places. Environmental variation arises when external factors influence how much protein is made from particular genes, or how the proteins work. When individuals experience different environments, they make different amounts of proteins or show differences in protein function. Genotype-by-environment interaction is the result of differences among individuals that are encoded into their DNA and that make them differ in their sensitivity to environmental influences. Different individuals thus react differently to a changing environment.

We will illustrate these generalizations with examples.

Genetic Variation

Humans show considerable variation in their perception of taste. One way to demonstrate this variation is to offer people small quantities of the chemical phenylthiocarbamide (PTC). Some individuals find it intensely bitter and unpleasant; others can scarcely taste it at all (Wooding 2006).

An experience of taste begins at a taste receptor protein in the surface membrane of a taste receptor cell in a taste bud on the tongue (Yarmolinsky et al. 2009). Taste receptor proteins have diverse shapes and chemical properties. Each kind of taste receptor protein binds with a subset of the chemicals in food, corresponding to sweet, sour, salty, umami (savory), and bitter flavors **(Figure 5.6a)**. When the right chemical binds to the receptors on its membrane, a taste receptor cell sends nerve impulses to the brain. The brain integrates messages from taste receptors across the tongue and generates a conscious sensation of flavor.

The receptor proteins responsible for bitter flavors are the type 2 taste receptors (TAS2Rs). The one that binds PTC is TAS2R38, encoded by a gene on chromosome 7 (see Figure 5.5). The coding region of the gene specifies a sequence of 333 amino acids. Un-kyung Kim and colleagues (2003) examined the TAS2R38 genes of a number of individuals. They found three places where different versions of the gene encode different amino acids. The 49th codon in the gene may specify either proline or alanine, the 262nd codon may specify either alanine or valine, and the 296th codon either valine or isoleucine. Different versions of a gene are called **alleles**. The most common TAS2R38 alleles, named for the amino acids they specify at the variable sites, are *AVI* and *PAV*.

Everyone has two chromosome 7s: one inherited from their mother, the other from their father. The two chromosomes may carry the same allele of the TAS2R38 gene, or they may carry different alleles. The combination of alleles an individual carries is called his or her **genotype**. Considering just alleles *AVI* and *PAV*, the three possible genotypes are *AVI/AVI*, *AVI/PAV*, and *PAV/PAV*.

The suite of traits an individual exhibits is called his or her **phenotype**. The aspect of phenotype we are interested in here is sense of taste. To show that TAS2R38 genotype influences sensory phenotype, Richard Newcomb and colleagues (2012) asked people with different genotypes to taste a standard PTC solution and rate the intensity of the flavor. Figure 5.6b presents the results. There is variation among the subjects plotted on each graph, showing that factors other than TAS2R38 genotype influence an individual's sensitivity to PTC. But TAS2R38 genotype clearly matters (see also Bufe et al. 2005). Individuals with genotype *PAV/PAV* are most sensitive, those with *AVI/AVI* are least sensitive, and those with *AVI/PAV* fall in between. Switching just 3 of the 333 amino acids in TAS2R38 changes the protein's shape and/or chemical properties enough to alter either the protein's ability to bind PTC (Figure 5.6c), its ability to trigger a nerve impulse in response to binding, or both (see Biarnés et al. 2010).

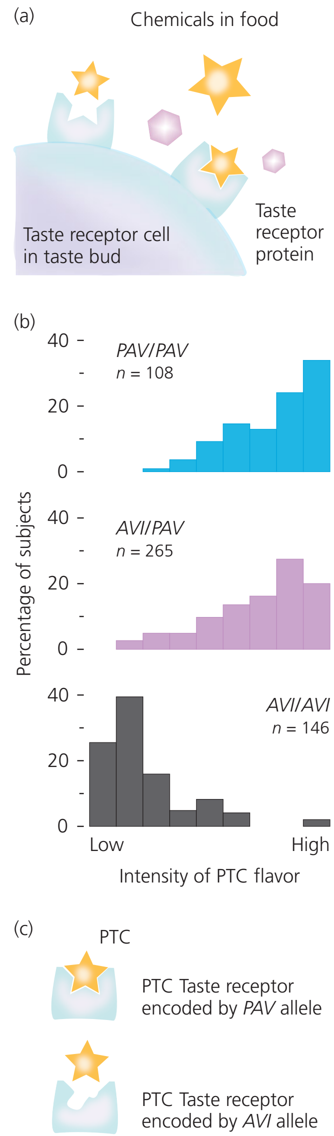

Figure 5.6 Genetic variation for bitter taste perception (a) Taste receptors bind chemicals in food. (b) PTC tastes different to people with different versions of TAS2R38, perhaps because (c) the version encoded by allele *PAV* binds PTC more strongly. Graphs from Newcomb et al. (2012).

