

COLOR CODE

Using hair color to make a clear connection between genotype and phenotype

J. José Bonner

Students may wonder why they look the way they do, maybe seeing Dad's nose and Mom's eyes when they glance in the mirror. The answer lies in genetics, the branch of biology that deals with heredity and the variation of inherited traits. However, understanding how an organism's genetic code (i.e., genotype) affects its characteristics (i.e., phenotype) is more than a matter of idle curiosity: It's essential for understanding heredity and the processes of mutation and evolution. Yet, students often have trouble making the connection between genotype and phenotype. This article offers a simple way to illustrate that connection—through a discussion of human hair color.

Common Misconceptions

In creating a new generation, parents pass DNA to their offspring. The DNA carries genes that hold the information for the proteins and RNA molecules that will determine the offspring's traits. We can't see the DNA, RNA, and protein molecules, but we can see some of the traits they produce. It is challenging to work backward, inferring invisible mechanisms from a handful of visible traits. Yet this is precisely what 19th-century Austrian scientist Gregor Mendel did.

Mendel, the founder of genetics, studied generations of pea plants. Peas are self-fertilizing, and Mendel's pea population was largely separate from other peas. Self-pollination leads to a loss of genetic diversity, leaving Mendel with a number of traits for which only two variations were left (e.g., green pea pods versus yellow pea pods). The variations were determined by *alleles*, which are different genetic variations of a particular gene (e.g., *y* [for the recessive yellow] and *Y* [for the dominant green]).

It is common to introduce genetics using Mendel's examples, but this can lead to misconceptions. Consider, for example, a simple genetic cross between two homozygotes (identical alleles): $YY \times yy = Yy$. The offspring, the F_1 generation, are all heterozygotes (different alleles). Crossing the F_1 s among themselves produces the F_2 s: $Yy \times Yy = YY, Yy, \text{ and } yy$, in a 1:2:1 ratio (YY, Yy, Yy, yy) of genotypes but a 3:1 ratio of phenotypes, 3 green peas to 1 yellow.

A similar series of genetic crosses cannot be performed with humans (as it would require sibling marriages), but the *pattern* of inheritance fits many human traits. Yet students sometimes generalize from particular examples and develop misconceptions. A particularly durable one is that all traits have two alleles: one dominant, the other recessive. This belief leads students to infer that alleles are stable and can't change, which, in turn, leads to thinking that genetics has no role in evolution—a conclusion that may have been shared by Mendel himself (Callender 1988). Students with this view imagine that evolutionary mutations are some kind of magical transformation of individuals from one species to another, entirely unrelated to changes in DNA sequence.

We can help students avoid these misconceptions by clarifying the definition of *mutation* and by expanding students' understanding of alleles and the most common mechanism of dominance.



From peas to hair

Peas may be a terrific organism for the study of genetics, but students naturally find a discussion of human genetics more relevant to their lives. But human genetics is messy and complicated. Yet, there is a way to take advantage of our tremendous genetic diversity and simultaneously address the genotype and phenotype connection: hair color.

Have your students look around the classroom. Does everyone look the same? Does everyone have the same hair color? There are many shades of brown hair, from light brown (blonde) to medium brown to dark brown to a brown that is so dark it looks black (Figure 1). Why is this?

People aren't peas or fruit flies, so students can't just "set up the crosses"—mix the parents together and collect the F_1 s and eventually the F_2 s. But students *can* look at their own families. Ask students to create pedigree charts of their families, showing hair color (e.g., Figure 2, p. 66; see "On the web"). Many genes influence hair color, but the *Skin, Hair, and Eye Pigmentation* gene (*SHEP1*; see "On the web") shows the greatest allelic diversity and can, in principle, produce the entire story told here. To simplify, I recommend referring to a hypothetical gene called *brown*.

As students study their pedigrees and those of their classmates, ask them to think of possible explanations for the results. It may be helpful to show a sample pedigree chart (Figure 2) to give the discussion a common focus. Guide their discussion as needed. In general, it should become evident that darker-hair parents sometimes have lighter-hair chil-

dren, but lighter-hair parents don't have darker-hair children. Darker appears to be dominant to lighter. Why?

Again, guide the discussion. Point out that the visible trait is pigment; it's not a gene itself or an allele of that gene. It is necessary to talk about what the gene *does*. In an introductory high school biology class, students might describe this as "the gene required for the production of brown pigment"; alleles that cause more pigment to be produced would be expected to be dominant to alleles that cause less pigment to be produced. For an advanced biology course, or in a course with a previous unit on enzymes and gene expression, students should use more detailed phrasing: "These alleles affect the activity level of the enzyme required to produce the pigment." Regardless of the phrasing, the bottom line is the same: Darker hair is dominant to lighter hair because the enzyme makes more of the pigment.

