Genetic Variation

National DNA Day

April 25, 2008

Acknowledgements

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- Presentation intended for classroom use only

Human Genetic Variation

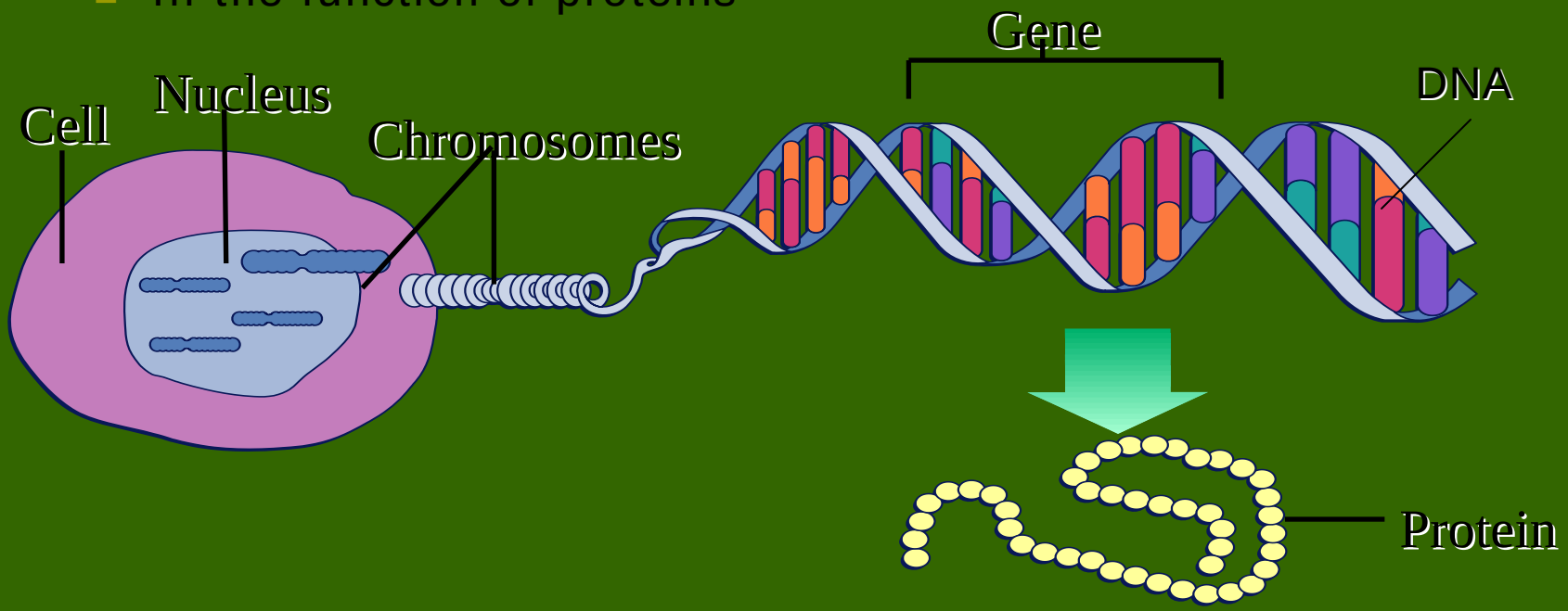
- *Genetics* is the scientific study of inherited variation
- *Human genetics* is the scientific study of inherited human variation
- We study this variation in order to better understand ourselves as a species and use this knowledge to improve our health and well-being

Understanding human genetic variation

- *Homo sapiens* are a relatively young species
  - We have not had much time to develop genetically and produce variations
- We each have approximately $3x10^9$ base pairs of DNA
  - No two people, except for identical twins, are genetically identical
  - Any two people have about $6X10^6$ base pairs which are different; this may seem like a lot, but in fact is only 0.1% of the entire human genome.
- And yet around the world, all populations of humans are essentially the same – the differences lie among individuals, not among populations
  - This is leading some geneticists to question the validity of defining race – the biological differences between the races are much fewer than the differences among individuals in one race

What are genetic variations?

