

INHERITANCE: It's More Complicated Than That

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For the past 60 years, teaching and learning the science of inheritance and biological variation has largely been centered in Mendelian genetics. In classrooms, genetics instruction generally focuses on traits controlled by a single gene, with genotype the primary determinant of phenotype and little to no effect from other genes or of the environment (McElhinny et al. 2014). Traits used as phenomena generally have two to three discrete phenotypes (wrinkled or smooth, short or tall), which are inherited in a dominant/recessive pattern. Students participating in learning environments designed from the perspective of Mendelian genetics should be able to use a Punnett square to make predictions about the genotypic ratios of offspring from parental crosses and should understand how genotype determines phenotype in traits inherited in a dominant/recessive pattern. However, the reliance on this framework of inheritance does not support students to appreciate or explain the true complexity of human variation. After learning the Mendelian curriculum, many students attempt to apply deterministic Mendelian logic to the inheritance of all traits, assuming

that there must be "a gene for" traits like eye color, skin color, personality, and intelligence and that they are inherited in the same dominant/recessive pattern as the Mendelian traits they studied in the classroom (Mills Shaw et al. 2008; Radick 2016).

When students start to explore human variation through their own observations, they notice that most human traits are not discrete, but are more complicated than that. Traits from skin and eye color to the risk of complex diseases are not easily divided into two or three clear buckets. These traits exist on a continuum within human populations and therefore are unlikely to be controlled by a single gene alone. Twenty-first century geneticists have explored the genetic basis of these complex traits equipped with the power of the complete human genome sequence, millions of individual samples of genomic DNA, and the computing power to run genome-wide association studies. We now know that most single gene variants confer some level of risk or probability of a particular trait, but very rarely determine phenotype in and of themselves. Most human traits are influenced by dozens, hundreds, or thousands of genes working together, not by single genes. Although some genes' effects are stronger and others are weaker, few genes and gene variants have large effects on phenotype. Rather, the tiny effects of many genes and gene variants, in concert with an individual's environment, are integrated to produce a particular phenotype (Visscher et al. 2017). Although polygenic traits are sometimes discussed in the biology classroom, they are rarely emphasized and are not always explicitly compared to Mendelian traits.

The incongruence between the single-gene traits explored in most biology classes and the polygenic traits that make up most visible (and invisible) human variation provide an opportunity to deeply engage students in the science practice of evaluating and revising models to build a more accurate and complex understanding of human variation. In this article, we describe a series of activities that support students to explicitly evaluate the Mendelian model of inheritance and to model additive polygenic inheritance using the phenomenon of human variation in height.

Activity sequence description

The following activities take two class periods that last approximately 55 minutes each. We describe the learning sequence through the 5E framework (Bybee and Landes 1990); however, each of the Es is not attended to each day. The 5 Es are stretched over two days to give the students ample time to explore variation in human height with a polygenic model of inheritance.

The activities are part of a larger unit on genetic inheritance. Prior to these activities, students should engage in a variety of activities that explore chromosomes as biophysical structures and that demonstrate Mendelian models of genetic inheritance. Students should be familiar with using Punnett squares to determine the potential probability of offspring having a particular phenotype given the genetic makeup of the parents.

CONTENT AREA

Biology

GRADE LEVEL

6–8

BIG IDEA/UNIT

Genetic inheritance and variation

ESSENTIAL PRE-EXISTING KNOWLEDGE

Dominant and recessive gene expression, Mendelian inheritance, Punnett squares

TIME REQUIRED

Two hours (two class periods of 55 minutes; best to do over two days if possible)

COST

N/A

SAFETY

N/A

Engage

To begin, students receive a black-and-white picture of college students organized in a histogram according to height (Figure 1). Students take a few minutes to write down in their science notebooks what they notice and wonder about the picture. Once they finish their quick-write, the teacher invites students to share their observations with their table mates before sharing with the whole class. Some examples of students' observations might include the following: (a) the people are organized by heights; (b) overall, the people in the white shirts are shorter than the people in the black shirts; and (c) there are more people clustered in the center with fewer at each end.

