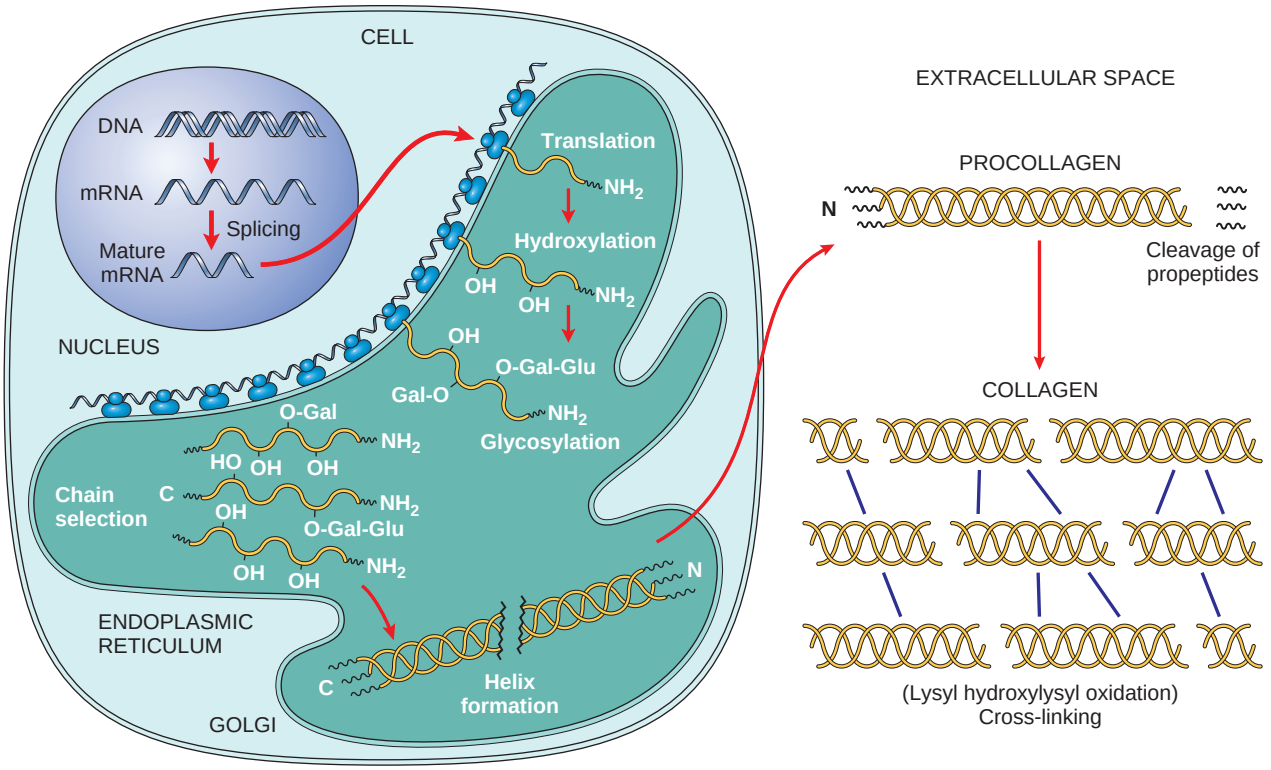

Figure 1-15 Collagen biosynthetic pathway. The α-chains that make up a fibrillar collagen molecule are synthesized as precursor pro-α-chains, with large globular polypeptide regions flanking the central triple-helical domain. After proline and lysine hydroxylation and lysine glycosylation within the endoplasmic reticulum, three procollagen chains align to form a triple helix. For all the fibrillar collagens, the C-propeptide is completely removed by endoproteinase activity after secretion, and the resulting triple-helical rod-like domains polymerize in a staggered fashion into fibrillar arrays. After secretion, the collagen achieves lateral stability though collagen cross-linking involving lysyl oxidase and the previously hydroxylated residues. Defects in primary sequence, procollagen endopeptidase processing, hydroxylation, or cross-linking can all lead to weak connective tissues. The specific tissues affected (e.g., blood vessels, skin, bone, ligaments) by such disorders is based on the type of collagen that predominates in that tissue.

- *Water-hydrated gels* such as proteoglycans and hyaluronan that permit compressive resistance and lubrication
- *Adhesive glycoproteins* that connect ECM elements to one another and to cells

Collagens. Collagens are typically composed of three separate polypeptide chains braided into a ropelike triple helix (Fig. 1-15). About 30 collagen types have been identified, some of which are unique to specific cells and tissues.

- Some collagen types (e.g., types I, II, III, and V collagens) form linear fibrils stabilized by interchain hydrogen bonding; such *fibrillar collagens* form a major proportion of the connective tissue in structures such as bone, tendon, cartilage, blood vessels, and skin, as well as in healing wounds and particularly scars. The tensile strength of the fibrillar collagens derives from lateral cross-linking of the triple helices, formed by covalent bonds facilitated by the activity of lysyl oxidase. Since this process is dependent on vitamin C, children with ascorbate deficiency have skeletal deformities, and people of any age with vitamin C deficiency bleed easily because of weak vascular wall basement membrane, and heal poorly. Genetic defects in collagens cause diseases such as *osteogenesis imperfecta* and certain forms of *Ehlers-Danlos syndrome* (Chapter 5).
- *Non-fibrillar* collagens may contribute to the structures of planar basement membranes (type IV collagen); help regulate collagen fibril diameters or collagen-collagen interactions via so-called **f**ibril-**a**ssociated **c**ollagen with **i**nterrupted **t**riple helices (FACITs, such as type IX collagen in cartilage); or provide anchoring fibrils to basement membrane beneath stratified squamous epithelium (type VII collagen).

Elastin. The ability of tissues to recoil and recover their shape after physical deformation is conferred by elastin (Fig. 1-14). This is especially important in cardiac valves and for large blood vessels (that must accommodate recurrent pulsatile flow), as well as in the uterus, skin, and ligaments. Morphologically, elastic fibers consist of a central core of elastin with an associated meshlike network composed of fibrillin. The latter relationship partially explains why fibrillin synthetic defects lead to skeletal abnormalities and weakened aortic walls, as in individuals with Marfan sydrome (Chapter 5).

Proteoglycans and hyaluronan (Fig. 1-14). Proteoglycans form highly hydrated compressible gels that confer resistance to compressive forces; in joint cartilage, proteoglycans also provide a layer of lubrication between adjacent boney surfaces. Proteoglycans consist of long polysaccharides, called *glycosaminoglycans* (examples are keratan sulfate and chondroitin sulfate) attached to a core protein; these are then linked to a long hyaluronic acid polymer