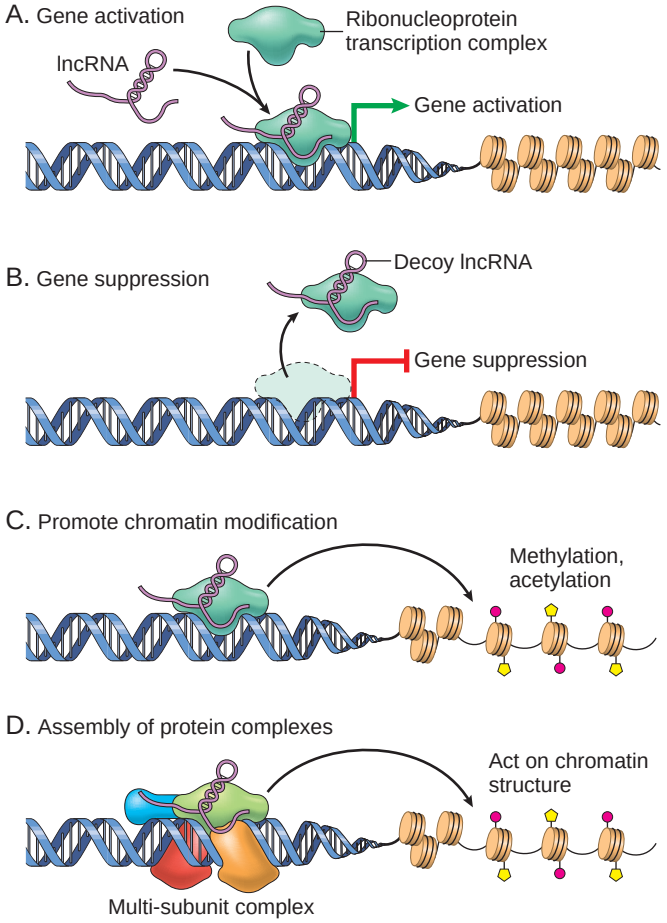

Figure 1-4 Roles of long noncoding RNAs. **A,** Long non-coding RNAs (lncRNAs) can facilitate transcription factor binding and thus promote gene activation. **B,** Conversely, lncRNAs can preemptively bind transcription factors and thus prevent gene transcription. **C,** Histone and DNA modification by acetylases or methylases (or deacetylases and demethylases) may be directed by the binding of lncRNAs. **D,** In other instances, lncRNAs may act as scaffolding to stabilize secondary or tertiary structures and/or multi-subunit complexes that influence general chromatin architecture or gene activity. (Adapted from Wang KC, Chang HY: Molecular mechanisms of long noncoding RNAs. Mol Cell 43:904, 2011.)

Cellular Housekeeping

The viability and normal activity of cells depend on a variety of fundamental housekeeping functions that all differentiated cells must perform. These functions include *protection from the environment, nutrient acquisition, communication, movement, renewal of senescent molecules, molecular catabolism*, and *energy generation*.

Many normal housekeeping functions are compartmentalized within membrane-bound intracellular organelles (Fig. 1-5). By isolating certain cellular functions within distinct compartments, functionally important, potentially injurious degradative enzymes or reactive metabolites can be concentrated or stored at high concentrations in specific organelles without risking damage to other cellular constituents. Moreover, compartmentalization allows the creation of unique intracellular environments (e.g., low pH or high calcium) that may then selectively regulate the function of enzymes or metabolic pathways.

New proteins destined for the plasma membrane or points beyond are synthesized in the *rough endoplasmic reticulum (RER)* and physically assembled in the *Golgi apparatus*; proteins intended for the cytosol are synthesized on free ribosomes. *Smooth endoplasmic reticulum (SER)* may be abundant in certain cell types such as gonads and liver where it is used for steroid hormone and lipoprotein synthesis, as well as for the modification of hydrophobic compounds (for example, drugs) into water-soluble molecules for export.

Proteins and organelles must also be broken down if they become damaged, as must proteins and other molecules that are taken up into the cell by endocytosis. Catabolism of these constituents takes place at three different sites and serves different functions. *Lysosomes* are intracellular organelles that contain degradative enzymes that permit the digestion of a wide-range of macromolecules, including proteins, polysaccharides, lipids, and nucleic acids. *Proteasomes,* on the other hand are a specialized type of "grinder" that selectively chews up denatured proteins, releasing peptides. In some cases the peptides so generated can be presented in the context of class I major histocompatibility molecules (Chapter 6). In other cases signaling molecules trigger the proteasomal degradation of negative regulatory proteins, leading to activation of pathways that alter transcription. These are described in more detail later in the chapter. *Peroxisomes* play a specialized role in the breakdown of fatty acids, generating hydrogen peroxide in this process.

The contents and position of cellular organelles are also subject to regulation. *Endosomal vesicles* shuttle internalized material to the appropriate intracellular sites or direct newly synthesized materials to the cell surface or targeted organelle. Cell movement—both organelles and proteins *within* the cell, as well as movement of the cell in its environment—is accomplished through the *cytoskeleton*. These structural proteins also maintain basic cellular shape and intracellular organization, requisites for maintaining *cell polarity*. This is particularly critical in epithelium, in which the top of the cell (*apical*) and the bottom and side of the cell (*basolateral*) are often exposed to different environments and have distinct functions. Most of the ATP that powers cells is made through oxidative phosphorylation in the *mitochondria.* However, mitochondria also serve as an important source of metabolic intermediates that are needed for anabolic metabolism; they are sites of synthesis of certain macromolecules (e.g., heme), and contain important sensors of cell damage that can initiate and regulate the process of programmed cell death.

Cell growth and maintenance require a constant supply of both energy and the building blocks that are needed for synthesis of macromolecules. In growing and dividing cells, all of these organelles have to be replicated (*organellar biogenesis*) and correctly apportioned in daughter cells following mitosis. Moreover, because the macromolecules and organelles have finite lifespans (mitochondria, for example, last only about 10 days), mechanisms must also exist that allow for the recognition and degradation of "worn out" cellular components.

With this as a primer, we now move on to discuss cellular components and their function in greater detail.

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