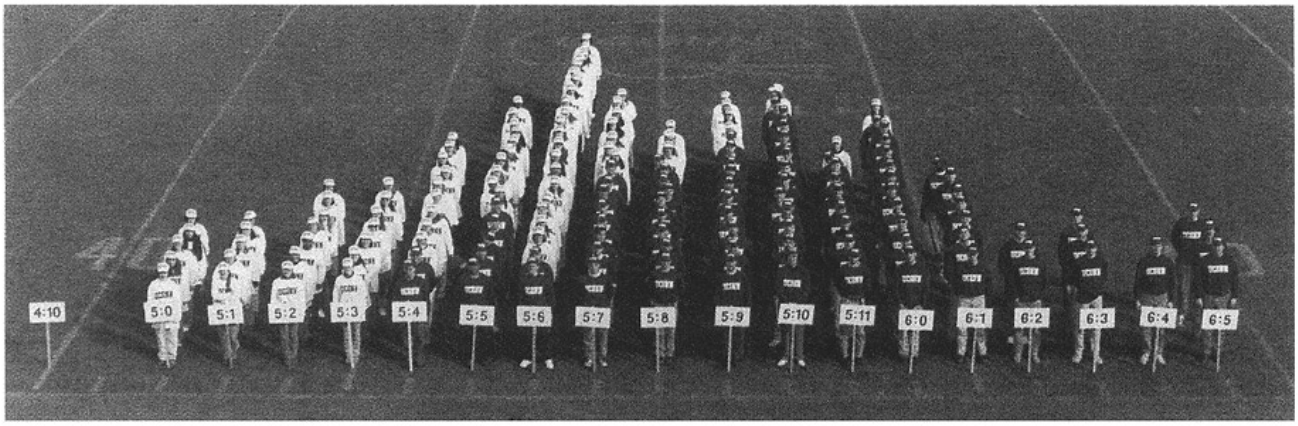
This initial activity should take about 20 minutes and is meant to initiate students' sensemaking about if and how the Mendelian model for genetic inheritance works for other human traits. The simple Mendelian model for dominant and recessive traits that students should have experienced prior to this activity had only two or three possible outcomes for phenotype. The living histogram shows considerably more phenotypic variation than this, leading to an opportunity to evaluate the prior model based on new evidence. The teacher can prompt this sensemaking by asking students if the variation they notice in the photo follows patterns of inheritance they had observed with Mendelian traits. The students should recognize that there is considerably more variation in height than could be explained by the Mendelian model and that therefore the model must need to be revised for the trait of height.

Explore

The explore phase takes about 30 minutes and introduces students to a model for inheritance of a polygenic trait. To start, the teacher provides students with a handout that describes a model for the contribution of four genes (rather than one) to the determination of an individual's height (see the polygenic height model in the box; it is also available in Supplemental Materials). Each gene is represented by a different coin and has two alleles, one that increases the height of the offspring (heads) and the other that decreases the height of the offspring (tails). As genes can vary considerably in the strength of their effects on particular traits, the genes in the model differ by the amount of height added/subtracted. The quarter and dime genes have a larger effect on height, adding or subtracting 2 or 1.5 inches to an average height, respectively, and the nickel and penny genes have a smaller effect, adding or subtracting 1 or .5 inch to an average height, respectively.

After the teacher goes over the model as presented in the handout, the students practice doing a calculation of height using a sample coin genotype. It is helpful if the sample genotype is heterozygous at some genes and homozygous at others. This is an

FIGURE 1: Living histogram of 143 university students.

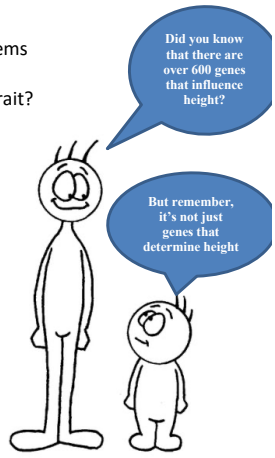


[SCHILLING, WATKINS, AND WATKINS 2002].

