ACTIVITIES AND DISCUSSION QUESTIONS FOR CLASSROOM USE

Most suitable for Grades 11 and 12, but some content can also work for Grades 8 to 10.

Daniel Drucker, Joel Habener, and Jens Holst:

Read: F. Qaiser and A. Mortazavi. "**The Molecular Elements of Diabetes**" (article, comic and/or video). *Canada Gairdner Awards 2021 Laureates Education Materials,* pp2 - 6

Learning Objectives:

1. Define blood sugar homeostasis.

2. Clarify the roles of insulin and glucagon in managing blood glucose levels.

3. Define an incretin.

4. Describe the role of proglucagon as a gene and GLP-1 and GLP-2 as peptides.

5. Characterize the role of an inhibitor as treatment for disease

6. Understand GLP-1 and GLP-2 as treatments for type 2 diabetics and short bowel syndrome.

Supplementary Reading:

Keywords: insulin, glucagon, proglucagon, glucagon-like peptide-1, glucagon-like peptide 2, dipeptidyl peptidase-4

Our bodies want to be in a healthy state and we call this **homeostasis**. For us, healthy means to be in a stable equilibrium (or balance) between interdependent elements, specifically maintained by physiological processes. Humans' internal body temperature is a great example of homeostasis. When someone is healthy, their body maintains a temperature close to 98.6 degrees Fahrenheit (37 degrees Celsius). When you get shivery in the cold, or sweat in the summer, that's your body trying to maintain homeostasis.

Our bodies are constantly at work maintaining **glucose homeostasis** - the balance of insulin and glucagon to maintain blood glucose. Glucose is a sugar that we consume and our bodies have to decide to either use it immediately to make energy or to store it for energy later. Our bodies know which choice to make through hormone signalling, like what insulin and glucagon do. Insulin is secreted by the pancreas in response to elevated blood glucose after a meal. Insulin lowers blood glucose by increasing glucose uptake in muscle and adipose tissue. A fall in blood glucose increases the release of **glucagon** from the pancreas to promote glucose production to raise blood sugar levels.

Proglucagon is a protein encoded from a gene and the precursor of glucagon. It is also generated in the pancreas and cleaves into several components in different organs. **Glucagon-like peptide 1** (GLP-1) and **glucagon-like peptide 2** (GLP-2) are cleaved from proglucagon and secreted at the intestine.

GLP-1 is an **incretin**; thus, it has the ability to decrease blood sugar levels in a glucose-dependent manner by enhancing the stimulating the release of insulin. People who suffer from **type 2**

diabetes are insulin resistant meaning that their cells don't respond well to insulin and have a tough time taking up glucose from the blood. As a result, the pancreas attempts to create more insulin. GLP-1 as a treatment for type 2 diabetes is attractive because it enhances insulin secretion. Normally GLP-1 would be degraded by **dipeptidyl peptidase-4** (DPP-4). In the treatment plan of a type 2 diabetic DPP-4 inhibitors may be included to disrupt this pathway. A way to avoid DPP-4 would also be to find a GLP-1 analogue that is comparable to GLP-1's activity.

GLP-2 is also cleaved from the proglucagon at the intestine. This peptide enhances intestinal growth and metabolism with nutrient intake. Ultimately GLP-2 enhances intestinal function. GLP-2 and related analogs similar to it may be treatments for conditions like **short bowel syndrome**. In this condition the body is unable to absorb enough nutrients from the foods you eat because you don't have enough small intestine. The small intestine is where the majority of the nutrients you eat are absorbed into your body during digestion..

Classroom Activity: Symptom Scenario

Supplies: one piece of paper per group and a pen.

Time: 15 minutes for activity, 15 minutes for discussion.