Human hair color is determined by too many alleles to use only two symbols (e.g., *B* and *b*). Instead, we must refer to specific alleles, such as *brown^{ebony}*, *brown^{oak}*, and *brown^{honey}* (Figure 1). The general rule that darker hair is dominant to lighter hair indicates that dark brown is dominant to medium brown and medium brown is dominant to light brown. So is medium-brown hair dominant or recessive? It depends on the allele with which it is paired. An allele itself cannot be either



Keywords: Genotype/Phenotype
at www.scilinks.org
Enter code: TST121102

FIGURE 1

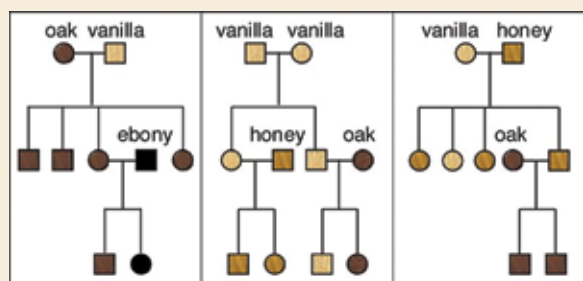
Many alleles of the brown hair color–determining genes.



FIGURE 2

Family pedigrees of hair color.

Students can learn about pedigree charts by making charts showing generations of their families. Treating these colors as phenotypes from different alleles of a single gene, students can infer that ebony is dominant to oak, honey, and vanilla; oak is dominant to honey and vanilla; and honey is dominant to vanilla. Intermediate colors are recessive in some heterozygous combinations but dominant in others.



dominant or recessive; it is more accurate to speak of a particular allele being dominant or recessive in a particular combination.

I suspect that coming face-to-face with alleles like “medium brown” that are dominant to some alleles (lighter colors) but recessive to other alleles (darker colors) encourages students to ponder why it works that way. This moves them from memorizing “received wisdom” to figuring out the basis of dominance, which builds the connection between genotype and phenotype.

From hair pigment to morphology

When students reach the unit on evolution, some ask questions about body shape (i.e., morphology). Like hair color, morphology is controlled genetically, but the mechanisms are more complicated. In general, the critical events for

What causes mutations?

DNA damage, followed by imperfect repair, causes most mutations. The DNA-repair enzymes are more prone to making errors than the DNA-replication enzymes. Radiation (e.g., x-rays, radioactivity) or chemicals (e.g., pollutants, plant toxins, oxygen radicals) can cause DNA damage. None of these DNA-damaging agents can choose where to damage DNA. As a result, mutations occur in a statistically random fashion. It is impossible for individuals of any species to avoid occasional DNA damage and subsequent mutation. Therefore, there is always a measurable background rate of mutation, which is the ultimate origin of new alleles.

morphological features occur in small tissue primordia during embryogenesis in animals and in the meristems of plants. In recent years, an entire subdiscipline has developed around the study of developmental evolutionary biology, *evo-devo* (Carroll 2005) or *devo-evo* (Raff 1996).

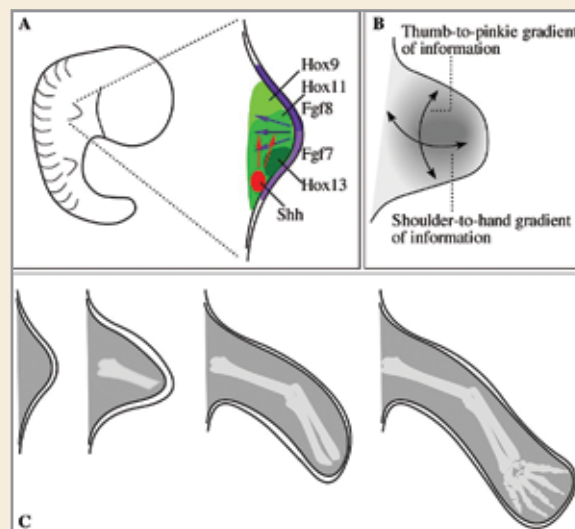
To a large extent, morphological events in embryogenesis depend upon cell–cell contact and short-range diffusible molecules. For example, during vertebrate limb development (Tickle 2006), limb buds form on the flanks of embryos shortly after the cell movements of neurulation (Figure 3). Within each limb bud, cells communicate to activate various developmental control genes that determine how individual cells differentiate. Expression of those genes depends on the cells’ positions in the embryo.

Students asking about evolutionary changes in morphology should be told that the “rules” are the same as with hair color: The genes are passed from parents to offspring and are subject to occasional mutations. The difference is that these

FIGURE 3

Limb development.

- Vertebrate embryos form a limb bud on the embryo’s flank. Within this limb bud, different cells activate different genes depending upon local cell–cell communication. The result is that cells differentiate according to their positions in the limb bud.
- The complex patterns of gene expression (A) enable the limb bud to establish “gradients of information.” Each cell acquires information on its relative location in the limb bud and develops accordingly.
- As the limb grows outward from the side of the embryo, the information established by differential gene expression leads each cell to develop into the appropriate parts of the limb.