- Variations are simply differences in genetic sequence
- Variation can be seen at every genetic level:
  - In the DNA
  - In the genes
  - In the chromosomes
  - In the proteins
  - In the function of proteins



Major types of genetic variations

- Mutations – changes at the level of DNA; one or more base pairs has undergone a change; change could be at random or due to a factor in the environment
- Major deletions, insertions, and genetic rearrangements can affect several genes or large areas of a chromosome at once
- Polymorphisms – differences in individual DNA which are not mutations
  - Single-nucleotide polymorphisms (SNPs) are the most common, occurring about once every 1,000 bases or so
  - Copy number variations – some DNA repeats itself (i.e. AAGAAGAAGAAG) and there can be variation in the number of repeats

Understanding human genetic variation

- Most variation is “meaningless” – it does not affect our ability to survive or adapt
  - Example: “silent mutations” in DNA, which change the DNA, but does not change the amino acid the DNA codes for. Other mutations may change the amino acid sequence of a protein, but not the overall function of that protein
  - Many polymorphisms do not seem to affect our survivability

Understanding human genetic variation

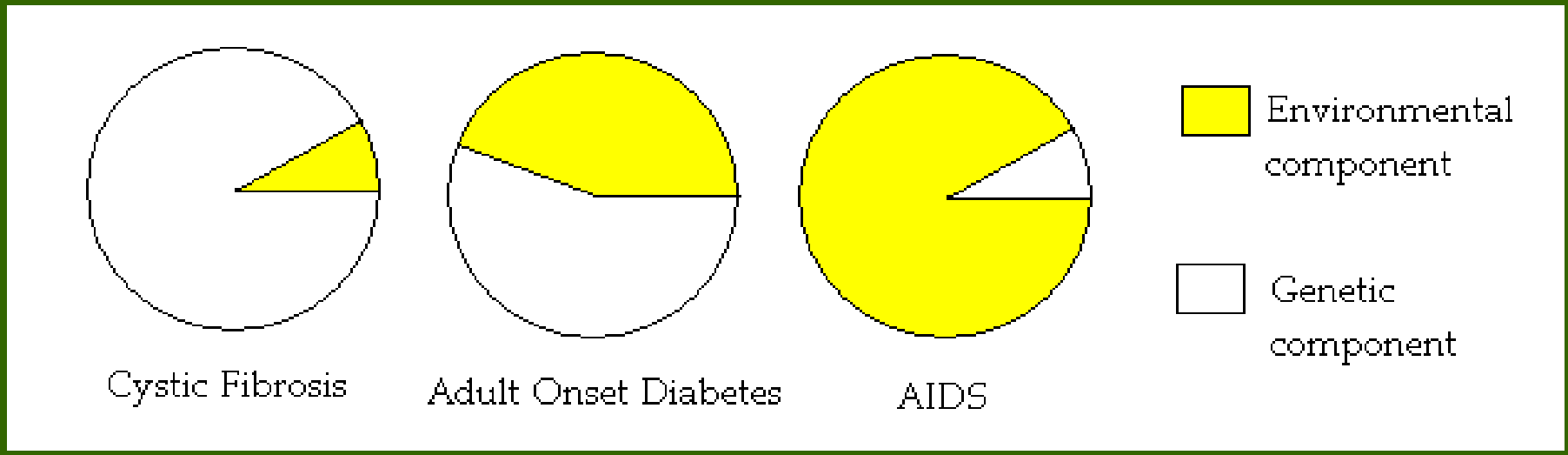
- Some variation is positive – it improves our ability to survive or adapt
  - Mutations in the *CCR5* gene provide protection against AIDS – makes it harder for HIV to bind to the surface of cells and infect them
  - Genetic mutations which cause the disease sickle cell anemia have also been found to have a protective effect – individuals with sickle cell trait (i.e. carriers of the recessive gene) are less likely to die from the disease malaria, which is caused by parasites and spread by mosquitoes

Understanding human genetic variation

- And, of course, some variation leads to disease
  - Single-gene disorders like cystic fibrosis and Huntington disease
  - We are also learning more about the contribution of genetic variation to more “common” conditions, such as heart disease, cancer, diabetes, and psychiatric disorders like schizophrenia and bipolar disorder; variation may give us a predisposition to one of these conditions, though not the condition itself

Understanding human genetic variation

- For those mutations/variations which make us more likely to develop a condition such as diabetes, environment also plays a key role.
  - Environment may be interacting with several different genes to cause a condition, instead of just one gene
- We now believe that genetics plays a part in virtually all human diseases, except perhaps trauma



Understanding genetic variation

- The following activities are designed to highlight the application of human genetic variation principles.
- Variation in Human Traits
  - Will exemplify just how similar we are, but also how very different
- Rolling the Dice
  - Will demonstrate the interaction between environment and genetics in causing human disease

Activity: Variation in Human Traits

Introduction

- One goal of the Human Genome Project was to provide the complete sequence of the human genome.
- Another goal was to illuminate the extent of human genetic variation by providing a detailed picture of human differences and similarities on the genetic level.
- Any two individuals are 99.9% identical in their DNA