Description: Break the students up into groups of three. In this activity, each student will represent one of the three symptom scenarios listed below:

Student 1: fatigue between meal times, alert, normal washroom times and types

Student 2: increased thirst, frequent urination, fatigue, increased hunger

Student 3: stomach ache, diarrhea, weight loss, fatigue

Once the students have their symptom prompts they will begin discussing with their group what could possibly be wrong (hint: there were two abnormal conditions mentioned in the article and supplemental reading). Have them write down their symptoms and the name of their current state as well as any treatment options that may be available to them.

Purpose: The purpose of this activity is to work through the information discovered by Holst, Drucker, Habener and apply it to a real-life scenario. By organizing the conditions that correctly match the symptoms and recommending treatment, students will better understand endocrine signal transduction and glucose homeostasis.

Discussion Questions:

1. Insulin and glucagon are antagonistic hormones in the body because they oppose or reverse the effect of one another. Can you think of other examples of hormones that are antagonists?

2. When administering things like GLP-1, GLP-2, or DPP-4, do you think dosage is important? Why?

3. If you were to make a flowchart of the various hormones and peptides involved in glucose homeostasis, you may realize that controlling this appears very complicated with many parts involved. Why do you think this complexity is a good thing? Another way to think about this is to imagine what if homeostasis was controlled only by a single thing - why might that be a bad thing?

Activity designed by Rhonda Thygesen.

Elizabeth Eisenhauer:

Read: Z. Sepehri, D. Ng, and A. Mortazavi. "**From the Lab Bench to the Hospital Bed**" (article, comic and/or video). *Canada Gairdner Awards 2021 Laureates Education Materials,* pp7 - 11

Learning Objectives:

1. Understand three treatments for cancer (chemotherapy, HAP, angio).

2. Define treatment toxicity.

3. Understand the importance of scheduled planning for drug treatment.

4. Able to describe acquired resistance. Identify acidic invasion.

Supplementary Reading:

Treatment of cancer requires effort from basic research scientists and clinical researchers, as mentioned in the article. Treatments developed in the lab will be tested by clinical researchers on existing cancer patients to figure out the best method of therapy. As you can imagine, there are multiple factors that play into the success of a treatment that clinical researchers must observe, some of which were previously discussed.

Chemotherapy is a very popular type of cancer treatment that uses one or more anti-cancer drugs as part of a standardized routine. However, while the purpose of chemotherapy medications is to reduce your cancer symptoms and lengthen your life, the drugs can also have unwanted effects on your body. Chemotherapy can poison your body and lead to harm, and this is known as treatment toxicity, a main indicator of how a patient is responding to the chemotherapy course.

Just as important as the type of treatment is the scheduled planning of it. By determining when a treatment will be administered researchers can predict and avoid a poor bodily response in the patient. Sometimes the body will react in unexpected ways such as with acquired resistance. Tumors that suddenly begin to grow while on a treatment regimen may be experiencing tumor resistance. In this case, researchers have to balance between slowing the tumor growth and causing resistance. Certain cancer cells may have hyperactive metabolisms that break down carbohydrate fuel at abnormal speeds, resulting in what's called acidic invasion. The acid produced from a tumor kills normal cells and allows it to grow faster.

Hypoxia activated prodrug (HAP) is a nice complement to chemotherapy, but it only works in hypoxic regions - areas with low oxygen. In a patient, a mix of chemotherapy and HAP may be necessary. This is called combination therapy. Angio drugs block angiogenesis - the growth of blood vessels. They do this by blocking nutrients and oxygen from a tumor, essentially starving it. Angio can boost the effectiveness of HAP by lowering the amount of oxygen in the tumor, inducing hypoxia (low levels of oxygen in your blood).

All three drugs (chemotherapy, HAP, angio) can be used to treat a cancer patient. One patient's cancer treatment may look very different from another's and requires unique treatment plans.

Classroom Activity: Cancer Crusade!

Supplies: Students will need to download a free app. Therefore access to a smartphone or computer (laptop or desktop) and to the Apple app store or the Google Play store is required

Time: 5 minute scenario/student, adjust total time as necessary for activity (for instance, students can go through 2 scenarios in 10 minutes, etc). 15 minutes for discussion.

