Genetic Variation - 

the Impact of Change

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Part 1 - Genetic Variation and Mutations

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Part 1:

Genetic Variation and Mutations

Introduction

My science fair project will focus on genetic variation, and why it is fundamental in understanding and preserving our ancestry as a species, as well as preventing genetic disorders.

In my project, I will

1. Explain genetic variation and evolution, and how certain mutations can imply harmful effects on humans through several generations.
2. Focus on genetic testing and how tests are used to prevent genetic diseases.
3. Discuss types of genetic tests, and pre-diagnosis and treatment for several common diseases so we can prevent them from an early stage in an individual's life.
4. Investigate three common genetic disorders, sickle cell anemia, cystic fibrosis, and Diabetes mellitus and discuss which ethnic groups are prone to that disease.
5. I will share a list of recommendations I have for initiatives AHS (Alberta Health Services) can take to make sure they are prepared to the full extent of providing the right care to individuals with genetic disorders.

Alberta is a multicultural hub, filled with many immigrants from many different countries. For a successful society, we must focus on the health of individuals suffering from familial genetics and strive to have the proper resources and equipment that are used to provide individuals with good health.

One of the main raw purposes of studying genetics and genetic variation is to develop efficient ways to provide care for our species and find cures and prevention of genetic diseases.

With this project, I aim to fill the gaps in Alberta's healthcare system that would help our province stay one step ahead of common genetic disorders with the proper resources, and pre-diagnose patients suffering from them. Now I will explain the fundamental terms related to this topic.

Important Terms

Variation: A change or difference in the level, amount, or condition of something.

Genes: The smallest units of deoxyribonucleic acid (DNA), or strands of nucleotides.

Genetic variation: Differences in the DNA sequences that make up genes of a particular species, causing evolution to occur.

Genetics: The study of hereditary, or the physical and mental characteristics passed from generation to generation in the evolution of a species.

Evolution: The gradual changes in the physical and mental characteristics of a particular species over many generations.

DNA: A molecule that carries the genetic information for an organism to grow, reproduce, and function.

Nucleotides: The building blocks of DNA, each made of a phosphate group, a sugar group, and one of the four nitrogen bases, adenine, thymine, cytosine, and guanine(A, C, G, T or U).
Allele: A pair of chromosomes.

Why does genetic variation occur? Homo sapiens, (humans), have lived on Earth for nearly 6 million years, without variation, would we have survived to this point? Without variation, will we continue to survive?

Cell Components and their Functions

Cells are the basic unit of life, found in every organism on our planet. They are the smallest unit of matter that can live and contain all our genetic material. The three major functions of the cell are;

1. Energy production so your body can carry out basic and biological functions.

2. Protein synthesis so your body has a structure.

3. Cell replication so your body can grow.

Components of the cell include

Cytoplasm: The gelatinous semi-fluid composed of water, organic molecules, and salts in which the rest of the components float.

A plasma membrane: The barrier that separates the inside of the cell from the external environment, made of many organic compounds including a lipid bilayer that consists of phospholipids and cholesterol, as well as proteins and carbohydrates.

Mitochondria: Organelles that produce energy in the form of ATP, (adenosine triphosphate) to support the chemical processes in the cell. They produce ATP using a process called oxidative phosphorylation. Nucleus: The primary organelle in the cell stores the cell's genetic information, and develops ribosomes. The nucleus consists of a cell membrane made of two layers, which have nuclear pores. The inside of the

nucleus is made up of several chromosomes, and in the middle is a densely compacted region of DNA called the nucleolus, which is responsible for ribosome assembly.

Chromosomes: Strands of DNA supercoiled around a protein called a histone. They are the primary carriers of genetic information. Humans have 23 pairs of chromosomes in each cell, or 46 chromosomes in total.

Nucleolus: Primary ribosome production site. It takes ribosomal RNA and proteins to develop a fully formed ribosome.

Ribosomes: Organelles that synthesize proteins by bonding amino acids together based on the instructions of messenger RNA.

Proteins: Organic molecules that provide structural support and tissue growth, and aid in many processes in the cell.

RNA: (Ribonucleic acid), is a nucleic acid like DNA, however, the four nitrogenous bases of RNA are adenine, cytosine, guanine, and uracil.

Messenger RNA: The set of instructions that tell a ribosome how to make a protein, and they are synthesized in the nucleus using a process called transcription.

Transcription: The process in which a series of nucleotides of a DNA strand are decoded by RNA polymerase to form mRNA. RNA polymerase is an enzyme with this specific job.

Ribosomal RNA: Transcribed in the nucleolus by mRNA.

Nuclear pores: Holes in the membrane of the nucleus so mRNA and ribosomes can get in and get out. ATP also needs to enter the nucleus so it can provide energy for the processes such as transcription and synthesis the nucleus carries out.

Cells must divide themselves, so your body can increase in size. When they divide themselves into two, they must also replicate the chromosomes to the new cell, so the hereditary information of the new cell is the same as every other cell, meaning the inheritance of genetic traits.

But how do they replicate? To understand DNA replication, we need to know DNA structure and all components that take part in replication.

The chemical structure of DNA

First, we need to understand the chemical structure of a DNA molecule. DNA is made of two strands intertwined in a double-helix structure, discovered by Watson and Crick in 1951. Each strand is made up of a sugar-phosphate backbone and base pairs. A nucleotide is composed of a single base, such as thymine for example, as well as a 5-carbon sugar molecule and phosphate group from the sugar-phosphate backbone. A base pair is two nitrogenous bases held together by hydrogen bonds. The 5-carbon sugar molecule also includes 10 hydrogen atoms and 4 oxygen atoms, held together by phosphodiester bonds. A phosphate group contains one phosphorus atom bonded to four oxygen atoms.

A hydrogen bond is when there is a dipole-dipole attraction between a hydrogen atom and another atom with a higher electronegativity. A phosphodiester bond is when the phosphate group of one nucleotide bonds with 2 5-carbon sugar molecules. It specifically bonds with the hydroxyl groups of these sugar molecules, which are oxygen atoms bonded with carbon atoms.