Different types of alleles.

A gene is a stretch of DNA that provides the code for the sequence of amino acids in a protein, such as the enzyme required to produce brown hair pigment. DNA sequence differences between alleles can potentially occur anywhere in a gene. Some, like those that determine lactose tolerance, are outside of the gene and affect the gene's expression (Tishkoff et al. 2007) without altering the amino acid sequence of the protein. Other DNA sequence differences can be inside the gene and cause amino acid substitutions.

Mutations that affect gene regulation can produce more total enzyme or less total enzyme, which for hair color, would produce darker or lighter hair, respectively. Mutations that alter the amino acid sequence of the protein can affect protein folding or the enzyme's active site (e.g., Saslowsky, Dana, and Winkel-Shirley 2000; Dana, Bevan, and Winkel 2006). Some of these kinds of alleles cause the enzyme to be nonfunctional (blonde hair). Some, called *partial loss-of-function alleles*, cause the enzyme to have less activity than normal (light brown, medium brown, dark brown, depending on the enzyme's activity). Geneticists refer to this variation from no-, to partial-, to higher-than-normal function as an *allelic series* (e.g., McClintock 1944).

Generally, alleles with more activity are dominant to alleles with less activity (e.g., hair color). Because there is so much variation in so many genes, geneticists rarely use the classical terms of *dominance*, *codominance*, *partial dominance*, or *multiple alleles*. Nearly all genes have multiple alleles, and their relationships fall along a continuum that includes complete dominance, partial dominance, and codominance.

particular genes control embryonic development rather than pigment. We can also say that

- ◆ we know many (but not all) of the genes involved in creating morphological features,
- ◆ mutations can cause slight changes in these genes' expression patterns, and
- ◆ slight changes in embryo development can cause changes in the final organism's morphology.

These points can be illustrated with limb development. Mutations that alter the anterior-to-posterior pattern can cause more (e.g., humans) or fewer (e.g., birds, horses) digits to form. Mutations that recruit more or fewer cells into the limb bud, or allow more or fewer cell divisions during growth, can affect the overall size of the limb (e.g., mice vs. elephants). Different animals share many of the same genes; it's where and when those genes are expressed that makes animals different (Carroll 2005).

Conclusion

I find it effective to introduce genetics with hair color. For teachers who begin with Mendel and his pea plants, it helps to move quickly to hair color, before students form the conception that all genes have only two alleles. Although this can be a more complex discussion, my students tell me it actually simplifies genetics for them; it helps them make sense of dominance, and they can see how high-activity alleles should be dominant to low-activity alleles. Students can see the effects in their families, their friends, litters of puppies, and, sometimes, even in plants. Knowing that it is the norm for there to be multiple alleles, and that new alleles appear every generation by mutation, they can also build the connection between the genetic diversity they see around them and the genetic diversity that is so important in natural selection. ■

J. José Bonner (bonner@indiana.edu) is a professor of biology at Indiana University in Bloomington.

On the web

Indiana University family pedigree charts: www.indiana.edu/~oso/lessons/Genetics/MyFamily.html

Mendelian inheritance in skin, hair, and eye pigmentation: www.ncbi.nlm.nih.gov/omim/227220

References

- Callender, L.A. 1988. Gregor Mendel: An opponent of descent with modification. *History of Science* 26: 41–57.
- Carroll, S.B. 2005. *Endless forms most beautiful: The new science of evo devo and the making of the animal kingdom*. New York: Norton.
- Dana, C.D., D.R. Bevan, and B.S. Winkel. 2006. Molecular modeling of the effects of mutant alleles on chalcone synthase protein structure. *Journal of Molecular Modeling* 12 (6): 905–914.
- McClintock, B. 1944. The relation of homozygous deficiencies to mutations and allelic series in maize. *Genetics* 29 (5): 478–502.
- Raff, R.A. 1996. *The shape of life: Genes, development, and the evolution of animal form*. Chicago: The University of Chicago Press.
- Saslowsky, D.E., C.D. Dana, and B. Winkel-Shirley. 2000. An allelic series for the chalcone synthase locus in Arabidopsis. *Gene* 255 (2): 127–138.
- Tickle, C. 2006. Making digit patterns in the vertebrate limb. *Nature Reviews Molecular Cell Biology* 7 (1): 45–53.
- Tishkoff, S.A., F.A. Reed, A. Ranciaro, B.F. Voight, C.C. Babbitt, J.S. Silverman, K. Powell, H.M. Mortensen, J.B. Hirbo, M. Osman, M. Ibrahim, S.A. Omar, G. Lema, T.B. Nyambo, J. Ghoris, S. Bumpstead, J.K. Pritchard, G.A. Wray, and P. Deloukas. 2007. Convergent adaptation of human lactase persistence in Africa and Europe. *Nature Genetics* 39 (1): 31–40.