Let's investigate some of the wonderings you have listed.

One idea that came up was the idea that maybe height is not an "either/or" kind of trait. It seems to be continuous but with more in the middle than on the ends. What if there were more than one gene that influenced height? What if height is a polygenic (poly=many, genic=gene) trait? What if height is determined by many genes? To make it simpler, let's imagine there are four genes that determine a person's height.

We will represent four different height-influencing genes with four coins: a quarter, a dime, a nickel, and a penny. For each of these genes, we will have two alleles. One allele, heads, increase height, and one allele, tails, will decrease height. Because each of the coins represents a different gene, each will have a different effect on the height of the person.



Quarter: Q^H will add 2 inches to a person's height
Q^T will subtract 2 inches from a person's height

Dime: D^H will add 1.5 inches to a person's height
D^T will subtract 1.5 inches from a person's height

Nickel: N^H will add 1 inch to a person's height
N^T will subtract 1 inch from a person's height

Penny: P^H will add .5 inches to a person's height
P^T will subtract .5 inches from a person's height

****All people will start at a height of 5 feet 9 inches.**

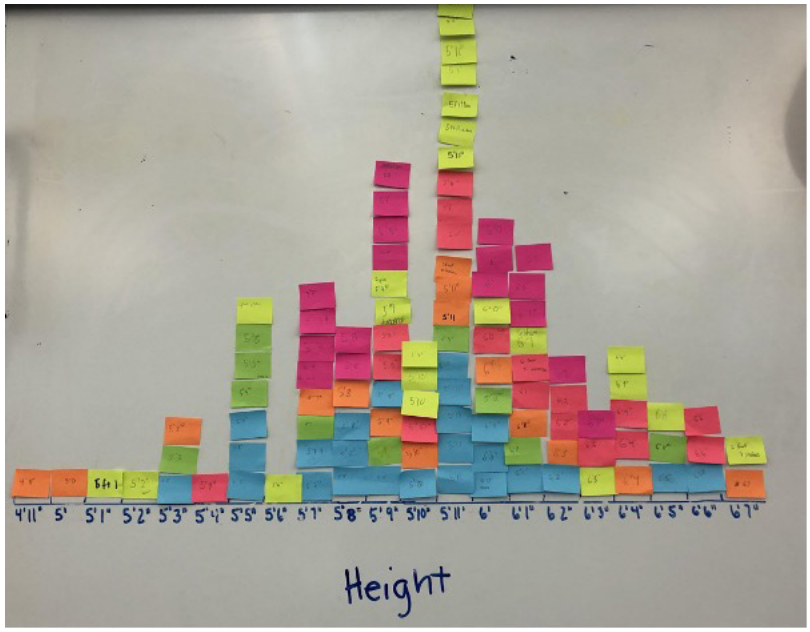
important step because the key piece of the model is the differential effect of each gene on height. Doing the calculation first before flipping the coins helps students understand that they are flipping the coins to see what effect each gene has on height.

Next, each student creates one offspring by flipping the four coins and calculating the height based on a standard starting height. The parents in the sample cross are both heterozygous for each of the four height-determining genes. Because the parents each have both alleles for each gene, the students flip each coin twice to determine which alleles they get from each parent. Once they have their genotype based on their coin flips, they calculate the height of their offspring from a standard starting height. Students then put their final height for their offspring on a sticky note and place it on a class bar graph on the whiteboard (Figure 2). Data should be collected across multiple classes to gather enough data so that clear patterns can be observed.