Models of DNA strands are depicted with 3’ and 5’ ends. So the end of one strand will be 3’, and the end of the other will be 5’. The 3’ and 5’ refer to the number of carbon atoms the phosphate groups bond to. Each sugar group which is referred to as a deoxyribose sugar molecule has a chemical structure in the shape of a pentagon, with a carbon atom at each vertex, forming a carbon backbone. The carbon atoms are labeled with numbers in a clockwise rotation, from 1’ to 5’. The 3’ and 5’ carbon bonds with the phosphate groups are at the end of each strand. Base pairs can be adenine and thymine, and cytosine and guanine. So whenever there is a base of guanine for example in one strand, there will be a cytosine base that forms a hydrogen bond on the other strand, same for adenine and thymine. In scientific language, we refer to the four bases as (A) adenine, (C) cytosine, (G) guanine, and (T) thymine. Now that I’ve given you a brief overview of the chemical structure of DNA, let's look at the key players involved in DNA replication. These key players are enzymes, and proteins that accelerate chemical reactions, and there are a total of 7 in this process.

1. Helicase
2. Primase
3. Ligase
4. DNA Polymerase 1
5. DNA Polymerase 3
6. SSB Proteins
7. Topoisomerase

DNA Replication

Helicase breaks the hydrogen bonds holding the nucleotides together, separating the double helix into its two strands. While it’s separating the DNA molecule, it forms a replication fork, with the two strands being separated and the DNA molecule that remains intact. DNA is a coiled molecule, so separating DNA strands would cause torsional strain and supercoiling to occur.

To prevent supercoiling and tangled strands, the enzyme **topoisomerase** travels ahead of helicase and unwinds the tangled DNA and puts it back into its double helix structure before it separates.

SSB (single-stranded) proteins will bind to the two open strands to prevent them from reassociating.

DNA **primase** initiates an RNA primer, about 5-10 nucleotides long, at a specific location in the leading strand. The leading strand starts from 5’ and ends at 3’. Once the primer is initiated, it serves as a template for DNA polymerase 3 which starts the replication process.

Since A (adenine) bonds with T (thymine), and C (cytosine) bonds with G (guanine), the polymerase needs to add bases complementary to the bases of that strand. For example, if guanine was on the leading strand, DNA polymerase 3 would initiate a cytosine nitrogenous base. For the leading strand, bases are added at a constant rate. However, the lagging strand which starts at 3' and ends at 5' would cause more difficulty for the enzymes. The leading strand goes from left to right, while the lagging strand goes from right to left. Primase initiates an RNA primer at the 5' end, and then **DNA polymerase 3** starts adding bases. However, several primers are added as bases cannot be added at a constant rate. The bases between these primers are called Okasaki fragments and are 100–500 nucleotides long.

Once helicase separates the entire molecule into two strands, and primers and bases are added to both completely, DNA Polymerase 1 switches the RNA primers for DNA bases. RNA contains uracil instead of thymine. **DNA Polymerase 1** switches the uracil for thymine, so the molecule is completely DNA. DNA Polymerase 1 scans the two strands for any mistakes made by DNA Polymerase 3, and if two bases shouldn't be together, DNA Polymerase switches them for the correct pair.

Finally, **ligase**, the "gluing" enzyme attaches the primers and bases, to form a complete sugar-phosphate backbone. In the end, we have two identical copies of the first DNA molecule.

Mutations

Mutations are what cause genetic variation. To put it simply, mutations are changes in the sequences of nucleic acids of an organism, such as DNA and RNA. If the DNA molecule in a chromosome in your body reads ATTGCC, and once replicated it reads ATTGCC, this would be a mutation. DNA is transcribed into mRNA, and mRNA synthesizes proteins, which help develop your cell structure, convert food into energy, and build more proteins. If the DNA is different, the mRNA will be different, and if the mRNA is different, the proteins will be different, and if the proteins are different, you will be different. Mutations can be neutral, cause harm, or benefit an organism.

An example is if I have a chocolate cake recipe, and in the ingredients list it says 2 cups of sugar. A neutral mutation would be if it said 2 kups of sugar. You'd still understand the typo, causing no difference to the finished chocolate cake. A harmful mutation would be if it said 2 cups of vinegar. Vinegar is not used in chocolate cake, and would probably end up making it taste horrible. A beneficial mutation would be if the recipe read 1 cup of sugar. In the sense of health, one cup of sugar means less carbohydrates for your body, and since the chocolate already contains sugar, it means less fat you have to burn off. Mutations can be spontaneous, or induced.

Spontaneous mutations occur in the inside of a cell, most commonly when DNA is being replicated. Induced mutations occur as a result of the environment and external factors, such as smoking, increased UV radiation caused by sunlight, and dietary factors. One thing to remember is that mutations are always random, and aren't meant to happen. Let's talk about a few types of spontaneous mutations. The most common mutation throughout all organisms are point mutations. Point mutations occur when a single base pair is added, changed, or deleted. A substitution point mutation occurs when the wrong base is added. Say we have cytosine and adenine as a base pair. The result from a mistake caused by DNA

Polymerase 3, and one DNA Polymerase 1 did not fix. Luckily, there is protection. Proteins will travel along the DNA strand and look for these false base pairs. Once they find one, they will switch to say cytosine for thymine. But in other cases, they will switch adenine for guanine, and now there are two nitrogenous bases which weren't there in the original DNA strand before replication. There is also deletion. Radiation and chemicals can cause a DNA molecule to lose a base pair, moving all the nucleotides up the strand. The last type of point mutation is an insertion mutation. When radiation and chemicals enter the body and break the hydrogen bonds holding nucleotides together or even the sugar-phosphate backbone, proteins will rearrange the nucleotides into their original shape. However, in some cases they add an extra base pair, changing the sequence of one of the two strands. 50% of the time, proteins rearrange and substitute bases correctly, the other 50% these mutated strands keep getting replicated, and now your body has two or several types of DNA.

Natural Selection

So genetic variation is the result of mutations, which are mistakes in our nucleic acid sequences. **How does this help us and other species on our planet? Has it helped us for 6 million years?** The answer is yes, and the explanation is natural selection. In 1859, Charles Darwin published his book On the Origin of Species. He is known as the father of evolution and natural selection. Here is a made-up simulation that depicts natural selection.