Description: Students will download the game "Cancer Crusade" onto a smartphone or a computer. If possible, have them pair up in groups of two to share a device and work through the app together. The students will run through the instructions of how the game works and then will begin digitally experimenting to treat tumour growth. By playing the game, the students will be testing different variations of treatments, becoming real-life data for cancer researchers. Students will receive a good score in the game by preventing both tumor size and toxicity from becoming too high for too long.

Purpose: Many combinations exist for cancer treatments, however, it is difficult to know how much, at what time, and for how long. Students will play the role of a clinical researcher from their cell phones and laptops and observe how a fake cancer cell grows and shrinks in response to their treatments. By playing the game and testing out new possible treatment combinations the students are contributing to research collections that otherwise would have taken years of trial and error.

Discussion Questions:

1. How did it feel to be responsible for finding the right treatment and dose? Was it frustrating or exciting? Did anyone have a particularly good score?

2. What do you think is the biggest challenge a clinical researcher faces in their day to day work?

3. What are some ways we can improve cancer research, specifically between basic research scientists and clinical researchers?

4. Tumors occur in many parts of the body resulting in breast, lung, brain, skin, and other associated organ cancers. How might you think treatments of these individual cancers would vary in dosage, method of administration, time of treatment, and length of treatment?

5. Politicians tend to fund clinical research rather than basic research, why do you think this is?

6. A pharmaceutical company seeking FDA approval to sell a new prescription drug must complete a five-step process: discovery/concept, preclinical research, clinical research, FDA review and FDA post-market safety monitoring. What do you think is the most difficult part and why? What specific challenges might each of these steps face?

Activity designed by Rhonda Thygesen.

Yi Guan and Joseph Malik Peiris:

Read: N. Wang and A. Mortazavi. "**Virus Trackers and Preventing Pandemics**" (article, comic and/or video). *Canada Gairdner Awards 2021 Laureates Education Materials,* pp12 - 16

Learning Objectives:

1. Describe what a virus is.

2. Explain the role of memory cells in viral infections.

3.Discuss some reasons for tracking viruses.

4.Describe what zoonotic viruses are and explain why they present a larger threat to humans.

5.List the three main objectives that scientists have when a virus outbreak occurs.

Supplementary Reading:

Memory cells are a critical component of our immune response, as they are how we remember viruses we have encountered before. Memory cells are made after our first encounter with a virus, so that the next time we are infected by the same virus (or a similar virus), our immune system can recognize it and jump into action much more quickly.

In the last two years we have all experienced and witnessed the effect that viruses can have on society. When a virus outbreak or pandemic occurs, not only is it important to understand how the virus is spreading, but it is also critical to gain an understanding of how the virus works. Scientists work hard to identify the source of the virus, develop a diagnostic measure and treatment, as well as learning how the virus interacts with human cells. An understanding of the biological mechanisms behind the virus and disease are crucial to develop a vaccine, and in some cases, a cure.

Classroom Activity: Tracking a Virus.
A virus tracking simulation followed by a discussion period. Students will represent sharing close contact with each other by mixing the water in each others' cups. After several exchanges, a chemical indicator will reveal "virus" present in some of the cups, and students will try to uncover who the original "infected" students were.

Supplies:
- 24-32 clear plastic drink cups, ½ cup to 1 cup in size (1 per student, for best results should be a multiple of 4)
- Water, about 1 liter
- Phenolphthalein solution, about 5 ml
- Sodium carbonate (aka washing soda), 1 scant teaspoon
- Disposable pipette or eye-dropper
- Beaker, flask, or cup
- Permanent marker
- 24-32 index cards

Optional:
- 24-32 small test tubes (1 per student, for best results should be a multiple of 4)
- Test tube rack

Time: 15 minutes for simulation, 15 minutes for virus tracking, 5-10 minutes for discussion

Description:

Set up:

1. Set the cups out on a table and optionally place the test tubes in the rack. Using a permanent marker, number the cups 1 to 24, 28, or 32, depending on class size. Please read the information about class size in step 3 of the Conducting the Simulation section (below) before you start! Number the test tubes in the same way. It is important that the total number of cups and test tubes used is a multiple of four.