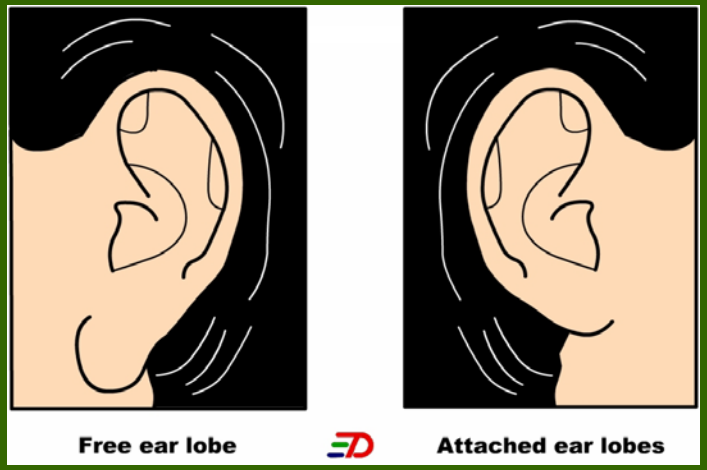
Introduction

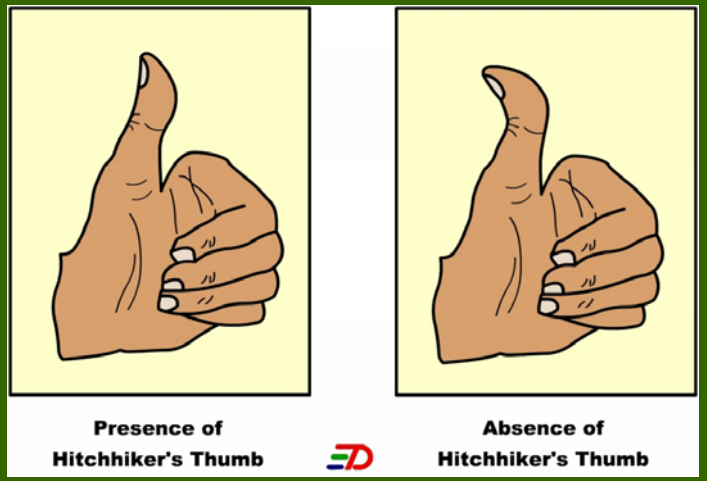
- That 0.1% is VERY important in defining our differences.
- We are all very similar, but all very different
  - Visitors to our planet would have a tough time telling us apart at first, but would slowly begin to notice the differences
- The 0.1% of unique DNA, plus the interaction of genetic and environmental factors, is what leads to our different *phenotypic* features
- Let's see just how similar you all are!

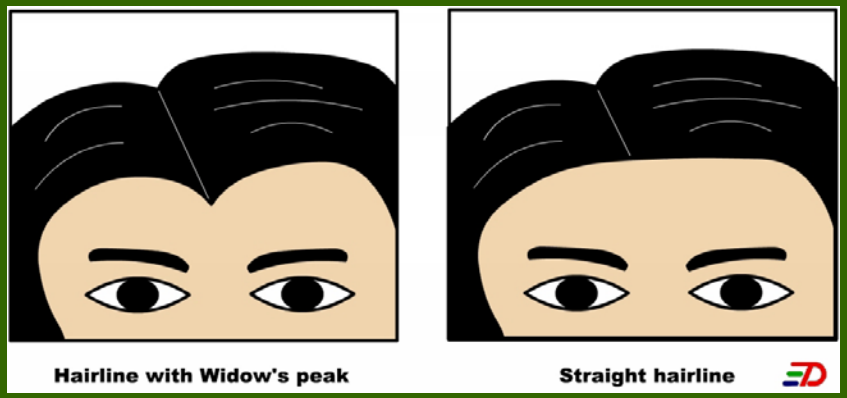
Instructions

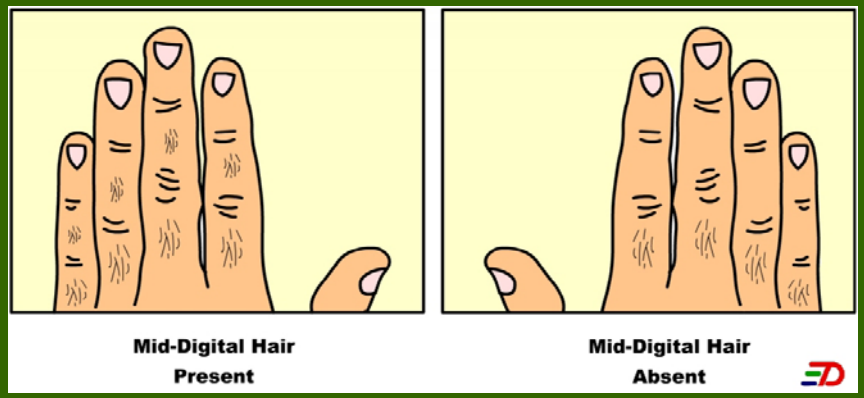
- Split up into pairs. Go down the "Inventory" worksheet and fill it out for your *partner's* traits.
- Compare your worksheets once finished.