You are a blob-like herbivorous creature, you live in a humid climate with plenty of tropical plants and fruits to feed on. There are around fifty of you and the same species on this small, remote, tropical island. However, there is a population of bird-like predators who often feed on your species. Its teeth are smooth and conical, making it easy for it to grasp on your soft, rubbery flesh. You are an invertebrate, with very little bones. You move slowly, making it difficult to escape. Let's say your first cousin has a substitution point mutation, and now he is slowly growing legs. Of course, in a real-life scenario, there would have to be time and reproduction present. He reproduces with another blob creature and has one offspring. Your second cousin has a deletion point mutation where he gains speed. He also reproduces and has one offspring with another blob creature. Over many generations, these offspring will continue to reproduce, and their offspring will continue to reproduce and so on, until half the population has legs, and half the population can move quickly. Now, the birds have a harder time finding their food, the variant species with legs are more agile and able to have a wider range of senses. The variant species with quickness can easily escape the predator's grasp without hiding in the first place. A few more generations pass by, and soon, the variant species with legs are all that remain. Why did this happen?

For natural selection to occur, there needs to be genetic variation, reproduction or inheritance of traits, environmental pressures, and differences in mutations between phenotypes. Phenotypes are physical traits we can observe, such as extra limbs or speed. Variation started with your two cousins, both your cousins started a long chain of hereditary, passing along these traits, the environmental pressure is the birds with conical teeth, and there is the obvious difference between these two phenotypes, legged and quick. The legged phenotype has desirable traits that allow it to endure the environmental challenges the other phenotype does or doesn't do so well. Certain phenotypes of a species are "selected" to

continue to thrive and reproduce, while the other phenotypes do not. Remember, mutations are always random, but when the mutation is beneficial, natural selection has a chance to occur.

Natural selection is a long process, taking millions to hundreds of millions of years. There's a high chance natural selection is occurring within our species right now, but we cannot predict the future and know which of us will survive. Charles Darwin came up with natural selection in 1835 in the Galápagos Islands when studying phenotypes of finches, specifically the shape of their beaks. Genetic variation can also be the long necks of giraffes so they can reach the leaves of tall trees, or the development of gills, so fish can breathe underwater. Without natural selection, there is no evolution.

Part 2:

Impacts of Genetic Mutations on Humans

Introduction

In part 1, I have explained how mutations occur in several generations through DNA replication and reproduction. In part 2, I will discuss three common genetic disorders that dominantly affect three ethnic groups. These are the examples that prove the process of inheritance of mutated genes, as each disease occurred in a specific population at a specific time, and through tens of thousands of years that specific population now has a higher chance of carrying that mutated gene. The three diseases I will discuss are sickle cell anemia, cystic fibrosis, and Diabetes.

Sickle Cell Anemia

Overview and Symptoms

Hemoglobin, an iron-rich protein found in your red blood cells, is responsible for delivering oxygen to the tissues in your body. Too much hemoglobin clumped together means blood clotting, and too little means not a sufficient amount of oxygen for your body to function properly. Sickle cell anemia is part of a group of inherited disorders referred to as sickle cell disease. It causes hemoglobin molecules to stick together, affecting the shape of your red blood cells. Red blood cells are round and pliable, so they can move easily through your blood vessels. However, this disease causes your red blood cells to be shaped like crescent moons or sickles. Rigid sickle cells can slow down or block blood flow, causing clotting.

Symptoms that are introduced include episodes of extreme pain when sickle cells block the arteries in your chest, abdomen, and joints. Red blood cells have a lifespan of 120 days before they are engulfed by macrophages, and sickle cells have a lifespan of a mere 10–20 days. A shortage of sickle cells means a shortage of hemoglobin, which in turn means a shortage of oxygen for the body, causing fatigue and shortness of breath. Blocking blood circulation can also cause swelling of hands and feet, severe infections in the spleen, delayed growth, and vision issues.

Genetic Causes

This is a genetic disorder, meaning a gene has undergone a mutation in both parents of an offspring. If both parents have this mutation in one copy of a specific gene, then the offspring has a 50% chance of carrying one copy of the mutated gene, a 25% of carrying no mutated copies of that gene, and a 25% of inheriting sickle cell anemia, meaning both copies are mutated. When a disorder follows these patterns, it is called recessive.

The gene that is mutated to cause sickle cell disease is called the HBB gene, found in chromosome 11p15.5. This gene encodes a protein for your hemoglobin, specifically the two beta-globin subunits out of the four genes that code for hemoglobin. This type of mutation is a single base-pair point mutation.

During DNA replication, a single base pair has been added, deleted, or changed in the HBB gene, and this mutated strand of DNA has been replicated through a series of sexual reproduction and cell replication, where the new gene is replicated for several generations.

Demography and origin of mutation

Mutations are random and are rarely beneficial to an organism. 50–150 years ago in sub-Saharan Africa, around 50% of the population was suffering from a disease known as malaria. In broad terms, malaria is a disease carried by a parasite which infects a mosquito, and the mosquito later bites a human, introducing a series of high fevers, shaking chills, and flu-like symptoms. Researchers say sickle cell anemia battled malaria germs and made it very difficult for them to survive in your body. Due to the low amounts of oxygen, it creates a hostile environment, giving more time for the immune system to react and terminate the parasite before it starts growing. In this case, sickle cells are beneficial, however, the disease itself hurts a human's body and therefore cannot be completely beneficial. In present times, about 1 in 12 African Americans or people of northern African descent carry this defect.

Sickle Cell Anemia: Care and Treatment

Sickle cell anemia (SCA) is a lifelong disease and one of the oldest and most common genetic disorders. Individuals who suffer from SCA require lifelong medical care and treatment, otherwise, the irregular crescent-shaped red blood cells can lead to life-threatening issues, such as stroke, and multi-organ failure. People with SCA often lead full and healthy lives, as we have been providing methods of prevention for over one hundred years. Fortunately, our medical world has advanced in genetic technology for mere decades, and we have found ways to edit the HBB gene that causes this defect. From yearly checkups, prescribed medicine, and lifestyle changes such as increased hydration and pain control, using gene therapy as a possible cure, we can switch the HBB gene's very base pairs and reverse its mutation.