2.Put about a cup of water into the beaker, and stir in one scant teaspoon of sodium carbonate (washing soda) until it is all dissolved and the water is clear. Choosing three of the numbered cups at random, pour this solution into them so that each cup is about one-quarter full. If choosing to use the test tubes, then pour some of the remaining solution into three of the test tubes whose

numbers correspond with the cups, so that each test tube holds about an inch of solution.

3. Fill the other cups about one-quarter full with water. Fill the remaining test tubes with about one inch of water. Put the test tubes somewhere out of sight.

Conducting the simulation:

1. Give each student an index card on which to write their name. Have each student obtain a prepared cup, and then write the number that appears on the cup next to their name on the index card.

2. Explain to students that they will each "share close contact" with three other students, one at a time, following a certain procedure:

- After choosing a classmate to "be in close contact" with, one member of the pair pours all the water from their cup into the partner's cup. Then the partner will pour half of the combined liquids back into the first member's cup. This way the students have mixed their two liquids, but in the end, each has the same amount they started with. Both students should record the number of the cup belonging to the person they just exchanged liquids with. (Demonstrate this exchange process with two extra cups containing tap water, emphasizing the need to record the numbers of the cups.)

- Repeat this "close contact" 2 more times, for a total of 3 exchanges. Ensure the students record the number of the cup that they are in contact with each time.

3. Note: This number 3 is important for the problem solving aspect of the exercise that follows. It is also important that the total number of participants is a multiple of 4, so classes of 24, 28 or 32 will work perfectly. If you don't have quite enough students to make a multiple of four, it is best if you recruit extra students or adults (including yourself) rather than leave any students out. Any recruits need only be present for the few minutes it takes to do the liquid exchanges. If you have 20 or fewer students, use only two "infected" cups (and test tubes) for the simulation, instead of three.

4.Have students return to their seats with their index cards and cups of water. Tell the class that, unfortunately, a few of the cups were "infected" with a virus at the start of the simulation. By sharing close contact with their friends, it is likely that several more students are now "infected." Then walk around the room, placing a drop or two of phenolphthalein in each cup. Those cups with water that turns bright pink contain the "virus", so each student whose water is pink is now "infected" -- and contagious. Typically, at least two-thirds of the class will have become infected during the exchange process.

Tracking the Virus:

1. Give the students a chance to comment on the results of their experiment. They may ask who the original "infected" people were, so you should return the question to them, asking, "How can we find out?" Point out that epidemiologists are scientists and medical doctors who try to solve these kinds of puzzles, and epidemiology is a branch of medicine that is concerned with the causes, spread, and control of diseases in populations.

2. Students will likely realize they need to start by eliminating those students who were not infected at the end of the experiment, and then try to work backwards from there. Treat this as a puzzle for them to solve. Give them time to realize that they will need to get organized and devise a systematic way to look at the data they have. It may be useful to have one or two students at the board to lead the discussion and record information as they go along. Initially it may be easy to eliminate students who could not have been the initially infected ones, but it will then become more difficult. They may not be able to deduce the original three infected persons, but they should be able to eliminate all but 4-6 students.

3. Optional: At this point you can tell them that, fortunately, you took a "blood sample" from everyone before they started. If you choose not to use the test tubes for this optional step, you can just tell them which were the infected cups. Produce the rack of test tubes, and show how they are numbered to correspond to the cups that were used. Then explain that you can test for the presence of the virus using the same chemical indicator as before. Have a student volunteer put

a drop of phenolphthalein in each test tube, and students will then be able to see how close they got to determining the original sources of the virus.