PTC does not naturally occur in food. The ability to taste it might seem unimportant. However, different versions of TAS2R38 also respond differently to other bitter flavors (Sandell and Breslin 2006). Among these flavors are chemicals found in broccoli and its relatives, including mustard greens, turnips, and horseradish. People with genotype *PAV/PAV* rate these vegetables as more bitter than do people with genotype *AVI/AVI*. There is some evidence that *AVI/AVI* individuals eat more vegetables than individuals with other genotypes (Tepper 2008; Duffy et al. 2010; but see Gorovic et al. 2011).

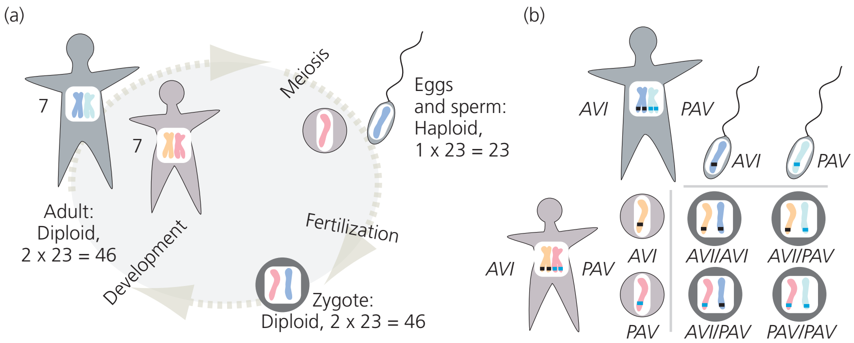

Figure 5.7 The human life cycle (a) We spend most of our lives in a diploid phase, carrying a complete set of chromosomes received via the egg and a complete set received via the sperm. Each gamete we make receives one member of each chromosome pair. (b) We can thus use a Punnett square to calculate the odds that a zygote will have a particular genotype.

Genetic variation consists of differences among individuals that are encoded in the genome and transmitted from parents to offspring.

To the extent that differences among individuals in the ability to taste bitter flavors are due to differences in genotype, they are transmitted from parents to offspring. **Figure 5.7a** shows the human life cycle. The figure does the bookkeeping for chromosome counts, highlighting chromosome 7 as an example. For most of our life cycle, our cells carry two chromosome 7s. When we make gametes, each egg or sperm receives a copy, selected at random, of one chromosome 7 or the other. When egg and sperm unite, they yield a zygote that once again has two chromosome 7s. If the gametes were produced by parents who both carried allele *AVI* on one chromosome 7 and allele *PAV* on the other, then all three genotypes are possible among the offspring (Figure 5.7b). In a large sample of offspring, we expect the genotypes to occur in a 1:2:1 ratio.

Given that the *PAV* allele tends to make people who carry it dislike broccoli and related vegetables, and that eating vegetables is good for one's health, we might expect that individuals with allele *PAV* would be less likely to survive and reproduce, and that the allele would disappear. Consider, however, that vegetables contain natural toxins—an adaptive trait that discourages animals from eating them. Consuming a healthy diet thus requires balancing one's intake of nutritious plants against one's ingestion of the toxins they contain, some of which taste bitter. That alleles *PAV* and *AVI* are both common in human populations all over the world suggests that historically the best genotype for survival and reproduction has been *AVI/PAV* (Wooding et al. 2004).

Stephen Wooding (2005, 2006) speculates that although the version of the PTC receptor encoded by allele *AVI* is less sensitive to the toxins in broccoli and its kin, it is perhaps more sensitive to toxins found in other plants. If this is so, then individuals with genotype *AVI/PAV* would be able to detect a wider variety of toxins in their food than individuals with either genotype *AVI/AVI* or *PAV/PAV*. Such individuals might have an advantage in seeking a nutritious diet that avoids an overdose of any particular plant toxin. Note that this is a hypothesis, not an established fact. It will have to be tested with careful experiments.