Individuals of sub-Saharan African descent are most commonly affected by this disease. 10 - 40% of Africa's entire population is affected, roughly 40 countries, and with a steadily growing population, inheritance of the recessive gene will continue to spread. The vast region of sub-Saharan Africa lacks the modern medical equipment and hospital infrastructure needed to carry out cures, including gene therapy and bone marrow transplants.

As a possible cure to this threat, gene therapy equipment must be made affordable and practical in low-resource environments. **Now, you may ask, what is gene therapy?**

Gene therapy in broad terms is when a patient's cell is extracted from the body, its specific gene is modified to not carry that mutation, and later reintroduced into the body through bone marrow transplants. Through DNA replication, that modified cell will continue to replicate until it greatly lowers the risk for symptoms of SCD. This specific type of gene therapy is called CRISPR.

Bone marrow transplants are in most cases applied to youth under 16, as eradicating the mutated cell before adulthood would greatly increase the chance for a healthy lifestyle. First, a bone marrow stem cell is taken from someone who has similar bone marrow, often a sibling. Next, drugs are applied to the child to destroy his mutated cells, and the healthy bone marrow donation is inserted. There are many risks associated with bone marrow transplants, including the risk of infection and immune system problems.

If the child's immune system is not weakened before the transplant, it may recognize the foreign bone marrow cells as dangerous, and quickly eliminate them. This is why gene therapy is becoming a much more popular option. However, the vast majority of hospitals have not included gene therapy, and rely solely on pre-diagnosis, and lifestyle.

Lifestyle choices include staying hydrated, plenty of physical exercise, eating and sleeping well, and avoiding smoking and drinking. Individuals older than 2 are recommended to get checkups once a year. Infants 1–2 years old are recommended to get checkups every 3 months, and newborn babies up to a year old are recommended to get checkups every 2–3 months.

Using newborn screening, we can see if a child carries the recessive gene for SCD 24 hours after his birth. Hematologists say individuals with SCD should drink 8–10 glasses of water every day, and keep a healthy lifestyle composed of physical exercise, but to make sure to rest when tired and not overdo their lungs.

There is also a plethora of prescribed medication for SCD, including; Hydroxyurea, L-glutamine oral powder, Crizanlizumab, Voxelotor, and pain-relieving medicines. Hydroxyurea, L-glutamine oral powder, and Crizanlizumb are taken by injection to relieve extreme episodes of pain, however, Hydroxyurea is not recommended for those who are pregnant, and Crizanlizumab may have side effects including nausea, joint and back pain, and fever. Voxelotor, which is taken through oral intake, improves blood flow and reduces the risk of anemia. It is not prescribed to children younger than 12 years of age and may have side effects including headache, nausea, diarrhea, fatigue and fever. Pain-relieving medicines including narcotics are often prescribed to patients to help alleviate pain during an extreme episode of pain.

Major organizations elaborating on the importance of SCD gene therapy and providing new methods include SCDAA, Casgevy, NOVARTIS, and several CRISPR technology companies such as Vertex Pharmaceuticals. The majority of sub-Saharan Africa lacks a vast amount of professionally trained healthcare specialists, biotechnology, sufficient medicines and safe vaccines. 50-80% of infants born in Africa with SCD are deceased before five years of age. AHS, (Alberta Health Services), solely relies on bone marrow transplants as a cure for SCD. If CRISPR gene editing technologies are made more affordable and accessible to the consumer market for hospitals, regions of Africa and Alberta may be able to rely on gene editing as their main source of care and treatment.

Cystic Fibrosis

Overview and Symptoms

Mucus. You may have second thoughts about its importance in your body, but it plays a vital role, acting as a lubricant for tubes and passageways, and trapping bacteria and viruses. Cystic fibrosis is an inherited disorder that causes the usually thin and consistent mucus to become thick and sticky. This secretion now plugs into tubes and passageways, especially in the lungs and pancreas. Blocked passageways in the lungs may cause wheezing, coughing of thick mucus, lung infections such as pneumonia and bronchitis, stuffy nose, sinusitis, and inability to do exercise. This disorder also creates an unusually high concentration of water in your sweat.

Cystic fibrosis also blocks the tubes that carry digestive enzymes from your pancreas to your small intestine, meaning your intestines cannot completely absorb the nutrients in your food. **Symptoms** caused by this include severe constipation, slow growth and weight gain, intestinal blockage, and foul-smelling stools.

Genetic Causes

Like many genetic disorders, symptoms of cystic fibrosis are caused by a mutation in a specific gene which encodes for a specific protein. In this case, the gene is the CFTR or cystic fibrosis transmembrane conductance regulator gene, which encodes for the CFTR protein. The CFTR protein is a type of protein called an ion channel protein and regulates the amount of ions moving in and out of cells. It maintains the balance of water and salt moving in and out of cells and through the surfaces of specific organs, such as the lungs. The CFTR gene undergoes a frame-shift mutation, meaning there has been an insertion or deletion of nucleotide bases of a large number. Like sickle cell anemia, CF is a recessive disease. This means the offspring must have two copies of the mutated gene to inherit it, not just one. And so the same rules apply, a 25% chance of inheriting cystic fibrosis, a 25% chance of inheriting no mutated genes, and a 50% chance of inheriting one mutated gene, that is, if each parent carries one mutated gene. This mutation causes the CFTR gene to encode for a protein which does not maintain a healthy balance of salts, so your mucus is consistent, and instead malfunctions and causes it to thicken.

Demography and origin of mutation

In modern times, Caucasians and especially those of northern European descent are affected the most by CF. 20,000 individuals from Europe have this disease, and 30,000 from America. Researchers have traced its first mutation to 50,000 years ago in Northern Europe, most likely the Basques of Spain. This mutation was random, and not influenced by any environmental factors, and unfortunately harmed the organism it has evolved in.