Purpose: By simulating a virus being spread around the class and its subsequent tracking, students will place themselves in the role of an epidemiologist or virologist to track a virus and gain a deeper perspective on the challenges that scientists often face in this field.

Discussion Questions:

1. What percent of the class became infected after sharing close contact? What percent of the class was infected originally, before sharing close contact?

2. Why is it usually not possible to determine exactly who the originally infected persons were in a situation like this? *Usually the sources can be traced back to 4-6 possibilities, but the actual three can only be determined if all the students did their first exchanges simultaneously, then all did their second exchanges simultaneously, and finally completed the third exchanges simultaneously. Instead, during the simulation some students will have already completed their third exchanges before others completed their second. Without knowing exactly who exchanged fluids when, it is nearly impossible to determine who the original three "infected" persons were.*

3. What assumptions did we make about the virus in this tracking activity? *For instance, we assumed that we knew that the virus was spread only through close contact; what happens when it spreads more easily than that? How can we track viruses that spread in other ways?*

4. What challenges do epidemiologists face when trying to track viruses? What are some solutions to these challenges?

Activity designed by Brenna Hay, with material adapted from the University of Colorado https://www.teachengineering.org/activities/view/duk_virus_mary_act

Mary-Claire King:

Read: S. Laframboise and A. Mortazavi. "**Discovering the Breast Cancer Gene**" (article, comic and/or video). *Canada Gairdner Awards 2021 Laureates Education Materials,* pp17 - 21

Learning Objectives:

1. What is the role of DNA?

2. Describe what a gene is and how we inherit them.

3. Explain the difference between dominant and recessive alleles.

4. Name two genes that are known to be involved in the development of breast cancer.

Supplementary Reading:

DNA contains information grouped into small segments called genes. The DNA molecule contains 4 chemical bases that are represented by the first letter of its name: adenine (A), thymine (T), cytosine (C), and guanine (G), which pair up together to make DNA. A DNA molecule consists of 2 strands of bases, that are always paired together: A pairs with T, and C pairs with G. Out of convention, we only discuss the sequence of the primary DNA strand (the complementary second strand is just assumed to be paired correctly to the primary strand). The order of these bases is what specifically encodes the detailed set of instructions required to build an organism's traits. The human genome (our complete set of genetic material) contains 23 pairs of chromosomes and over 22,000 genes that are coded for by over 3 billion base pairs.

As students select each DNA Strip and tape them together in order, they are creating one chromosome containing 6 different genes that are coded for by the 4 chemical bases. This is what allows researchers to "map" the location of a gene to a specific place on a chromosome, regardless of the sequence variability itself. For example, we can "map" where the gene for hair colour is (the third gene on the chromosome), regardless of different students having different hair colours (brunette, blonde, etc.). It is the small sequence variations within each gene that lead to differences in traits. Usually, there are a limited number of sequence variations for a gene. Each form of the gene is known as an allele. In this activity, the genes have between 2 and 4 different alleles (different forms/possibilities that influence the trait). In this activity, a single gene determined each human trait. Typically, however, a trait is influenced by multiple genes as well as environmental factors.

Classroom Activity: A Recipe for Traits.
Create and decode a "DNA recipe" for a human to demonstrate how variations in DNA lead to the inheritance of different traits. Alleles for 6 genes are randomly chosen by selecting a DNA Strip out of the envelope and taped together to form a chromosome. Follow the traits key to decode the DNA and create a drawing of a person, then compare it with others to note similarities and differences.

Supplies:
- Copies of traits key (1 per student/pair)
- Drawing paper (1 per student/pair)
- Crayons or colored pencils
- Envelopes (1 per student/pair)
- Tape
- Coloured paper for preparing DNA strips (4 colours needed)

Time: 30 minutes, optional additional 15 minute activity.

