes and vision problems; however, they typically have red hair instead of the usual yellow, blond, or light brown hair seen with this condition. (*NIH, 2014*)

Organize your thoughts: by reviewing the phenotypic traits that appear in humans with this genetic disorder in the reading above, complete the table below.

Albinism Type	Skin color	Hair color	Eye color	Certain people affected?	Gene affected
OCA1					
OCA2					
OCA3					
OCA4					

What do all types of albinism have in common? Use the traits discussed in the reading as evidence.

_____

_____

_____

_____

What is the function of the protein melanin? Explain its importance by citing evidence from the reading.

_____

_____

_____

_____

_____

Construct an explanation below that explains why there are different variations of this disorder and why it results in the same basic phenotype. Cite specific evidence *without* copying any part of the passage directly below.

_____

_____

_____

_____

_____

_____

_____

Name: _____

Going through the motions…
Genotypes to Phenotypes

In this activity, you will observe a normal gene and compare it to three (3) mutated sequences. By transcribing and translating each gene sequence, you will determine both where the mutation is located and what type of mutation has occurred. Finally, you will determine how the gene was changed and how it affected the person's phenotype.

Procedure:

1) Each student will analyze one of four genes ***on the back*** of this sheet: ***TYR***, ***OCA2***, ***TYRP-1***, or ***SLC45A2***. Each student will have a different gene and be responsible for reporting their findings to the other group members.
2) Each form has an original DNA strand and 3 different mutated strands. For each, you will transcribe the mRNA sequence and then translate the mRNA into the amino acid sequence (AAs).
3) With a ***colored pencil***, you will then do the following:
   - ✓ *First, circle the mutation(s) on each of the three mutated strands that differ from the original DNA strand at the top of your form. (Note: not all sequences start at beginning of gene.)*
   - ✓ *Second, lightly shade over each **codon that differs** in the mRNA strand from the original mRNA strand at the top of your form.*
   - ✓ *Lastly, lightly shade over each **amino acid that differs** in the amino acid sequence from the original amino acid sequence at the top of your form.*
4) Using the amino acid sequences, match **one** of them to the "Individual" cards at your table to view phenotype.
   Analysis: Making sense of your data **Your gene: _____ Individual # ____ & ____**

Mutation	Mutation Type	Cite your evidence here for mutation type	Change in Phenotype
Mutation 1			
Mutation 2			
Mutation 3			

Which of the above mutations caused a change in the phenotype? _____

How did this change occur? _____

_____

Which mutation did not result in a change in the phenotype? _____

Why did this mutation not result in a change in phenotype? _____

_____

Original DNA Strand **Gene: TYR (OCA1)** **Name: _____**

DNA: TACGAGGACCGACAAAACATGACGGACGACACCTCAAAGGTCTGGAGGCGACCGGTAAAG

mRNA:

AAs:

Mutation 1

DNA: TACGAGGACCGACAAAACATGACGACGACACCTCAAAGGTCTGGAGGCGACCGGTAAAGG

mRNA:

AAs:

Mutation 2

DNA: TACGAGAACCGACAAAACATGACGGACGACACCTCAAAGGTCTGGAGGCGACCGGTTAAGG

mRNA:

AAs:

Mutation 3

DNA: TACGAGAACCGACAAAACATGACGGACGACACCTCAAAGGTCTGGAGGCGACCGGTAAAGG

mRNA:

AAs:

Original DNA Strand **Gene: OCA2 (OCA2)** **Name:** _____

DNA: TAGCACGTGTCTTGAGACCGCCGGTACGACCCAAGGGAACGTCGTGACCGTCGTGACCGA

mRNA:

AAs:

Mutation 1

DNA: TAGCACGTGACTTGAGACCGCCGGTACGACCCAAGGGAACGTCGTGACCGTCGTGACCGA

mRNA:

AAs:

Mutation 2

DNA: TAGCACGTGTCTTGAGACCGCCGGTACGACCCAAGGGAACGTCGTGACCGTCGTGACCAA

mRNA:

AAs:

Mutation 3

DNA: TAGCACGTGTCTTGAGACCGCCGGTACGACCCGAGGGAACGTCGTGACCGTCGTGACCGA

mRNA:

AAs:

Original DNA Strand **Gene: TYRP-1 (OCA3) Name: _____**

DNA: CGGACACTGGTCTCCCAAGAGTATCAGTCCTCTTTAGAAGACCTGAATTCATTTCTTCTT

mRNA:

AAs:

Mutation 1

DNA: CGGACACTGGTCTCCCAAGAGTATCAGTCCTCTTTAGAAGACCTGTAAGTCATTTCTTCT

mRNA:

AAs:

Mutation 2

DNA: CGGACACTGGTCTCCCAAGAGTATCAGTCCTCTTTAGAAGACCTGAACTCATTTCTTCTT

mRNA:

AAs:

Mutation 3

DNA: CGGACACTGGTCTCCCAAGAGTATCAGTCCTCTTTAGAAGACCTGAATTCATTTTTTCTT

mRNA:

AAs:

Original DNA Strand **Gene: SLC45A2 (OCA4)** **Name:** _____

DNA: CTCCGTCGCATACACTGGGGTCAGGACGAGTCGCATCCAGACGGGTCGTCGGACATGTCG

mRNA:

