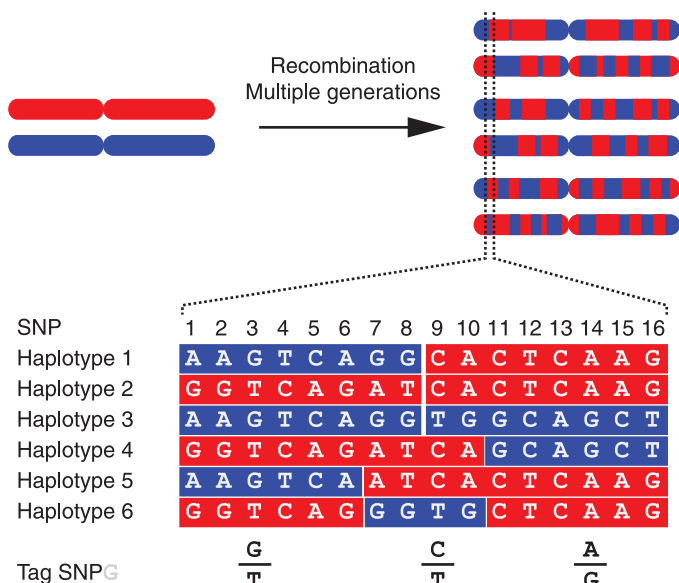


**FIGURE 82-3** Chromosome 7 is shown with the density of single-nucleotide polymorphisms (SNPs) and genes above. A 200-kb region in 7q31.2 containing the *CFTR* gene is shown below. The *CFTR* gene contains 27 exons. More than 1900 mutations in this gene have been found in patients with cystic fibrosis. A 20-kb region encompassing exons 4–9 is shown further amplified to illustrate the SNPs in this region.



**FIGURE 82-4** The origin of haplotypes is due to repeated recombination events occurring in multiple generations. Over time, this leads to distinct haplotypes. These haplotype blocks can often be characterized by genotyping selected Tag single-nucleotide polymorphisms (SNPs), an approach that facilitates performing genome-wide association studies (GWAS).

because the complement of mRNAs transcribed by the cellular genome is called the *transcriptome*.

Most studies of gene expression have focused on the regulatory DNA elements that control transcription. However, it should be emphasized that gene expression requires a series of steps, including mRNA processing, protein translation, and posttranslational modifications, all of which are actively regulated (Fig. 82-2).

**Epigenetic Regulation of Gene Expression** *Epigenetics* describes mechanisms and phenotypic changes that are not a result of variation in the primary DNA nucleotide sequence, but are caused by secondary modifications of DNA or histones. These modifications include heritable changes such as X-inactivation and imprinting, but they can also result from dynamic posttranslational protein modifications in response to environmental influences such as diet, age, or drugs. The epigenetic modifications result in altered expression of individual genes or chromosomal loci encompassing multiple genes. The term *epigenome* describes the constellation of covalent modifications of DNA and histones that impact chromatin structure, as well as non-coding transcripts that modulate the transcriptional activity of DNA. Although the primary DNA sequence is usually identical in all cells of an organism, tissue-specific changes in the epigenome contribute to determining the transcriptional signature of a cell (transcriptome) and hence the protein expression profile (proteome).

Mechanistically, DNA and histone modifications can result in the activation or silencing of gene expression (Fig. 82-7). DNA methylation involves the addition of a methyl group to cytosine residues. This is