Description:

Set up:

1. To prepare for this activity, make 6 copies each of DNA Strip pages A, B, C, and D on coloured paper choosing one colour for each type of DNA Strip (this will make enough for 30 student DNA envelopes). For example: 6 copies on blue of DNA Strips A, 6 copies on green of DNA Strips B, 8 copies on yellow of DNA Strips C, 6 copies on pink of DNA Strips D.
2. Cut out the DNA strips on each page (a paper cutter works well). Place 2 DNA strips of each

colour in each envelope; each envelope should contain 6 DNA strips total with 2 of each colour. Note: this is the minimum number of DNA strips per envelope needed to carry out the activity; adding more DNA strips of each colour increases the variety of possibilities for each trait.

A Recipe for Traits:

1. Students work individually or in pairs to randomly select a DNA Strip out of their envelope to determine which allele they will get for each gene.

2. Have them circle the picture for the corresponding trait after each selection and tape the strips together in order.

3. Repeat these steps for all 6 of the traits.

4. When they have finished, draw a person with all of these traits. Allow students to compare how the different people turned out.

Optional extension (15 minutes):

1. As a class, make a "map" of your human genome. Compare the different DNA recipes of each student. Point out that the gene for height is always at the top of the DNA molecule (or chromosome), the gene for hair texture is always second, and so on. Draw a representation of a chromosome having 6 segments. Have students come up with a name for each gene. Label the segments with the gene names and specify the trait they encode. Point out that although each person looks differently (has a different combination of traits), it is still possible to make a general map of the human genome. Show students a completed map of the human genome (for example, the Human Genome Landmarks Poster *https://public.ornl.gov/site/gallery/highres/GenomePoster2009.pdf*) and discuss how researchers have mapped the over 22,000 genes to particular locations on each of the 23 pairs of human chromosomes.

Purpose: This activity helps students visualize the simplified structure of DNA, from whole genome, to chromosome, to gene, and finally to individual chemical bases. By random selection of sequences, they will experience how genes can be inherited and influence corresponding traits.

Discussion Questions:

1. Are any two people alike? Everybody shares some traits in common with others, but each has an overall combination of traits that is unique. In this example, we only looked at a person using 6 genes; in reality, humans have over 22,000 genes!

2. Based on the class results, how could we calculate the probabilities of inheriting certain genes?

3. Compare how dominant and recessive traits were demonstrated in this activity (using probability of randomly selecting a DNA Strip) to how they are actually inherited (inheriting one allele from each parent).

4. Give some examples of traits that are clearly genetically inherited, and some traits that are due to environmental factors. Are there any that may be a mix of both genetics and our environment?

5. How can computers help us compile genetic information?

Activity designed by Brenna Hay with material adapted from the University of Utah https://teach.genetics.utah.edu/content/heredity/#item8