Explain

On day two, the teacher begins by facilitating a conversation about whether the generated histogram of heights calculated the previous day better represents the variation in height they noticed in the original photo. During this discussion, the students should notice that there are more offspring with heights in the middle and fewer offspring at either extreme, similar to the photo of the human histogram. The teacher should ask the students to think about their calculations from the previous day and how the genotypes of the offspring at either extremes differ from the genotypes of offspring in the center. Students might notice that some heights are not as well represented as others, exposing a weakness of the model. For example, in the class histogram shared in Figure 2, the height 5'11" is over-represented as compared to the height of 5'10" because there are multiple genotypes that result in the 5'11" phenotype in this model. The teacher can support students to

FIGURE 2: Histogram of heights of offspring of the same two parents, both heterozygous for each of four genes influencing height in this model. Each class had a different color sticky note.



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hypothesize about why that is and come to the idea that there are likely many more than four genes that impact human height. This discussion should take about 10 minutes and sets the students up for the next phase of the activity to pick a parent cross they want to explore further.

Elaborate

Next, the students come up with crosses that they think would be interesting to explore, such as two shorter parents or one taller parent and one shorter parent. To generate enough data with each cross, the teacher should provide students with the genotypes for each of the parents they want to cross (see Supplemental Materials for suggested genotypes for student crosses). In this way the "short" parent's genotype will be the same with various crosses, supporting students to see that a "short" parent does not always have short offspring. These genotypes should include some heterozygous genes to show variation among offspring, again demonstrating that "short" people do not necessarily have all "short" genes and can have taller offspring.

For this part of the activity, students are organized in small groups of three to four. Together they decide on crosses they want to explore and what they predict the heights of the offspring will be. Next, students flip their coins to determine the genotypes of four offspring each and calculate their heights. They only need to flip their coins for genes that were heterozygous for each parent. If a parent was homozygous at a particular gene, then students know that the offspring can only get that allele. Students then create individual bar graphs of the heights of the offspring calculated from their crosses (examples of student work are shown in Figure 3).

Once their graphs are complete, students compare their graphs to one another in a gallery walk. The teacher can prompt students' sensemaking by asking students to look for patterns for the different parental phenotypic combinations. How does a cross between two short parents compare with a cross between two tall parents? How are the graphs similar or different to one another? Students should notice that two short parents tend to have relatively short offspring and two tall parents tend to have relatively tall offspring; however, there is a distribution

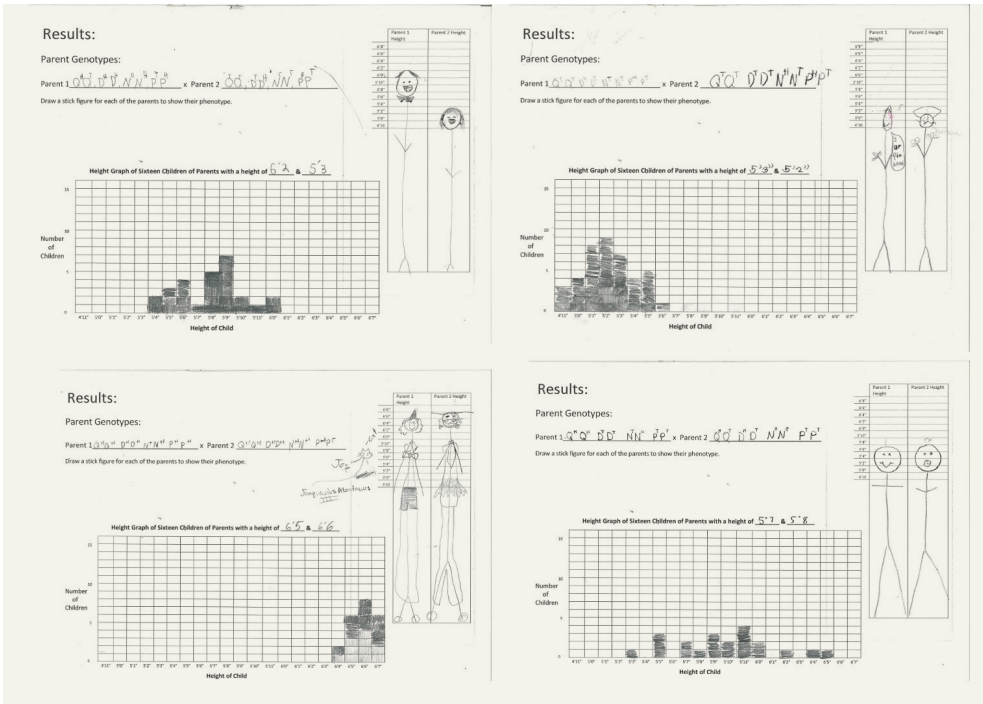
of heights that vary beyond the two heights of the parents. They might also notice that the offspring of two medium height parents create a wider distribution around their parents' heights. Last, they might notice that there is also a wide distribution of heights between the height of the two parents when one parent is tall and the other is short.

