The Amazing Race

Grade 11 and 12

A FACILITATOR'S GUIDE

Photo

*Developed for in-person outreach by **Pascale Charette** for Let's Talk Science in Ottawa.*
This activity was revised to be virtual in 2021 with help from Claire Poulin.

Thank you for volunteering for Let's Talk Science! The following manual will help guide you through the workshop. Please read this manual before visiting the group you are working with.

Important Notes

Introduction & Guidelines

- This manual is meant as a guide to help you prepare for your activity. The introduction includes questions that get at the curriculum link/science concept the workshop covers. You are not expected to memorize this manual. It is a guide and we want you to bring your own experiences and your style of teaching into it.

- As a general guideline, do not speak longer than the age of the students at one time.

- Most workshops fit well in a 1-hour time period but some like bridge building or some high school activities are a little longer.

- Practice your introduction and test out the activities beforehand so you can anticipate sections that may take more time or may be difficult for students.

- If you are working with a partner, work out roles and responsibilities before the visit.

Safety

As a Let's Talk Science volunteer, safety must be foremost in our minds during all activities. As STEM role models, volunteers must always also model safe science practices.

Always keep in mind the following precautions:

- Emphasize and demonstrate appropriate safety procedures throughout the presentation.
- Be professional but have fun.
- Keep workspaces clean to avoid tripping hazards.
- Allergens should have been checked before reserving the kit (e.g. allergies to latex).
- **Activity Specific Safety:** n/a

WHMIS

An overview of Canada's Workplace Hazardous Materials Information System (WHMIS) is included in these materials at the end of this manual where needed. No WHMIS sheets are included with this activity.

Overview of the Workshop

Grade Level and Curriculum Learning

Grade 11/12: Apply the concept of genetic variation to tailoring personalized therapeutics. Note, some knowledge of DNA and gene expression is best before doing this activity, however, there is an extra slide to explain DNA transcription and translation if needed.

Materials (per group or individual depending on whether students can work in groups)

Amazing Race PowerPoint presentation
1 Amazing Race answer key
Send the link to the YouTube video to the teacher: https://youtu.be/MvuYATh7Y74?t=96
The rest of the materials below are per group or individual depending on whether students can work in groups. These documents could be printed for each group or just given electronically in Folders if the students have tablets or phones they can view the documents on. You might want to ask the teacher which they would prefer or if they would like both.
Part 1 envelope: Ethical Dilemma prompt
Part 2 envelope: 2 documents - Sequencing prompt and the sequence
Part 3 envelope: 13 documents – Gene Selection prompt and 12 Gene Cards
Part 4 envelope: 2 documents – Data Analysis prompt and the data
Part 5 envelope: 4 documents – Treatment prompt, patient1 chart, patient2 chart, drug options

Materials (if not dropping off materials to the school)

Amazing Race PowerPoint presentation
Send the link to the YouTube video to the teacher: https://youtu.be/MvuYATh7Y74?t=96
1 Amazing Race answer key
The rest of the materials below are sent to the teacher to give the students. Since they need to do Part 1 before moving to Part 2, and Part 2 before Part 3 and so on, it is better if the teacher can load these on her google classroom but not have the students have access to them until the volunteers say to go ahead with Part 1. All of these are also on the slides in case the students can't access the folders, however, it is better if they can access the folders.
Part 1 folder: Ethical Dilemma prompt
Part 2 folder: 2 documents - Sequencing prompt and the sequence
Part 3 folder: 13 documents – Gene Selection prompt and 12 Gene Cards
Part 4 folder: 2 documents – Data Analysis prompt and the data
Part 5 folder: 4 documents – Treatment prompt, patient1 chart, patient2 chart, drug options

Timing (note you can reduce the time if needed by shortening the intro/discussion)

	Approx. Time	Description
Introduction and PowerPoint presentation	10-12 minutes	Introduce yourselves Powerpoint.
Activity: The Amazing Race	40 – 50 minutes	Activity: 5-10 minutes per each of 5 parts
Wrap up	10-15 minutes	Each group presents their findings to the whole group and a quick wrap up by you.

Activity

*The **questions** you might ask are in **bolded blue font**. Some things you might say are in blue font and the possible answers are in square brackets in black font. Actions are in purple font.*

Introduction

Hi everyone! We are Let's Talk Science volunteers. We come to schools and do hands-on activities. I study [simple terms] _____ at the University of Ottawa/Carleton University. I decided to study _____ because [when I was your age I loved… I think it's important to… I'm curious about…].