DNA STRIPS A

A T G C
A T G C
A T G C
A T G C
A T G C
A T G C
A T G C
A T G C
A T G C
A T G C

DNA STRIPS B

T A C G
T A C G
T A C G
T A C G
T A C G
T A C G
T A C G
T A C G
T A C G
T A C G

DNA STRIPS C

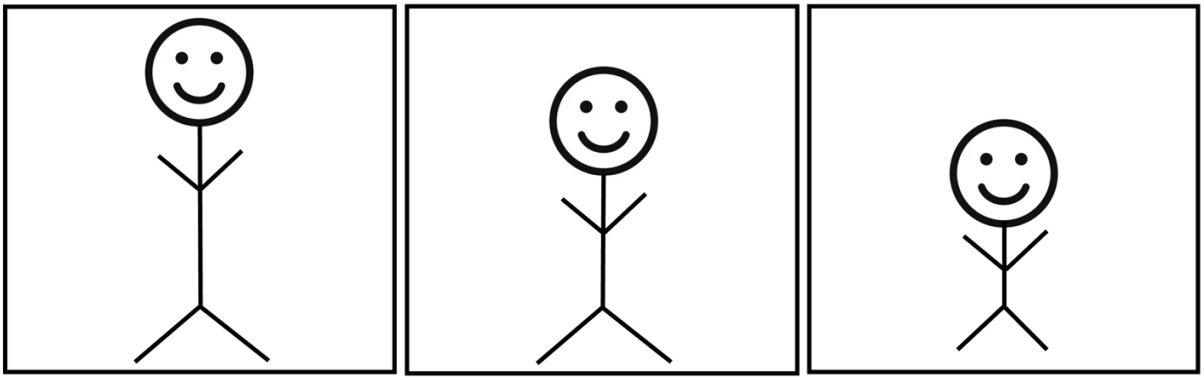
C T G A
C T G A
C T G A
C T G A
C T G A
C T G A
C T G A
C T G A
C T G A
C T G A

DNA STRIPS D

G A C T
G A C T
G A C T
G A C T
G A C T
G A C T
G A C T
G A C T
G A C T
G A C T

Traits Key

Height

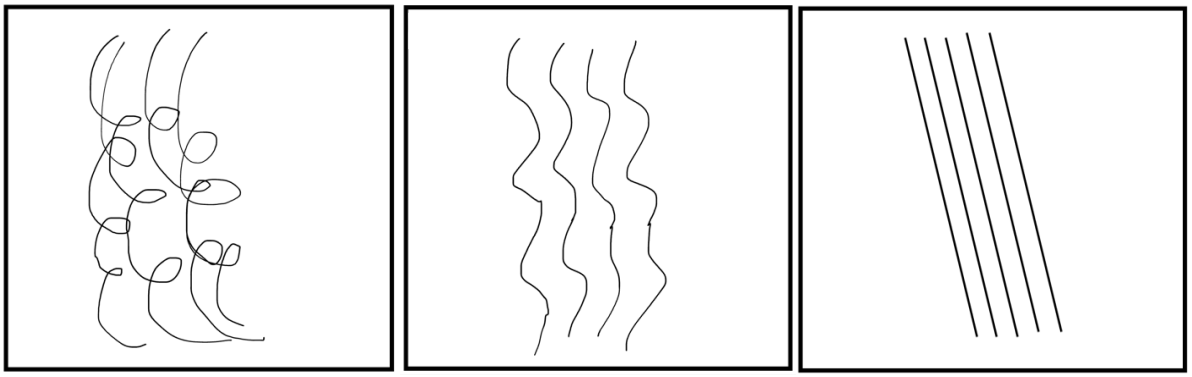


Tall
ATGC

Average
TACG or GACT

Short
CTGA