A little help . . .









Photos courtesy of the Ministry of Education in Singapore

Comparing four traits

- We will now create histograms of four traits: sex, number of noses, height and hair color.
- What do the histograms of these four traits show us?
  - How are we most similar?
  - What are our greatest differences?

Distribution of traits

- Discontinuous trait: distinct categories with no “in-betweens”
- Continuous trait: no distinct categories; rather, there is a wide variety which covers a broad spectrum
- Normal distribution (e.g. the bell curve): majority of data points at an average point, with fewer and fewer data points as you move away from the average
- Bimodal distribution: a type of normal distribution with two peaks instead of one (may see a peak for two populations within one larger population)
- What kind of distribution(s) do we see with our four traits?

How different are we?

- Look again at your inventory of traits.
- How many traits would be needed in order to identify any one of you as unique, or sharing a combination of traits with no one else in the room?
  - Give me your best guess!

Questions for Discussion

- Some human traits can be changed by human intervention and some cannot. What are some examples of each?
- Name some traits which reflect an interaction between genetic and environmental factors.
- What are some benefits of human genetic variation? What are some potential problems it can cause?

Activity: Rolling the Dice

A Sad Story . . .

- Ekaterina Gordeeva and Sergei Grinkov, young married Russian figure skaters, had won two Olympic medals in the pairs competition and were expected to continue their success. But in November of 1995, 28-year-old Sergei suddenly collapsed and died during a practice session. He was a non-smoker, physically fit, and there had been no warning signs. What happened?

An answer . . .

- Sergei Grinkov was born with a mutation in a single gene which affects the formation of blood clots. This mutation, called *PL(A2)*, can cause clots to form in the wrong place in the wrong time – like in the heart, causing a heart attack
- Sergei Grinkov had an increased *relative* risk for a premature heart attack, though his *absolute* risk was still low. In other words, his risk for a heart attack was higher than most people in the general population (maybe 20% higher), but his overall risk of having a heart attack by age 50 was still low (maybe about 5%).

Could anything have been done?

- It seems as though *PL(A2)* mutations interact negatively with cholesterol in the blood
- Someone with a *PL(A2)* mutation, like Sergei Grinkov, may be able to reduce their risk of a heart attack by maintaining a low cholesterol diet and exercising regularly.
- While genetic mutations such as these are very rare, we continue to learn more about how genetic factors interact with the environment in causing conditions like heart disease. This knowledge could help to better define individuals' health risks.

Introduction to Activity

Imagine that you are going to live your entire life in the next 10 minutes and that your choices in life are going to be made by a roll of the dice.

How will your choices affect the rest of your life? What else will influence the course of your life? How will your genetic makeup affect your life?

Instructions

- Begin with your “Life Stage 1: Choices as a Teenager” worksheet.
- Roll the die to determine how many points you will receive for each behavior (diet, exercise, school/job/relationships, and smoking). Record your points in the right-hand column.
- Share the die among your group members so everyone can roll for points
- Add up your total risk points for Life Stage 1. If the total is more than 85, you are done – you have had a fatal heart attack. Sit back and wait until the rest of your group finishes.
- Repeat these same steps for Life Stages 2 and 3.

Instructions

- Draw a strip of paper from the container the presenter passes around. This strip has your genetic factor written on it.
- Write your scores in the “Review” column of your “Combining the Factors” worksheet and your total score at the bottom.
- Write your “Genetic Factor Points” in the “Recalculate Column.” Re-record your life stage points beneath that. Add your Heart Points and Life Stage points together and record the total at the bottom. Whenever you reach 85 points, stop – you have had a fatal heart attack.

Questions for Discussion

- What effect did including your points for genetic risk have on your outcome?
- Think about the behavioral choices you made in each life stage.
  - Did everyone make the same choices?
  - Were all of the choices equally risky?
  - Were the risk factors associated with the choices reversible?
  - Were the choices under personal control?
- Now think about the effects of the genetic risk factors in each life stage.
  - Does everyone have the same genes?
  - Did all of the genetic factors have the same effect?
  - Were the genetic factors reversible or under personal control?

Questions for Discussion

- How is this game like real life? How is it NOT like real life?
- Assume that genetic testing showed that you were at increased risk for a fatal heart attack 20 years from now. Would you want to know? Would it cause you to change your behavior?
- How will increased knowledge of the genetic factors associated with heart disease (or cancer or diabetes) have a positive impact on individuals and society? How will it have a negative impact?