Open the "Amazing Race Personal Genomics" PowerPoint presentation.

We're going to run through a few points on the slides with respect to DNA, genes, and cancer. We'll then challenge you to take the learning and apply it to scenarios through an Amazing Race type game.

Slide 2

What is DNA? [The class should come up with answers about the basic structure – DNA is made of 2 antiparallel (run in opposite directions) strands of nucleotides in a double helix, held together by hydrogen bonds; nucleotides are composed of bases Adenine, Thymine, Cytosine, and Guanine which we abbreviate A, T, C, G].

What are genes? [Genes are packages of heritable (passed down) information from our parents]. Each gene has a special job to do. The DNA in a gene spells out specific instruction (much like in a cookbook recipe) for making proteins in the cell. Proteins are the building blocks for everything in your body.

How are genes encoded or expressed? [transcription and translation should come up here but if not, move to the next slide and talk about transcription and translation] Note: Slide 4 has a graphic showing transcription and translation in case you are in a class that has only just begun to study these processes but only use it if it's clear the class hasn't studied this yet.

Slide 3

This is the *Central Dogma* of molecular biology. It explains how one set of our genome can be expressed in different ways to create different proteins in our bodies. Then those proteins help carry out the various functions in our bodies.

Slide 4 (optional)

This slide is here in case you have a class that hasn't gone through transcription and translation yet in their studies (a class in Grade 11 at the beginning of the year might not have gone over these two processes yet).

Slide 5

In 1990, a group of international researchers began what was called *The Human Genome Project (HGP)*. These researchers decided to map the entire human genome and identified over

6 billion base pairs from 23 chromosomes. By 2003 *The Human Genome Project* successfully coded roughly 20,000 genes that each coded for a different protein!

Slide 6
In the end, those researchers also found out that we are all (regardless of race) *99.9%* genetically identical. **What accounts for that 0.1% difference?** [Various answers – looking for mutations].

Slide 7
There is natural variation in our genome itself, such as point mutations (single nucleotide polymorphisms), variable number of short and long repeats. These happen about 1 in every 1,000 base pairs of DNA (0.1%).

Although mutations are often thought of as indications of some health defects, there can also be *non-deleterious mutations*, where even though a mutation is present it causes no negative or lethal effects.

There are also natural variations that can happen. Where different levels of protein or different activity levels of some proteins are made. For example, skin colour, or identical twins can differ depending on their surrounding environments.

It is important to remember that your physical, mental, and behavioural states are the result of complex interaction between multiple genes in combination with your environment and lifestyle.

Slide 8
How is genome sequencing actually done? Let's take a look at this video.

Play the YouTube video (https://youtu.be/MvuYATh7Y74?t=96) and let the students watch. Make sure the start time is at 1 minute 36 seconds and that the speed in the bottom right corner is set to 1.25x fast.

New DNA sequencing technologies are quickly making it faster and less expensive to learn about one's DNA. In 2015, the cost to sequence your whole genome costed $1,000. In fact, the cost is anticipates to decrease so quickly that, within 10 years, your physician might request your genome be sequenced as part of routine blood-work, possibly covered by health insurance.

(Note: the graph that is shown on this slide can be seen more clearly at http://www.genome.gov/sequencingcosts/).

Slide 9
What do you think you can learn from your own DNA? [Various answers; insights about our health, behavior, family history, and other traits through genetic testing; can lead to targeted treatments for each patient; can provide personal information with personal, social, and familial impact]. Your DNA can reveal important information about your traits. Genetic screening will allow fast and specific diagnostic tests making it possible to treat countless conditions; it can be used by geneticists to detect carriers within families. Genomic information can indicate the future likelihood of some diseases (it does not tell the future).

Sequenced DNA can be used to look at the mutations within an individual and be able to create a personalized treatment for that patient. No two people are the same even if they have the same disease.

Slide 10
Now, let's take a look at different ways to sequence DNA.

Slide 11
First we are going to look at some different kinds of clinical testing.

Slide 12
What do you think hereditary disease testing is? [various answers]. Answer is on the next slide.

Slide 13
In hereditary genetic testing, an individual would have certain gees sequenced from their normal body cells (skin cells, hair cells, whole blood cells). These genes are selected based off the knowledge of their family medical history.

For example, if an individual's family has a history of heart disease, they might want to know if they carry a genetic risk for developing that as well.

Therefore a sample of normal body cells are collected, DNA is extracted and certain genes of interest that are related to Alzheimer's are sequences.

