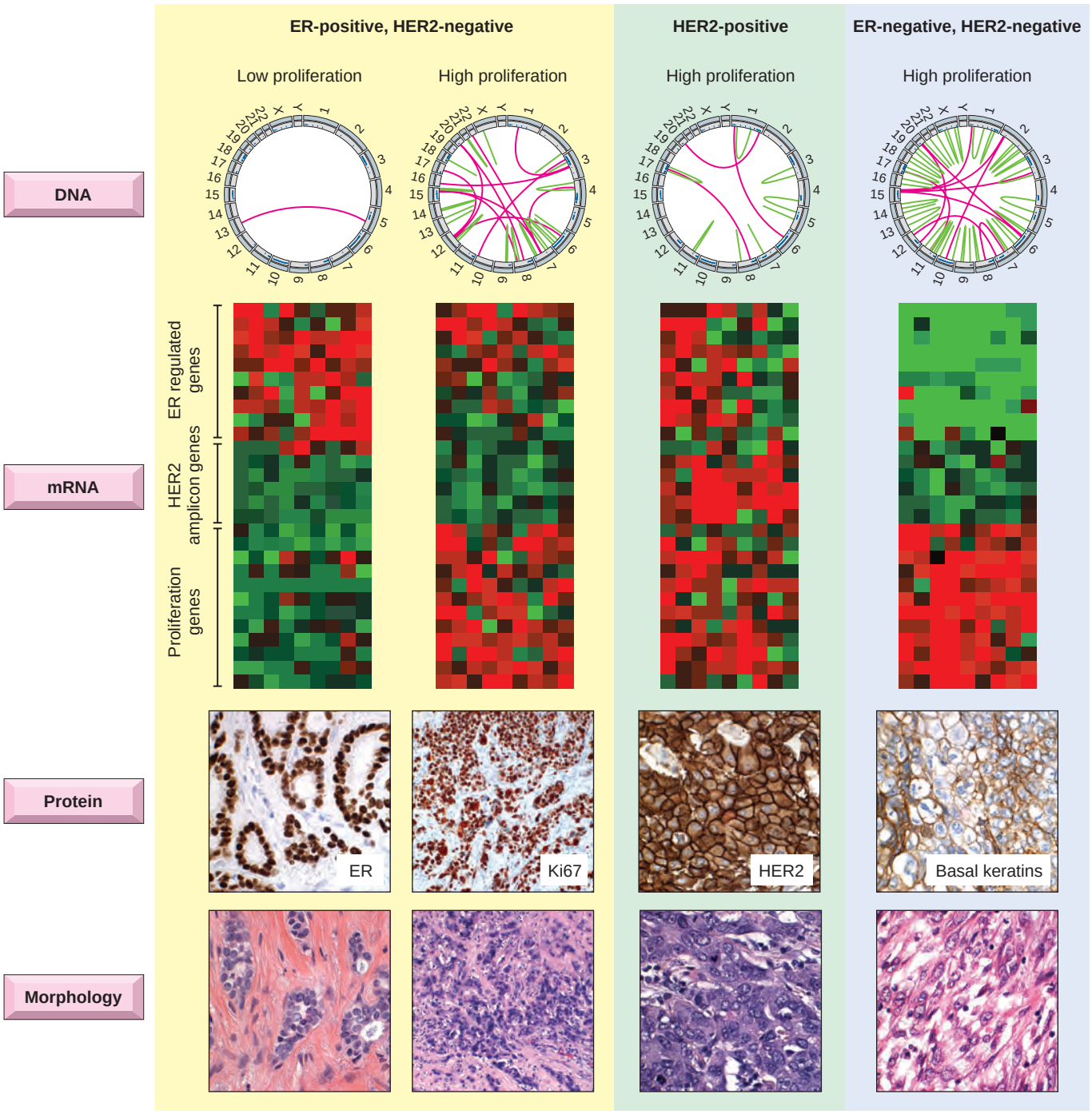

Figure 23-20 Major molecular subtypes of invasive breast cancer. Three major subtypes of breast cancer are distinguished by characteristic changes in genomic DNA, mRNA, protein, and morphology. Genomic abnormalities are shown in circos plots (Chapter 7), which present a snapshot of all of the genomic abnormalities within a particular tumor; these abnormalities are mapped onto the chromosomes, which are displayed at the periphery of a circle. Green loops show intrachromosomal rearrangements, while red loops show interchromosomal rearrangements. Gene expression profiling measures relative levels of mRNA expression. Red indicates a relative increase, green a relative decrease, and black no change in levels. Genes are arrayed from top to bottom and tumors from left to right. Immunohistochemical studies detect proteins using specific antibodies visualized by a brown chromogen. *ER-positive HER2-negative tumors* are diverse, ranging from well-differentiated cancers with low proliferative rates and few chromosomal changes to poorly differentiated cancers with high proliferative rates and large numbers of chromosomal rearrangements. All of these cancers express ER (an estrogen-dependent transcription factor). Proliferation is estimated by counting mitoses or by staining for cell cycle-specific proteins such as Ki-67. *HER2-positive cancers* may be ER-positive or ER-negative, but when ER is present, levels are typically low. HER2 positivity can be detected as an increase in HER2 gene copy number, an increase in HER2 mRNA, or an increase in HER2 protein, as shown here. *ER-negative, HER2-negative ("triple negative" or "basal-like") carcinomas* are characterized by genomic instability (denoted by numerous chromosomal changes), a high proliferative rate, and expression of many proteins typical of myoepithelial cells (e.g., basal keratins).