2017 01 14 https://en.wikipedia.org/wiki/Collagen **Collagen Synthesis** hydroxyl: **-OH**

First, a 3-dimensional stranded structure is assembled, with amino acids **glycine** and **proline** as principal components. This is not yet collagen but its **precursor,** procollagen. Step 2: **procollagen** is modified by addition of hydroxyl groups to amino acids proline and lysine. This step is important for later glycosylation and the formation of the triple helix structure of collagen. The **hydroxyl**ase enzymes that perform these reactions require Vitamin C as a cofactor, and a deficiency in this vitamin results in impaired collagen synthesis and the resulting disease scurvy[17] These **hydroxyl**ation reactions are catalyzed by two different enzymes: prolyl-4-**hydroxyl**ase[18] and lysyl-**hydroxyl**ase**.** Vitamin C also serves with them in inducing these reactions. In this service, one molecule of **vitamin C is destroyed** for each **H** replaced by **OH.** [19]
The synthesis of collagen occurs inside and outside of the cell. The formation of collagen which results in fibrillary collagen (most common form) is discussed here. β-sheet is the other form of collagen. All types of collagens are triple helices, and the differences lie in the make-up of the α peptides created in step 2.

1. **Transcription of mRNA**: About 34 genes are associated with collagen formation, each coding for a specific mRNA sequence, and typically have the "*COL*" prefix. The beginning of collagen synthesis begins with turning on genes which are associated with the formation of a particular α peptide (typically α 1, 2 or 3).
2. **Pre-pro-peptide formation**: Once the final mRNA exits from the cell nucleus and enters into the cytoplasm, it links with the **ribosomal** subunits and the process of translation occurs. The early/first part of the new peptide is known as the **signal sequence**. The signal sequence on the N-terminal of the peptide is recognized by a signal recognition particle on the endoplasmic **reticulum**, which will be responsible for directing the pre-pro-peptide into the endoplasmic **reticulum**. Therefore, once the synthesis of new peptide is finished, it goes directly into the endoplasmic reticulum for post-translational processing. It is now known as **pre-pro-collagen**.
3. **Pre-pro-peptide to pro-collagen**: Three modifications of the pre-pro-peptide occur leading to the formation of the **alpha peptide**:
    1. The signal peptide on the N-terminal is dissolved, and the molecule is now known as ***propeptide*** (not procollagen).
    2. **Hydroxyl**ation of lysines and prolines on **propeptide** by the enzymes 'prolyl-4-**hydroxyl**ase' and 'lysyl **hydroxyl**ase' (to produce **hydroxy**proline and **hydroxy**lysine) occurs to aid **cross-linking of the alpha peptides**. This enzymatic step requires vitamin C as a cofactor. In scurvy, the lack of **hydroxy**lation of prolines and lysines causes a **looser** triple helix (which is formed by three alpha peptides).
    3. Glycosylation occurs by adding either glucose or galactose monomers onto the **hydroxyl** groups that were placed onto lysines, but not on prolines.
    4. Once these modifications have taken place, three of the **hydroxyl**ated and glycosylated propeptides twist into a triple helix forming **procollagen**. **Procollagen** still has unwound ends, which will be later trimmed. At this point, the **procollagen** is packaged into a transfer vesicle destined for the Golgi apparatus.
4. **Golgi apparatus modification**: In the Golgi apparatus, the **procollagen** goes through one last post-translational modification before being secreted out of the cell. In this step, oligosaccharides (not monosaccharides as in step 3) are added, and then the **procollagen is packaged** into a secretory vesicle destined for the extracellular space.
5. **Formation of tropocollagen**: Once outside the cell, membrane bound enzymes known as 'collagen peptidases', remove the "loose ends" of the procollagen molecule. What is left is known as **tropocollagen**. Defects in this step produce one of the many collagenopathies known as Ehlers-Danlos syndrome. This step is absent when synthesizing type III, a type of fibrilar collagen.
6. **Formation of the collagen fibril**: 'Lysyl oxidase', an extracellular enzyme, produces the **final step** in the collagen synthesis pathway. This enzyme acts on lysines and **hydroxyl**ysines producing **aldehyde** groups, which will eventually undergo covalent bonding between tropocollagen molecules. This polymer of tropocollogen is known as a **collagen fibril. yaHoo!** edits by john@earthPa.us