Care and Treatment

Cystic fibrosis or (CF) is an inherited disease that damages multiple organs, including your lungs and digestive tract. The defective gene passed down generation from generation causes irregularities in your mucus, sweat, and digestive juices. It affects 70,000 people worldwide, and 30,000 are from the United States, as the gene affects Caucasians or whites of European origin dominantly. Most individuals who carry this genetic disorder have a high quality of life, and follow efficient treatment plans so that minor symptoms such as wheezing and shortness of breath do not lead to fatal outcomes including respiratory infection, predominantly pneumonia. The mortality rate of patients diagnosed with CF in the United States is 1 in 1.04 million.

Multiple healthcare organizations and systems in the States offer many forms of pre-diagnosis, prevention, and prescribed medication to make sure individuals lead normal, healthy lives.

First, I will describe forms of prevention. There are four types; controlling infections in the lungs, loosening mucus in the lungs, preventing intestinal blockage, and providing adequate nutrition.

Preventing and controlling infections in the lungs can come in the form of washing your hands often, getting a yearly Influenza vaccine, getting a yearly pneumococcal vaccine, avoiding first and second-hand smoking, and avoiding exposure to air pollutants. CF causes the cells in the lungs and respiratory system to absorb a high concentration of salt (sodium chloride), and water. The normal thin secretions of the lungs such as mucus become thick and sticky, leading to a high risk of infection.

Washing your hands decreases the chance of respiratory infection because germs and bacteria from your hands can rub off on surfaces and people. Those germs can be inhaled later and cause issues in your respiratory system, which is why it is important to wash your hands thoroughly with soap. Experts say you should wash your hands six to eight times a day.

Flu or Influenza is a highly contagious illness caused by a virus, and if this virus enters the body of an individual with CF, regular symptoms can worsen and lead to dangerous outcomes. Flu vaccines use antibodies, which are blood proteins released to defend your body from a specific antigen, to develop two weeks after injection of the vaccination. The vaccine includes a weaker copy of the virus that causes the flu, so your immune system has already exterminated the weaker copy before the more dangerous copy arrives, and so it is more prepared and can exterminate the virus more quickly. Side effects of the vaccine may include symptoms of the original virus, such as fever, cough, sore throat, and runny nose. The pneumococcal conjugate and polysaccharide vaccine protects your body from pneumococcal infections.

Pneumococcus is a type of bacteria that can cause sinus and ear infections, pneumonia and bloodstream infections. Similar to Influenza, Pneumococcus can worsen the already dangerous symptoms of CF, such as fever, bowel movements, and increased weight loss. It most commonly causes pneumonia, an infection where the air sacs of your respiratory system fill with pus and other secretions. It is recommended to get your pneumococcal vaccine once every five years.

Air pollutants such as particulate matter, nitrogen oxide, ozone, sulphur dioxide, and carbon monoxide are known to irritate your airways, which can lead to lung cancer, heart attacks, asthma episodes, wheezing, chest pains, and in some cases premature death. Air pollution moderates the severity of cystic fibrosis and lung phenotype of CS patients, similar to Influenza and pneumococcus.

Cigarette and tobacco smoke also include toxins such as tar and carbon monoxide, so it is important to avoid them as much as possible. The second form of prevention is loosening mucus in your throat, by gargling salt water, staying hydrated, and using nasal sprays and humidifiers.

By gargling salt water, the saline solution coats your mouth and throat, which also lessens inflammation and throat pain.

Drinking plenty of water every day means the mucus in your throat is thinner, lubricates your eyes and joints, and food moves through your digestive tract and gut. If you are over 14, doctors recommend 8–12 cups per day, and below 14 are recommended 4–7 cups per day.

Nasal sprays eradicate or lessen the number of nasal polyps, which interfere with the normal drainage or recylation of your sinuses.

Humidifiers increase the moisture or water vapour levels in the air, making it easier to breathe. Humidifiers are especially useful for individuals living in dry climates. There is also preventing intestinal blockage, by avoiding high-fiber foods, and raw fruits and vegetables.

An adequate diet for CF patients includes plenty of fats, carbs, and salts.

Diabetes Mellitus

Overview and Symptoms

Diabetes is a chronic disease, meaning it lasts for more than one year. It is where the pancreas, an organ located in your abdomen which plays the role of secreting digestive enzymes and hormones, makes little or even no insulin. Insulin is a hormone that turns glucose into energy and manages your blood sugar levels. Without insulin, your blood will have an increased concentration of sugar and become more acidic, due to increased levels of ketones, hormones produced by the liver to break down sugars.

Symptoms caused by increased blood sugar include dehydration, increased urination, loss of weight, mood swings, blurry vision, and fatigue. These symptoms can lead to extreme complications in major organs in the body, including; Heart and blood vessel diseases such as CAD, angina, heart attack, stroke, and atherosclerosis, nerve damage where you experience tingling and numbness all over your body and start to lose feeling of your limbs, kidney damage such as kidney failure or end-stage kidney disease, eye damage such as blindness, glaucoma and cataracts, infections can occur in the feet, skin and mouth, and pregnancy defects such as miscarriage, still birth, and birth defects.

Genetic Causes

Diabetes usually occurs as a result of two causes. The first is when your immune system, a network of organs and proteins that protect your body against harmful bacteria and viruses, destroys the islet cells in your pancreas which produce insulin. The other is genetics. In your DNA sequence, genes that provide instructions for producing proteins in the immune system encounter variation. These genes are HLA-DQA1, HLA-DQB1, and the HLA-DRB1 genes. These genes are located on chromosome 6p21.3. These mutations are point mutations, where a single letter of a gene is replaced, substituted, deleted, or added. Since point mutations have occurred in multiple genes, Diabetes is known as a monogenic disease. Diabetes is recessive, meaning it follows the same rules for the probability of an offspring inheriting it. Offspring who carry one mutated copy of a gene and one that is not affected are merely carriers, but offspring who carry both copies of the mutated genes inherit the disease.

Demography and origin

Its earliest records were in Egyptian papyri 1552 BC, and records have also been found in China, India, Greece, and the Middle East around that time. Although we have no concrete knowledge of when and where Diabetes originated, we know that North African Americans and African Americans are the two races most prone to it, so we can assume it has originated in Africa and South America, most likely in colder temperatures in the north and south. Diabetes is a chronic condition that affects 1.7 million adults

and 652,000 children around the world. About 40% of individuals diagnosed originate from China and regions of South Asia such as India, Bangladesh, Nepal, and Afghanistan. Currently, 537 million adults and 355 900 children have Diabetes.

