5

EXTENSIONS AND MODIFICATIONS OF BASIC PRINCIPLES

Birth weight of humans is influenced by genes that exhibit genomic imprinting, an exception to Mendel's rules of heredity. (PhotoDisc.)

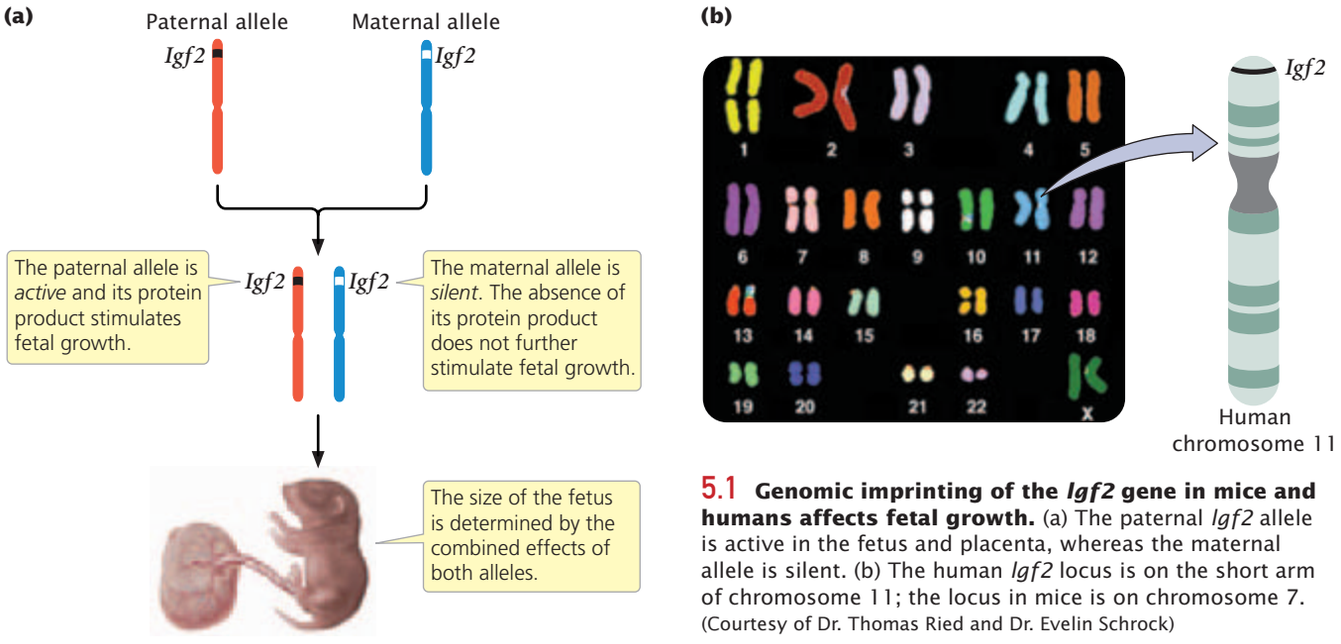
Birth Weight and Genomic Imprinting

When a new baby arrives, one of the first questions that people ask is, "How much does it weigh?" This preoccupation with birth weight is not surprising: birth weight is strongly associated with a baby's health and survival in the first few months of life. And, the effects of birth weight continue long after infancy; research shows that birth weight correlates with adult body weight, blood pressure, cardiovascular disease, diabetes, and a number of other adult conditions.

One of the genes that affects birth weight in mice and humans is *Igf2,* which codes for a protein called insulin-like growth factor II. This gene, along with a handful of others found in mammals, exhibits a peculiar mode of expression called genomic imprinting. A foundational principle of Mendelian inheritance is that the parental origin of an autosomal gene does not matter—reciprocal crosses give identical results. However, *Igf2* and other genomically imprinted genes clearly violate this fundamental principle of genetics. Was Mendel wrong?

The *Igf2* gene is located on human chromosome 11, and offspring inherit one *Igf2* allele from their mother and one from their father (FIGURE 5.1). The paternal copy is actively expressed in the fetus and placenta, but the maternal copy is completely silent. In a way that is not completely understood, the paternal *Igf2* allele (but not the maternal allele) promotes placental and fetal growth; when the paternal copy of *Igf2* is deleted in mice, a small placenta and low-birth-weight offspring result.

Why does genomic imprinting occur? One possible answer is the genetic-conflict hypothesis, which suggests that there is a conflict between maternal and paternal alleles for



5.1 Genomic imprinting of the *Igf2* gene in mice and humans affects fetal growth. (a) The paternal *Igf2* allele is active in the fetus and placenta, whereas the maternal allele is silent. (b) The human *Igf2* locus is on the short arm of chromosome 11; the locus in mice is on chromosome 7. (Courtesy of Dr. Thomas Ried and Dr. Evelin Schrock)

genes (such as *Igf2*) that affect fetal growth. From an evolutionary standpoint, paternal alleles that maximize the size of the offspring are favored, because birth weight is strongly associated with infant mortality and adult health. Thus, it is to the advantage of the male parent to pass on alleles that promote maximum fetal growth of their offspring. In contrast, maternal alleles that cause more-limited fetal growth are favored, because committing too many of the female parent's nutrients to any one fetus may limit her ability to reproduce in the future and because giving birth to very large babies is difficult and risky for the mother. This hypothesis predicts that genomic imprinting will evolve: paternal copies of genes that affect fetal growth should be maximally expressed, whereas maternal copies of the same genes should be less actively expressed or even silent. Indeed, *Igf2* follows this pattern: the paternal allele is active and promotes growth; the maternal allele is silent and does not contribute to growth. Recent findings demonstrate that the paternal copy of *Igf2* promotes fetal growth by directing more maternal nutrients to the fetus through the placenta.

As illustrated by *Igf2*, **genomic imprinting** is the differential expression of a gene depending on whether it is inherited from the mother or the father. Like a number of other genetic phenomena, genomic imprinting does not adhere to Mendel's principles of heredity. This lack of adherence doesn't mean that Mendel was wrong; rather, it means that Mendel's principles are not, by themselves, sufficient to explain the inheritance of all genetic characteristics. Our modern understanding of genetics has been greatly enriched by the discovery of a number of modifications and extensions of Mendel's basic principles, which are the focus of this chapter.

www.whfreeman.com/pierce Additional information about genomic imprinting

Dominance Revisited

One of Mendel's important contributions to the study of heredity is the concept of *dominance*—the idea that an individual organism possesses two different alleles for a characteristic, but the trait encoded by only one of the alleles is observed in the phenotype. With dominance, the heterozygote possesses the same phenotype as one of the homozygotes. When biologists began to apply Mendel's principles to organisms other than peas, it quickly became apparent that many characteristics do not exhibit this type of dominance. Indeed, Mendel himself was aware that dominance is not universal, because he observed that a pea plant heterozygous for long and short flowering times had a flowering time that was intermediate between those of