The sample is sent to a laboratory where technicians look for specific changes in chromosomes, DNA, or proteins, depending on the suspected disorder.

The laboratory reports the test results in writing to a person's doctor or genetic counselor, where a diagnosis is made. The results are interpreted to the individual who wanted to get sequencing done and a consultation is given of the limitations and risks of the results and what they mean moving forward.

If the individual was found to have a mutation in the genes of interest, ways of reducing the risk or preventing the disease from occurring may be possible, such as changing your lifestyle (eating better and exercising to prevent heart disease).

Slide 14 click and tumor sequencing highlights
Slide 15 Now we will look at what is called *Tumour sequencing*.

Slide 16
When sequencing tumour cells, a patient comes in already with cancer. The DNA is extracted (from cancerous cells, not normal body cells) and specific genes related to the specific cancer the patient has is sequenced as well as common other mutated genes known to be involved in cancer growth and survival.

The data is analyzed and the mutations are used to assess how the tumour cells of this patient grows. The results are conveyed to the patient and an Oncologist provides the specific treatment option that best fits the patient and targets the tumour cells effectively.

Slide 17

What is cancer? [Uncontrolled growth of abnormal cells; genetically unstable (mutations); develop when the body's normal control mechanism stops working]. By looking at the genetic profile of cancer cells compared to normal cells in a patient, the abnormalities in the genetic makeup of the tumour cells can be assessed. No 2 tumours have the same genetic profile therefore, by sequencing their genomes, we can find the reason as to why these cells are abnormal and are out of control.

Slide 18

These next couple slides will walk you through the *Hallmarks of Cancer*. These hallmarks indicate the characteristics that cancer cells display in order to thrive and continue to grow an invade the host. Any protein that has become defective as a result of an acquired mutation in cancer cells, is a prime target for creating personalized treatments that will selectively kill these abnormal cells of a specific patient.

Slide 19

The first hallmark is "Evading growth suppressors". For example, there are signals that keep your cells from dividing, you aren't growing extra limbs because of these signals. Without them the cells grow uncontrollably, and this forms a tumor.

Slide 20

The second is "Activating invasion and metastasis". This is when the tumor goes to other parts of the body.

Slide 21

The third hallmark is "Enabling replicative immortality" meaning that the tumor is now able to divide and divide and divide giving it a long lifeline.

Slide 22

Next is "Inducing angiogenesis". At this point the tumor can access the blood vessels in a person's body in order to obtain oxygen and nutrients for growth (similar to how parasites work).

Slide 23

"Resisting cell death", allows the tumor to prevent itself from dying (apoptosis).

Slide 24

And the final hallmark of cancer is a "Lack of immune rejection". This means that the cancer can hide from the body's own immune system.

Slide 25

Now that we've gone through what clinical genetic testing is, and some methods used: **What are some advantages/disadvantages to clinical genetic testing?** [various answers: advantages – can lead to proper diagnosis; provides reassurance and certainty; gives insight into risks of developing certain diseases (e.g. mutations that are known to increase risk of cancer); finds certain mutations in your genome that can lead to personalized treatments, change of lifestyle or prevention, regular check-ups, etc.].

In the clinical setting, the goal of patient DNA sequencing is not only to identify risk of disease development, but to help diagnose a variety of disease with a genomic basis. Clinic testing can involve the detection of infection disease, help in strategizing treatment approaches, assist in non-invasive prenatal testing, and more!

It is also under the control of a medical professional that can better interpret the results and relay the information to the patients. This is very important since potentially alarming information can adversely affect a patient, while other information may be overlooked and lead to health effect that could be prevented.

Validation and accuracy of home testing services are inconsistent, while testing by full-service clinical sequencing facilities are based on validated procedures (making them more reliable – you don't know how valid the company is or how they do it).

You can find the presence of a heritable genetic mutation that can be treated.

If there is history of a condition in the family knowing you are not a carrier can give you comfort or a better quality of life.

If a genetic test tells you that you have an increased risk of developing a condition later in life (such as breast cancer) you might be able to go for more regular check-ups, or take other measures to keep the risk to a minimum.

Some examples include:

(1) Personalized treatments: the process where patients are stratified and treated based on their genetic profile, which is used to assess expected drug responses and the risk of adverse side effects. Traditional medicine typically relies on the broad application of "standard of care" or "one size fits all" treatments to all patients with a given diagnosis, irrespective of their genetic context.
(2) Change of lifestyle: changing diet, exercising because I have a higher risk of heart disease.
(3) Regular check-ups: more aware of your risk therefore more active in your own health and go in for more check-ups.