AAs:

Mutation 1

DNA: CTCCGTCGCATACACTGGGGTCAGGACGAGTCGCATCCAGACGGGTCGTCGGAGATGTCG

mRNA:

AAs:

Mutation 2

DNA: CTCCGTCGCATACACTGGGGTCAGGACGAGTCGCATCCAGACGGGTCGTCGGACATCTCG

mRNA:

AAs:

Mutation 3

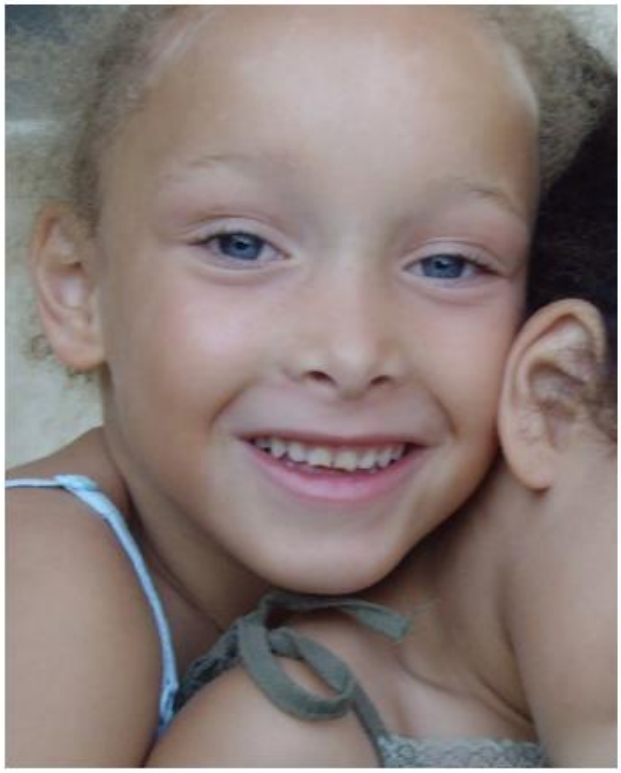
DNA: CTCCGTCGCATACACTGGGGTCAGGACGAGTCGCATCCAGACGGGTCGTCGGACATGCCG

mRNA:

AAs:

Individual #1

Individual #2



Individual #3

Individual #4

ile-val-his-
STOP-thr-
leu-ala-ala-
met-leu-gly-
ser-leu-ala-
ala-leu-ala-
ala-leu-ala

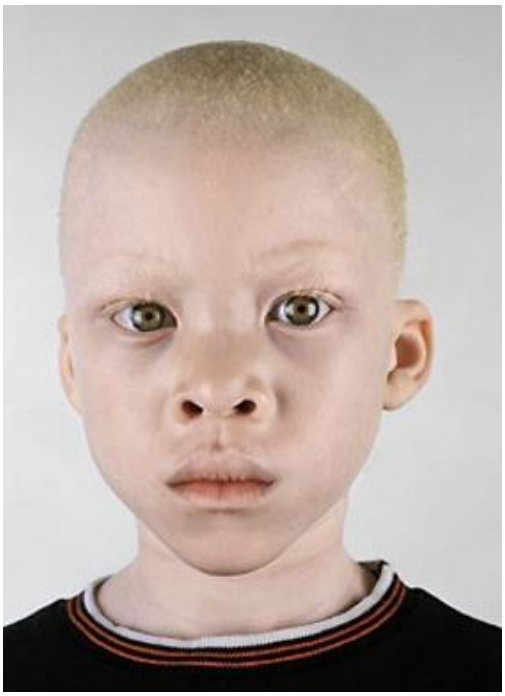
met-leu-leu-
ala-val-leu-
tyr-cys-cys-
cys-gly-val-
ser-arg-pro-
pro-leu-ala-
ile-ser

glu-ala-ala-
tyr-val-thr-
pro-val-leu-
leu-ser-val-
gly-leu-phe-
ser-ser-leu-
tyr-gly

ala-cys-asp-
gln-arg-val-
leu-ile-val-
arg-arg-asn-
leu-leu-asp-
ile-gln-
STOP-arg-arg

Individual #5

Individual #6



Individual #7

Individual #8

ile-val-his-
STOP-thr-
leu-ala-ala-
met-leu-gly-
ser-leu-ala-
ala-leu-ala-
ala-leu-val

met-leu-leu-
ala-val-leu-
tyr-cys-cys-
cys-gly-val-
ser-arg-pro-
pro-leu-ala-
glu-ser

glu-ala-ala-
tyr-val-thr-
pro-val-leu-
leu-ser-val-
gly-leu-phe-
ser-ser-leu-
STOP

ala-cys-asp-
gln-arg-val-
leu-ile-val-
arg-arg-asn-
leu-leu-asp-
leu-ser-lys-
lys-glu

Supplemental activity: Flow Chart **Name: _____**

By creating a flow chart below, trace the steps from DNA through to the resulting phenotype. It has been started for you below.

The following words must appear in this flow chart: ***transcription, translation, amino acid(s), protein, gene, mRNA, tRNA, phenotype***