Care and Treatment

Although there is no cure for Diabetes yet, a healthy lifestyle, blood monitoring and prescribed medication can improve an individual's health greatly. But for our most advanced methods of prevention, organizations must share their treatment with the ethnic groups suffering most from this disease.

First, I will describe several changes someone can take hold of to improve their lifestyle and decrease symptoms of Diabetes.

- Controlling the amount of carbohydrates, fats, and proteins you consume by eating healthy foods, and exercising regularly while maintaining your weight are all excellent initiatives an individual can take. These methods are all used for one goal, maintaining your blood sugar level. Increased blood sugar or hyperglycemia caused by overconsumption of carbs/sugars can cause permanent damage to multiple organs such as the kidneys, eyes, and lungs that require emergency care, while a low blood sugar level means not consuming enough carbs for the level of insulin in your body, resulting in nausea, headache, and multiple symptoms.
- Exercising helps lower the risk of hypoglycemia, by burning off glucose and improving the way insulin works. This is because working muscles cause more insulin sensitivity than resting muscles, so your muscle cells can take more available insulin to eradicate glucose after an activity.
- Cardio is the most efficient way of lowering blood sugar and comes in the form of walking, running, cycling, and aerobics. Specialists recommend at least 150 minutes of exercise per week and 150–250 grams of carbs per day.
- Now I will describe more practical treatments, including insulin and other medication. The four types of insulin medication are short-acting insulin, rapid-acting insulin, intermediate-acting insulin, and long and/or ultra-acting insulin. In broadest terms, each type of insulin differentiates by the amount of time before their peak effects occur, the duration of time before they start affecting the patient, and when they are injected.
- Other blood sugar medications include high blood pressure medications such as ACE and ARB inhibitors which are prescribed to individuals with high levels of mercury which keep your kidneys healthy, aspirin to lower the risk of a cardiovascular event, and cholesterol lowering drugs which lower cholesterol levels and in turn decrease the risk of heart disease.
- More recent or modern treatments for Diabetes include pancreas and islet cell transplants. Pancreas transplants are when a healthy pancreas is inserted in your body through surgery, and your body will no longer require insulin medication, as your new pancreas secrete normal and healthy amounts of insulin. They are available for individuals with extreme symptoms of

Diabetes, and individuals who also require a kidney transplant. Islet cell transplants are when islet cells which are insulin-producing cells from a donor pancreas are inserted in your body.

- 40% of individuals with Diabetes originate from Bangladesh. Without strong enough healthcare services, increasing poverty, and Diabetes on the rise, political will and economic resources are key success factors in raising awareness and lowering the percentage affected by Diabetes. The Diabetic Association of Bangladesh needs help from organizations such as JDRF, ADA, and NIH which are leading companies in pre-diagnosis and treatment for Diabetes. They must pool their collective resources and make them available for consumer markets in Bangladesh and Southeast Asia.

Part 3:

Initiatives and Recommendations for Alberta Health Services (AHS)

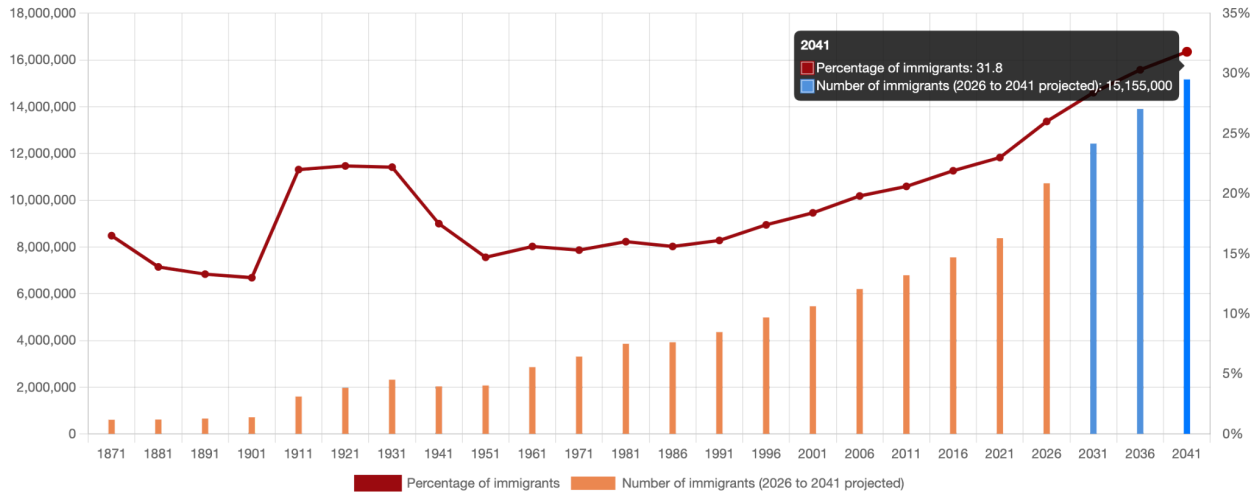
Introduction

Now I will discuss the practical implications of my project, by gathering all previous knowledge. I will share a list of 5 recommendations for the Alberta Health Services (AHS). These recommendations will be ways AHS can improve their program in terms of care and treatment for genetic diseases or initiatives they can take for pre-diagnosis and prevention of genetic diseases. Two of these recommendations will be short-term, or what AHS can accomplish now, while the other three will be long-term, initiatives that may take decades to have full effect. I will also discuss Alberta's demography and estimated future immigration levels of the three ethnic groups discussed in part 2, so you can understand the full scope and impact the health of these immigrants have in Alberta's society.