One key thing about genetic testing is the application it has in personalized medicine and both tie into treatment for patients with cancer.

Slide 26

Activity: Amazing Race Personal Genomics

So today we are going to apply what we have learned about genetic testing and personalized medicine and apply it to an activity that almost all of us know.

We are going to play "The Amazing Race".

What you will be doing is going through a pipeline of some of the tasks needed to be done for a patient to get their genome sequenced from point A, all the way to point B where the patient will receive their personalized treatment.

When you think you have answered and completed the task, one representative from your group will come up to us volunteers and give the answer. If you are right we will hand you the next envelope. If you are wrong you may try again.

You'll get into groups of 4 and the teacher will give each group an envelope labelled Part 1 (or you will use your electronic version starting with the folder labelled Amazing Race Part 1). You may open it when we say "Go". {If they are at home learners they may not be able to work in groups unless you can put them in breakout rooms, so they can work individually if needed. The teacher should have the folders for each of the 5 activities loaded up for the students to use. If they can't access the folders for some reason, there are slides that have each of the 5 activities on them you could use instead}

If you are ever stuck, you can ask us for help however a 1 minute pause will be applied.

Slide 27
Let's begin:

Two patients with breast cancer come in to get their tumour sequenced. The mother of Patient 1 was known to have breast cancer and for Patient 2, there was no known family history of cancer. Your job is to act as different medical professionals in each task of the race starting from the moment the patients come in and then ultimately ending back to the patients. The end goal is to create a personalized treatment plan that is unique to each patient and their tumour based on their tumour sequence.

Ask the teacher to split the class into groups of four. If there is an option to make breakout rooms for this, it would be easier because then others won't hear the answers. However, if not, ask one person from each group to come close to the computer when they think they have the answer and you can try to speak softly to give the answer. Have the teacher distribute Envelope 1 to each group (or allow individual students or groups learning online to view the folder "Amazing Race Part 1". As students finish one Part, have them move to the next Part. They will have to ask the teacher for the next envelope.

Once all the groups are settled with their envelopes begin the countdown.

Ready, …. Set,….GO!
(Note: DO NOT continue the PowerPoint from this point on, until the race has finished).

Set yourselves up in one spot in the classroom with an answer key that only you can see and wait for the students to approach you with each of their answers. If students are in groups in breakout rooms they can chat with you directly. If they are a whole class and there is a way for them to give you the answer without everyone hearing that can be done or they could just chat their group's response into the chat for you to see and not the whole class.

For the next part of this guide, each Part of the race will be explained (the answer key will be attached at the end of this document and is in a folder for you). Slides 27-37 have the 5 activities on them. Only use these if students don't have a hard copy or access to the folders for each activity – otherwise you can skip all but slide 27, run the race, and then start at slide 38.

Part 1: *Ethical Dilemma*
"Patient 1 is found to have a mutation in BRCA1 and wants her 14-year-old daughter to be screened for the mutation. The daughter does not want her genome sequenced in fear of finding out secondary information as well as having to share that personal information to anyone."

- Groups must decide if they (as the geneticist) would forego or refuse the test (i.e. do they listen to the parent or the daughter?).
- Students must come to you, tell you the ethical issues that arise in this situation, and what they would decide to do as a medical professional.
  (Note: there is no *right answer* as long as they have good reasoning)
- Ideal solution:
  "Giving the test would benefit the daughter because if she is a carrier then extra precautions can be taken. However, privacy of her own genetic information is important as well. As a 14-year-old who is underage, I would give her all the information she needs and all the consequences of getting a genetic test or not getting one. Once she is informed, she may make a decision, which I would respect."
- The Take-Home message: *students should realize that genetic testing raises many ethical dilemmas in relation to consent and confidentiality*.

Part 2: *Mutation Screening*
"The daughter consents to having her genome sequenced (Groups will receive a short sequence of the individual and a reference sequence). If an individual has a mutation, they have 55% increased risk of developing breast cancer. Scan through and find the mutation if there is one, name the kind of mutation (ex: insertions, point mutation), and give the results to the daughter."

- The volunteer will be acting as the daughter in this scenario.
- Groups will come to you to present their findings (the mutation and what kind it is).
- The daughter *will* in fact have the mutation, and when the group comes to you with the result follow up with a counter question:
  So I am going to get cancer? [students should be able to realize that even though an individual has a mutation it does not mean they will develop cancer; Genes are not destiny and there are sometimes prevention methods to minimize the risk of cancer].