Hair Texture

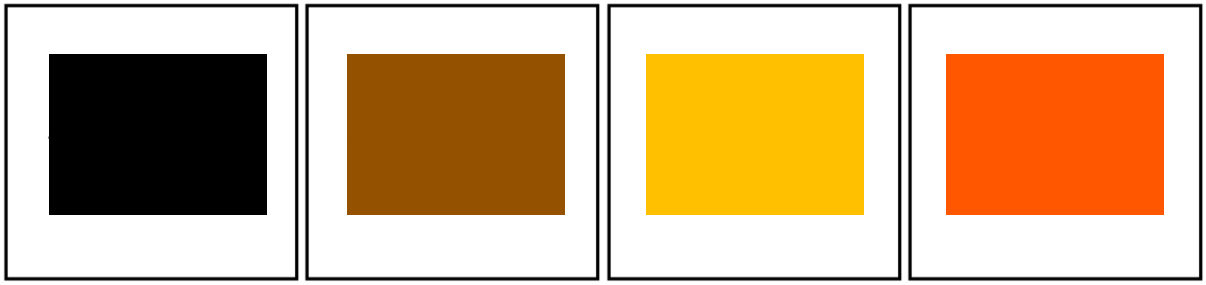


Curly
ATGC

Wavy
TACG or GACT

Straight
CTGA

Hair Colour



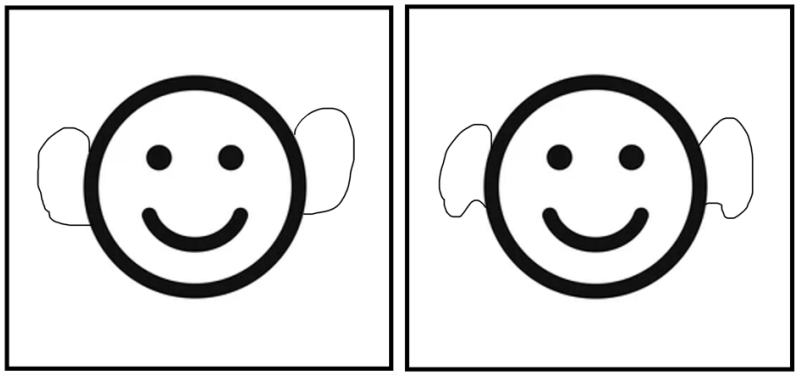
Black
ATGC

Brunette
TACG

Blonde
GACT

Red
CTGA

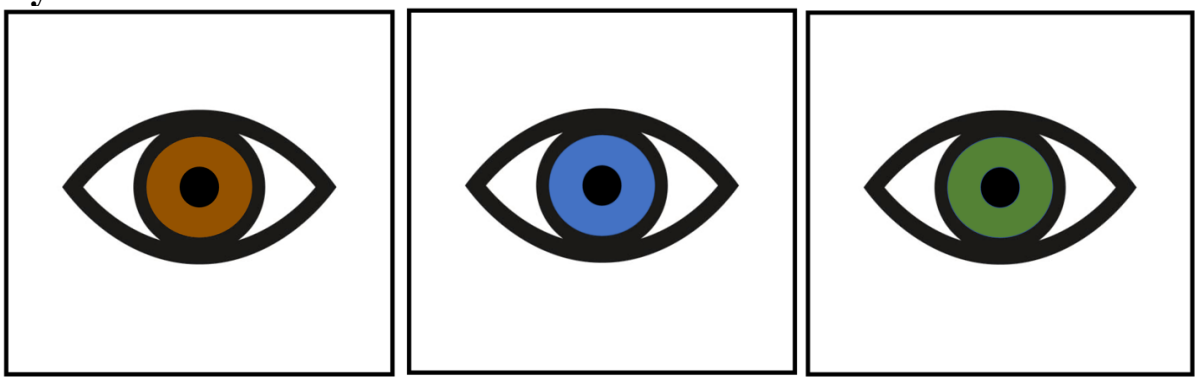
Earlobes



Attached earlobes
ATGC or TACG

Unattached earlobes
GACT or CTGA

Eyes

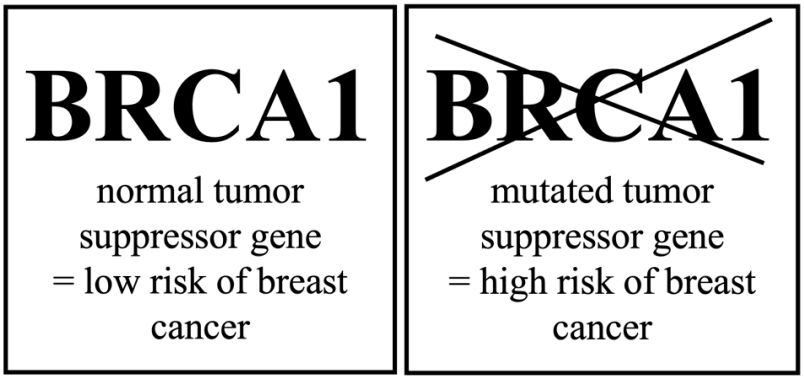


Brown eyes
ATGC or TACG

Blue eyes
GACT

Green eyes
CTGA

Breast cancer risk



Low risk of breast cancer
ATGC or TACG or GACT

High risk of breast cancer
CTGA