Alberta's Demography

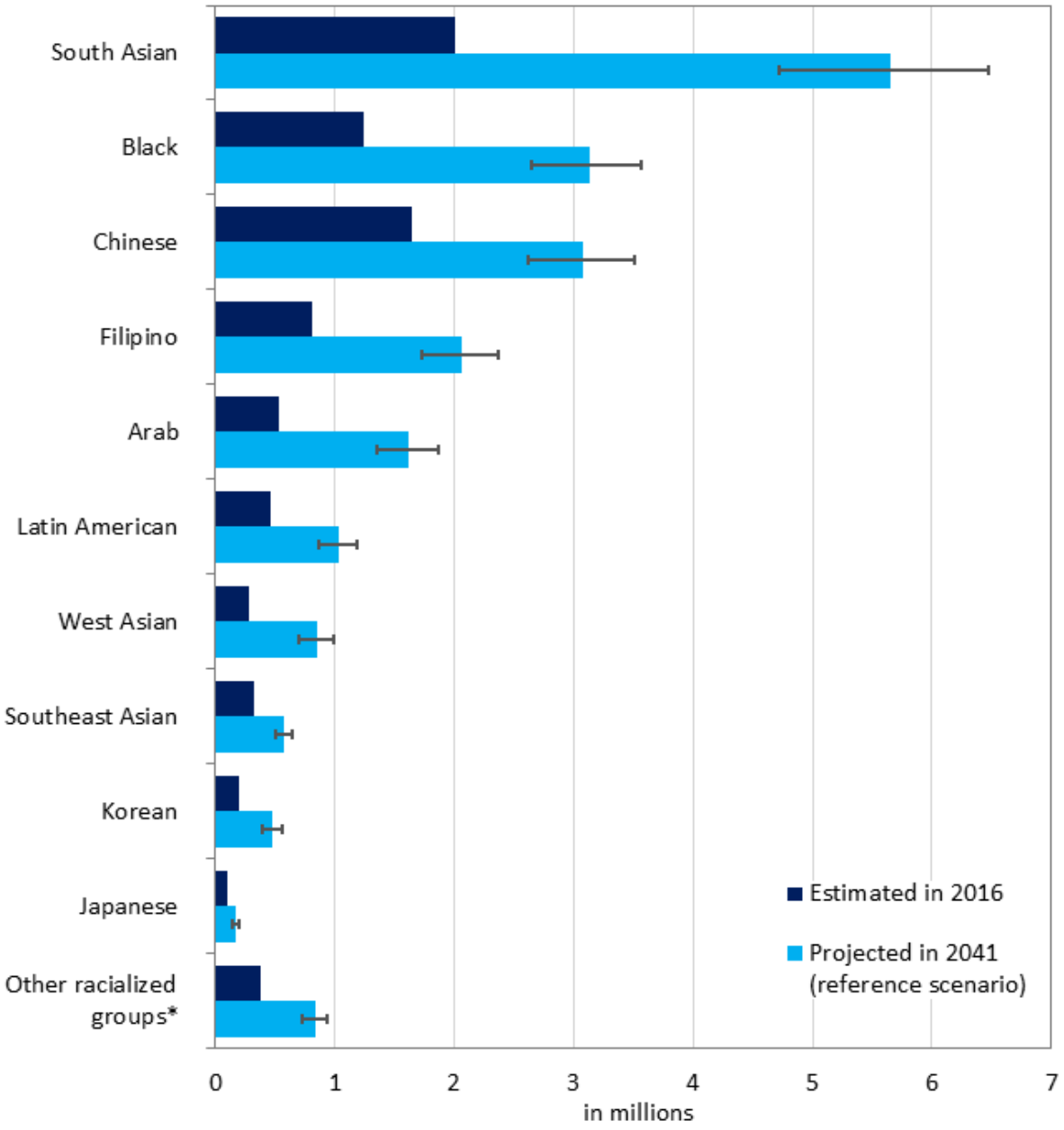
Sub-Saharan Africa, Southeast Asia, and Caucasians are all part of Alberta's population, and statistics show immigration levels from these regions will continue to rise. Immigrants play a pivotal part in our economy, and without optimal health, multiple sectors may go down, such as education, industrial production and even healthcare. It would be preferred If I included common genetic disorders tied to every ethnic group that has immigrated to Alberta, but for the sake and limitations of this project, I have chosen three.

The first statistical graph I have chosen shows general immigration levels and their estimated rise until 2041. It shows percent, and number of immigrants.



(from Immigration, R. a. C. C. (2023, December 20). Context. Canada.ca. https://www.canada.ca/en/immigration-refugees-citizenship/campaigns/canada-future-immigration-system/context.html)

The second graph I have chosen shows estimated future immigration levels of African, South Asian, and other ethnic groups until 2041.



* The category "Other racialized groups" includes people who belong to more than one racialized group or who belong to a racialized group not included elsewhere.
Note: The symbol " ⊢⊣ " corresponds to the minimum and maximum values projected by all 11 scenarios considered.
Sources: 2016 Census (adjusted) (3901) and *Population projections on immigration and diversity for Canada and its regions, 2016 to 2041* (5126).

(From Government of Canada, Statistics Canada. (2022, September 8). The Daily — Canada in 2041: A larger, more diverse population with greater differences between regions. https://www150.statcan.gc.ca/n1/daily-quotidien/220908/dq220908a-eng.htm)

Genetic Testing: The main form of prevention

Whenever an individual suspects he has a genetic disease or shows symptoms of a genetic disease, it is highly recommended to take a genetic test. Since my project revolves solely around immigrants and the genetic disorders prone to their ethnic group, it is important to discuss the process by which they find out whether they have that disease or the risk factor of inheriting it. A few of my recommendations in my final list also include genetic tests.

The last three diseases I have discussed can all be genetically inherited. Through methods of gene testing, we can see down to the last chromosome every mutation an individual has burdened to be diagnosed with this disease. However, none of these diseases have a definitive cure. A cure for CS or Diabetes has not been found, and right now bone marrow transplants for sickle cell anemia carry significant risks the majority of the population are not willing to take. So then, why do we research genetic diseases? Why don't we spend our time and resources on finding a cure instead? Well, it's because gene tests allow for the prevention of these diseases. Changes in the lifestyle, medication, and health of an individual may greatly reduce the risk of inheriting the full symptoms of a genetic disease before it is too late.