Part 3: *Gene Panel Selection*
Each group will have 12 gene cards with their associated functions on the flip sides.
"Select a panel of 7 genes for each patient to be sequenced. The reasoning behind your gene selection should be based off of the knowledge of how cancer cells work (i.e. proliferation, angiogenesis, metastasis) and the suspected type of cancer of each patient (ex: BRCA1 for breast cancer)."

- A representative from each group will come to you with their chosen panel.
- *IF incorrect*: students will be unable to move to the next stage
  Action: Tell the representative how many of their selected genes are wrong and that they must return to their group to try again.
- *IF correct:* students can move on to the next stage
  Action: Hand the group "envelope #2".

Part 4: *Data Analysis*
Groups will receive 4 sheets of mutations that were found (2 per patient – 1 from normal cells & 1 from cancerous cells). Each sheet will show the mutation and its outcome in the form of a graph, table, mechanism, OR schematic to allow the student to interpret the data.
(ex: *Gene X*: A → G = leads to a 2-fold increase in cell division by looking at a growth curve;
G → T = causes no significant differences compared to the normal variant.)
"Find which mutations are unique to the cancer cells and what the mutations with no outcomes imply. Compile all the relevant data from each patient and relay that information."
(Note: the pieces of information that the students' will find will be along the lines of:
"…it has been found that Patient 1 had a certain mutation in Gene X that is known to cause resistance to the chemotherapeutic drug cisplatin as well as the heritable mutation in BRCA1. Their tumour has a doubling time of…")

- Groups will come to you with their findings.
- You (and your partner volunteer if you came with one) will act as Patient 1 and Patient 2 receiving their results.
- *IF incorrect*: students will be unable to move to the next stage
  Action: Tell the representative how many of their selected mutations are wrong and that they must return to their group to try again.
- *IF correct:* students can move on to the next stage
  Action: Hand the group "envelope #3".

Part 5: *Personalized Treatment Plan*
Groups will combine their results from Parts 1 and 2 to create a treatment plan for each of the two initial patients. They will be given: a list of drugs, in-clinical trials or government-approved trials, and their method of action.

- Groups will come to you to present their personalized treatment plans for each patient.
- The first team to present a believable plan for each patient wins.

After the first team finished, give the rest of the groups 5 more minutes and then end the race. Give each team the opportunity to present their course of action for the patients.

Get the students to settle back down and draw their attention to the PowerPoint.

Slide 28

In Part 1 we had our *Ethical Dilemma*. A couple of things you may have noticed while discussing are:

(1) the concept of *age of consent*. In Ontario, there is actually no set age of medical consent.

(2) typically, with BRCA1 testing only the BRCA1 gene is actually sequenced!

(3) You could have decided to tell the mother to wait until her daughter is older. By then knowing if she is a carrier could lead to more courses of action (e.g. a mastectomy).

(4) In the end, genome sequencing quite often brings up a lot of controversial and ethical issues.

Slide 29

Part 2 was the *Screening for Mutation* step. In real-life situations, when a parent is known to be a carrier of a mutated gene, that specific gene is what is searched for in the children. Additionally, an average women has about a 12% risk of having breast cancer, compared to a 55% risk in women who actually have a BRCA1 or BRCA2 mutation.

Slide 30

By Part 3 you would have realized that the daughter did have the mutation and you would have followed up with the *Gene Panel Selection* step. Again some real-life examples of things you may have noticed that make this step a little more complicated could include:

(1) The fact that whole-genome sequencing is both time consuming and costly.

(2) When selecting your panel it was best to choose specific genes that would have been known to be associated with the particular type of cancer we were dealing with.

(3) Then the sequenced genes are ones that usually will have a solution to them if they have been mutated.

Slide 31

Part 4 was your *Data Analysis* step. It would have been important for you to note that not all mutations involved in cancer always lead to a loss of function. Once all your genes had been sequenced, the mutations you searched for would have been compared to what was already known (in real life this is taken from previous literature). Mutations in these cases that lead to no changes in the outcomes (compared to normal) are accounted for by variance.

Slide 32

The final part of the race had you developing a *Personalized Treatment Plan* for each of your original patients from Parts 1 and 2. It is important to remember: no two individuals are exactly the same, just as no two tumours are exactly the same. This is why different treatments are used to target different characteristics of the tumour cells based on the genome differences between the cancer cells and normal patient cells of each patient.

Action: Ask the students to help put the materials back in each of their envelopes and then return back to their individual desks.