Evaluate

By the end of these activities, students should be able to recognize that a polygenic trait displays greater phenotypic variation than what is predicted with a Mendelian model. To assess students' understanding, the teacher can ask students to think about how the height model supports what they notice in reality and how they might need to modify this model to better represent human height variation. Students should notice that the four-gene model, while more representative of human height distribution, still has a discrete number of phenotypes. Therefore, we want students to begin to think about what changes they can make to the model to better represent human height variation. These changes could include a greater number of genes that contribute to height, as well as potential environmental factors such as nutrition, exercise, and overall health. In the polygenic model presented, genotype is entirely predictive of phenotype—the set of alleles inherited from the parents allows us to precisely calculate the offspring's height. In reality, few human traits are fully predicted by genotype, as environmental factors nearly always affect phenotype to varying degrees. Genetics explains about 70%–90% of variability in human height (Silventoinen et al. 2003), with the remainder due to environmental factors or interactions that are not accounted for in this model.

As an exit ticket, teachers can ask students what other traits they think may be polygenic based on their observation of variation of that trait with humans. Some other complex polygenic traits students might notice in their environment are skin color, hair color, and/or weight. By the end of the lesson, students should be able to describe how phenotypic variation is the result of multiple genes and environmental factors.

FIGURE 3: Examples of student work of crosses of their choice.



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Discussion

We presented an activity that science teachers can use to push students' understanding of patterns of inheritance and variation past the single gene focus of Mendelian genetics, which focuses on the science practice of evaluating and using models—here, they evaluate textbook models of inheritance through their own observations of a phenomena and revise the model. Polygenic inheritance is not a content standard within the *NGSS* (NGSS Lead States 2013), but we argue that it is nevertheless important to teach in precollege classrooms. First, it is simply more accurate: Traits controlled by single genes are the exception rather than the rule. Teaching students Mendelian rules of inheritance does not help them to explain the majority of the variation they observe in humans and the rest of the natural world. Second, focusing on Mendelian explanations for biological variation may promote unrealistically deterministic understandings of genes and their effects on phenotypes (Jamieson and Radick 2017), which can lead to a number of negative outcomes for individuals and for society.

Genetic determinism is the belief that genes are the major, if not sole, predictor of human phenotypes, and that environment and epigenetics play no or minimal roles. Applied to human behaviors, conditions, or social groups, genetic determinism is linked to biological essentialism, which is in turn linked to stereotyping and prejudice (Dar-Nimrod and Heine 2011). For example, it has been shown that presenting genetic diseases (in which genes are the major determinant of phenotype) as linked to particular racial groups leads to students being more likely to attribute the U.S. racial achievement gap in education to genetic differences between groups (Donovan 2016). The Mendelian model's historic emphasis in science education thus has fundamental societal implications. While Mendelian inheritance is a necessary foundation for reasoning about inheritance, it is also important to help our students to elaborate on this model to account for the variation they can observe themselves—humans in a spectrum of shapes, sizes, colors, and behaviors.

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SUPPLEMENTAL MATERIALS

Suggested genotypes for student crosses—*https://tinyurl.com/ycy6cmy6*

Polygenic height model—*https://tinyurl.com/supcz77k*

Connecting to the *Next Generation Science Standards*—*https://tinyurl.com/y5tej4vr*

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