- The formation of procollagen begins with formation of interchain disulfide bonds between the C-terminal extensions of the pro-α-chains
  - This bring the three α-chains into an alignment favorable for helix formation
- The procollagen molecules move through the Golgi apparatus, where they are packaged in secretory vesicles
  - The vesicles fuse with the cell membrane, causing the release of procollagen molecules into the extracellular space

- **Extracellular cleavage of procollagen molecules**
  - After their release, the procollagen molecules are cleaved by N- and C- procollagen peptides, which remove the terminal propeptides, **releasing triple-helical tropocollagen molecules**
- **Formation of collagen fibrils**
  - Tropocollagen molecules spontaneously associate to form **collagen fibrils**
- **Cross-link formation**
  - The fibrillar array of collagen molecules serves as a substrate for **lysyl oxidase**
    - Lysyl oxidase one of several **copper containing enzymes.** Others include **cytochrome oxidase, dopamine hydroxylase, superoxide dismutase,** and **tyrosinase**.
      - Disruption in copper homeostasis causes **copper dificiency (X-linked Menkes disease)** or overload **(Wilson disease)**
- **Degradation**
  - Breakdown of collagen fibers is dependent of the proteolytic action of **collagenases,** which are part of a large family of matrix **metalloproteinases**
    - For **type I collagen,** the cleavage site is specific, generating **three-quarter** and **one-quarter** length fragments
      - These fragments are further degraded by other matrix proteinases
- **Collagen diseases**
  - **Ehlers-Danlos Syndrome (EDS)**
    - It is a **heterogenous group** of connective tissue disorders that result from **inheritable defects** in the metabolism of fibrillar collagen molecules.
    - It can be caused by a deficiency of collagen-processing enzymes or from mutations in the amino acid sequences of collagen type I, III, or V,
    - The classic form, caused by **defects in type V collagen,** characterized by skin extensibility and fragility and joint hypermobility
    - The **vascular form,** due to defect in **type III collagen,** is the **most serious form of EDS** because it is associated with potentially **lethal arterial rupture**
  - **Osteogenesis Imperfecta (OI)**
    - Known as **brittle disease;** a genetic disorder of bone fragility characterized by bones that fracture easily, with minor or no trauma