Wrap-Up

Action: If you have the time, continue with the PowerPoint before asking for any final questions.

Slide 33.

Aside from Clinical testing, there is also *Commercial testing*.

In the past, customers could buy kits online without a doctor's permission. They could then obtain their results about their genetic predisposition for serious diseases, their carrier status for mutations (that if inherited from both parents, can cause serious childhood diseases in their children), as well as interesting but not particularly consequential information about their traits.

In 2013, the United States Food and Drug Administration (FDA) intervened, and , in response, "23andMe" stopped providing most health information to new customers. At the time of this writing, the FDA had given approval to "23andMe" to offer carrier status and information about ancestry and non-medical traits to customers.

The market for direct-to-customer (DTC) genetic testing has undergone significant changes over the last several years. In 2016, the Food and Drug Administration demanded that a doctor's request was needed to request a genetic test for a patient. Now, with a doctor's permission, a patient can order a kit, spit into a tube, and send it back to the company for analysis. The doctor and patient both receive the results, and ideally will discuss any questions the patient has, and/or the doctor can refer the patient to a specialist for further consultation.

Slide 34. Discuss some potential advantages and disadvantages of *Commercial Genetic Testing*.

Slide 34

One thing to keep in mind with commercial testing is that sites like "23andMe" reserve the right to use your personal information – including your genome.

Action: Gesture to the image on the slide.

This is a screenshot taken directly from the "23andMe" website showing how they advertise the use of their product.

There are certain cases where an individual would use this product, find a long lost brother, for example, and realize that their parents put their baby up for adoption years ago. This breaks privacy, confidentiality, and respect of other people's lives. Understandably, this has created a big ethical debate.

If anything, you should be aware that this is *private information*.

Learning about your DNA is highly personal and also raises many questions about how we as a society are going to handle the accessibility of genetic information. As another example, if you learn your at risk for Alzheimer's disease, this may raise concerns for your mother, who might not want to know anything about her risk for Alzheimer's disease …something to think about at least!

Does anybody have any questions?

If you have extra time, you can ask if they have any questions about university or being a student or about your research.

Thank you for having us in your class today!

Additional Information

Answer Key on next page.

"The Amazing Race Personal Genomics" Answer Key

Part 1: *Ethical Dilemma*
(Note: Some issues include: age of consent and competence (autonomy), and the issue of secondary diagnosis from genetic testing such as finding a mutation in another gene that was not the initial reason to sequence the genome).

- Answer #1: "*I agree with the mother (or disagree with the daughter) and would do the test because the mother has her daughter's best interest and wants to know if she will develop breast cancer like herself."*
- Answer #2: *"I agree with the daughter (or disagree with the mother) because she has the right to her own privacy and if she is competent and understands the consequences then she can make her own decisions."*
- Answer #3: *"Tell the mother that her daughter can wait until she is older to get tested so that if she does carry the mutation, then there are reasonable steps to follow."*

Part 2: *Mutation Screening*

- Answer #1: *"Point mutation of A → G at nucleotide #126."*
- Answer #2: *"Inversion of of TGAGA (nucleotides #334 – 338) → AGAGT*

Part 3: *Gene Panel Selection*

Students should choose Genes #: *1, 5, 6, 7, 8, 10*, and *11*.

Part 4: *Data Analysis*

Answers for Patient 1:
- Gene #1: *"causes a 3-fold increase in proliferation"*
- Gene #5: *"has a BRCA1 mutation"*
- Gene #6: *"causes about a 9-fold increase in invasion. Cells are invasive (i.e. the tumor is more likely to spread."*
- Gene #10: *"causes an increase in angiogenesis."*

Answers for Patient 2:
- Gene #6: *"has no difference, but there is a tendency to increase (somewhat invasive) – or they can say there were large error bars (not valid) – or they can say the mutation has no different effect and could be a genetic variation.*
- Gene #7: *"causes a reduction in the number of dead cells (sign of cancer)."*
- Gene #8: *"causes a 1.5-fold increase in proliferation."*
- Gene #10: *"There is high expression of a protein marker that indicates an increase in angiogenesis."*

Part 5: *Personalized Treatment Plan*

Answer for Patient 1:
- *"Drug A (or E) is used to target proliferation."*
- *"Drug D is used to target HER2-positive status."*
- *"Enroll the patient in clinical trials to test Drug II – this is used to prevent high rates of metastasis."*

Answer for Patient 2:
- *"Drug B is used to target angiogenesis."*
- *"Drug E is used to target cell division."*

WHMIS Sheets na