The diagnosis of a genetic disease includes a physical examination, a family medical history, and laboratory testing if available. Common red flags for a genetic disease are symptoms, but another major factor is if a close relative carries that disease. That's why doctors ask for a detailed medical history or pedigree, to see if any family members carry that disease and the probability of you inheriting it if it is recessive. In genetic testing, a sample of your blood, skin, urine, or other tissue will be used. If the test was positive it means that the mutation of genetic change in your DNA that was being tested for has been found. If negative, then the mutation has not been found. You may also speak to your doctor about the risk of your offspring inheriting the disease or can go to genetic counselling, where a genetic therapist can ask any questions about your family or concerns you may have. **There are various methods of genetic testing used for specific situations and purposes:**

Carrier testing: Carrier testing is often used by couples with a familial history of a certain genetic disease, or if they are part of an ethnic group with a higher risk of mutated DNA sequences. Couples want to know the risk of their child(s) inheriting the disease. This is done by investigating if the father or mother carries a recessive allele, which is the mutated copy of a gene(s) individuals with that disease carry. Sickle cell anemia and CS are most often carrier tested.

Newborn screening: Newborn screening is the most common form of genetic testing. Newborns within 24 hours of leaving the womb are tested to see if they have certain metabolic disorders and abnormalities. This is so if a newborn does carry a genetic abnormality, care and treatment can begin from an early age. In the US every state has made it mandatory for an offspring to undergo newborn screening. Sickle cell anemia is one of the metabolic disorders newborn screening reveals.

Prenatal Diagnostic Testing: Prenatal testing is used to determine if during pregnancy a fetus has mutated genes in its sequence. Most commonly offered to couples who have an increased risk of

inheriting a disorder due to familial history. A tissue sample is obtained through an invasive amniocentesis. However, new methods to obtain a fetus's DNA include cell-free DNA by using a blood test from the mother.

Predictive or Presymptomatic testing: These tests are used by adults and adolescents with a family ancestry that includes multiple individuals of a particular disorder. For prevention of the disease down the road, a sample is obtained, and your sequence is investigated for the particular disease you are concerned about.

Diagnostic testing: If you have symptoms of a particular disease, such as cystic fibrosis, then diagnostic testing is done to analyze your DNA sequence to confirm if you have it. Diagnostic testing is not as useful as the other methods I have discussed, since it is used once the patient has already experienced the full extent of the genetic disorder.

Pharmacogenetics: Diagnostic testing is used to confirm if you have a genetic disease first aroused by symptoms, while pharmacogenetics is used to determine the medication and dosage you should consume to delay or prevent your health conditions.

Recommendations for Alberta Health Services:

Genetic Counseling: During immigration, if an immigrant has a high-risk factor of inheriting a genetic disorder or their child inheriting a genetic disorder, there should be a genetic counsellor. Genetic counsellors investigate individuals or families affected or at risk of inheriting a genetic disease and walk them through the impact on quality of life and medical complications in the future. Genetic counselling is important because it gives you recommendations and referrals to doctors and physicians who specialize in your disease and can reassure you so you are prepared for the full extent of your condition. **This would be a short-term plan** spanned to a maximum of a few months, as AHS already has a staff of genetic counsellors.

Genetic therapy for SCA: AHS has already implemented bone marrow transplants and stem cell transplants as part of their program. However, gene therapy has proven to be more successful as it does not require a donor and only requires the patient's cells. When the patient's cells are modified, there is no risk of graft-versus-host disease, or in other terms, the patient's immune system eradicates the foreign donor cells by mistake. In 2018, CRISPR Therapeutics and Vortex Pharmaceuticals funded CASGEVY's new gene-editing therapy using CRISPR Cas 9 for sickle cell disease, and the results were a success. CASGEVY also happens to be the first FDA, (Food and Drug Administration) approved gene editing technology in history. If AHS were to incorporate CASGEVY's CRISPR treatment, then the success rate of a 100% cure in the patient would increase. The only setback to this is that each CASGEVY treatment costs 2.2 million USD, which means that each CASGEVY treatment plan must be used for several patients, so I would recommend at least 3 treatment plans for a total of 6.6 million USD. **This would be a long-term plan, spanned over a few years.**

Immigration Genetic Tests: Every immigrant who comes to Canada must undergo a medical exam taken by a professional physician. This is called the IME, (Immigration Medical Exam.) This is so the possible

health condition of the immigrant does not endanger the safety of Canadians or put an excessive demand on Canada's healthcare services. During this testing, there is a physical examination, medical history, and several lab tests including chest and X-ray. However, if the medical history points out a close family member who has a genetic disorder, eg: a father, then there should be a carrier test or predictive test. Carrier testing will be used for couples with a history of familial genetics, or part of an ethnic group which is prone to a specific test. This is so they can know the risk of their child(s) inheriting a disease. An example would be a sub-Saharan African couple who wishes to know the likelihood of their child inheriting sickle cell anemia. Predictive testing will be used for individuals who have come to Canada and have a history of familial genetics. Carrier testing can be prenatal, meaning a blood sample of the fetus is taken before birth, and physicians will check if the child has a mutated recessive gene or not. This is highly efficient because the couple will know what specific measures to take for their child to lead a healthy life. **This would be a long-term plan, spanned over a few years.**

Raising Awareness: To raise awareness of the symptoms of a particular disease towards the public, there should be medical brochures that clearly outline the risks and dangers of that disease. These brochures should be conveniently placed in public locations such as the waiting areas of healthcare facilities. **This would be a long-term plan.**

Newborn Screening in Canada: In Canada, only Ontario provides newborn screening in hospitals. The United States offers newborn screening in all fifty-one states, and newborn screening has become the most common form of genetic testing across the world. It is when a blood sample from a newborn baby is taken during the 24 hours after his birth. A physician runs a genetic test to see if that child carries a genetic disorder and notifies the parents. Newborn screening is efficient because it tells parents any conditions a child may carry at the start of his life, so the necessary preemptive actions can be taken. It is also a genetic test which requires the least amount of time and resources, unlike prenatal or carrier testing which requires complex operations and tells you the likelihood of inheritance after a matter of weeks. **This would be a long-term plan, spanned over a few years.**

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