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Review Article

Review of Collagen in Health and Disease (Part 1 Collagen in Health)

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ABSTRACT

Collagen is the most abundant protein in the human body. It possesses triple helical protein molecule which forms the major part of the extracellular matrix. It forms integral part of skin, connective tissues, tendons, bones and cartilage. Also collagen is integral part of dental tissues such as enamel, dentin, pulp and periodontal ligaments. This review highlights the various physiological aspect of collagen.

Keywords: Collagen, Collagen disorders, Extracellular matrix, Fibroblast.

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INTRODUCTION

As collagen is integral part of body and its various organs. It had been studied extensively. It comprises a family of proteins rather than single type of protein and is distinguishable by their molecular compositions, morphologic characteristics, distribution, functions and pathologies. It is present in the skin, bone, cartilage, smooth muscle and basal lamina. It provides rigidity, elasticity and strength. Collagens are produced by several cell types. [1]

It is the major fibrous glycoprotein present in the extracellular matrix, inconnective tissue. It has a triple helical structure. Various studies have proved that mutations that modify folding of the triple helix result in identifiable geneticdisorders.[2]

Therefore, this review highlights the role of collagen in normal health and also the disorders associated with structural and functional defects in collagen.

Structure and Types of Collagen

In humans, collagenen compasses one-third of the total protein. It is the prevalent constituent of the extracellular matrix. Twenty-eight different types of collagens composed of at least 46 distinct polypeptide chains have been recognized in vertebrates. Common characteristic is the presence of hydroxyproline and hydroxylysine and glycine is present at every third position. Collagen fiber bundles are referred to as white fibers because of the fact that collections of collagen fibers appear white in living tissue.[3,4]

Microscopic Appearance

Collagen fibers appear as long, wavy, pink fibers bundles after staining with hematoxylin and eosin. Electron micrographs of collagen fibers stained with heavy metals display cross banding at regular intervals of67 nm, a characteristic property of these fibers. These fibers are formed from parallel aggregates of thinner fibrils 10 to300 nm in diameter and many micrometers in length.[3, 4]

Synthesis of Collagen

Mesenchymal cells and their derivatives (fibroblasts, osteoblast, odontoblast, chondroblasts and cementoblasts) are the chief producers of collagen. Other cell types synthesizing collagen are epithelial, endothelial, muscle and Schwann cells.[4]

Fibroblast

Fibroblast is the most common cell of connective tissue that produces and maintains the extracellular matrix. Fibroblasts provide a structural framework for many tissues and play animperative role in wound healing. The key function of fibroblasts is to maintain the structural integrity of connective tissues by continuously secreting precursors of the extracellular matrix, primarily the ground substance and a variety of fibers. They are recognized by their association with collagen fibers bundles. Fibroblasts exhibit contractility and motility which are important during connective tissue remodeling and formation and during wound repair. In certain tissues, fibroblasts have significant contractile properties and are called as myofibroblasts.[3,5]

Degradation of Collagen[3]

Mechanisms involved in degradation of collagen are:

1. Secretion by cells of enzymes that sequentially degrade collagen and other matrix molecule extracellularly,
2. Selective ingestion of collagen fibrils by fibroblasts and their intracellular degradation.
3. Collagen triple helix is highly resistant to proteolytic attack. Matrix metalloproteinases (MMP) is a large family of proteolytic enzymes that includes: Collagenases (MMP-1, 8, 13), gelatinases (MMP-2, 9), metalloelastases (MMP-12), stromelysins (MMP-3, 10, 11), matrilysin (MMP-7) that are involved in degradation of collagen. Collagenase 1, 2 and 3 degrades type I, II, III, Vcollagen, collagenase 3 can degrade type I, II, III, IV, IX, X,XI, fibronectin and other extracellular matrix component.

Collagen in Health

Collagen is sometimes referred to as the body's cement that holds everything in place. Collagen is important to health because it dictates the structure of skin, connective tissues, tendons, bones and cartilage.[6]

1. Skin health: Collagen plays an important role in skin health. Collagen maintains firmness and elasticity of skin. Collagen in the form of collagen hydrolysate keep skin hydrated. A lack of collagen becomes obvious during the aging process as skin begins to sag and lines and wrinkles begin to form. Information of scar tissue as a result of age or injury, there is change in the abundance of types I and III collagen as well as their proportion to one another. Type III collagen synthesis decreases with age resulting in changes in skin tension, elasticity and healing.[7]

2. Wound healing: Collagen is a key protein in connective tissue and plays an imperative role in wound healing by repair and formation of scar. Collagen deposition and remodeling contribute to the increased tensile strength of the wound. However, Collagen overproduction can form abnormal scars, which impede wound healing. A chronic wound burden among the elderly has been documented and much of this age-related, delayed wound healing is caused by impaired collagen synthesis and increased degradation. Increase infibroblasts and collagen during healing suggested that a correlation might exist between number of fibroblasts, quantity of collagen and tensile strength of a scar. [8]

3. Bone: Bone is a complex and dynamic tissue that provides structural support for the body, protection of internal organs and acts as levers to which muscles are attached, allowing movement. Out of 22 to 25% of organic component 94 to 98% is mainly collagen type I and other non-collagen proteins and 2 to 5% are cells. The combination of hard mineral and flexible collagen makes bone harder than cartilage without being brittle. Combination of collagen mesh and water forms a strongand slippery pad in the joint that cushions the ends of thebones in the joint during muscle movement. [9, 10]

4. Cartilage, tendon, ligaments: Collagen, in the form of elongated fibrils, is predominantly found in fibrous tissues such as tendon and ligament. It is a flexible and stretchy protein that is used by the body to support tissues and thus it plays a vital role in the maintenance of the cartilage, tendons and ligaments. Normal tendon consists of soft and fibrous connective tissue that is composed of densely packed collagen fibers bundles aligned parallel to the longitudinal tendon axis and surrounded by a tendon sheath also consisting of extracellular matrix components. Collagen constitutes 75% of the dry tendon weight and functions chiefly to withstand and transmit large forces between muscle and bone.[11] Collagen also forms a major constituent of cartilages. Cartilage collagen fibrils consist of collagen II, the quantitatively minor collagens IX and XI. [4,5]

5. Muscles: In muscle tissue, it serves as a major component of the endomysium. Collagen constitutes 1 to 2% of muscle tissue, and accounts for 6% of the weight of strong, tendinous muscles. [4,6]

6. Dental tissues:

a. Dentin: The mature dentin is made up of approximately70% inorganic material, 20% organic material and 10%water by weight. The organic phase is about 30%collagen (mainly type I with small amounts of types III and V) with fractional inclusions of lipids and noncollagenous matrix proteins. Collagen type I acts as a scaffold that accommodates a large proportion(estimated at 56%) of the mineral in the holes and pores of fibrils.[12]

b. Pulp: The extracellular compartment of the pulp ormatrix consists of collagen fibers and ground substance. The fibers are principally types I and III collagen. The overall collagen content of the pulp increases with age, the ratio between types I and III remains stable and the increased amount of extracellular collagen organizes into fiber bundles.[13]

c. Cementum: Predominant collagen present in cementum is type I collagen (forms 90% of the organic matrix). Other collagens associated with cementum include type III, a less cross linked collagen found in high concentrations during development and repair and regeneration of mineralized tissues and type XII that binds to type I collagen and also to noncollagenous matrix proteins. Collagens found in trace amount in cementum are types V, VI and XIV.[14]

d. Periodontal ligament: Periodontal ligament is composed of collagen fibers bundles connecting cementum and alveolar bone proper. The predominant collagens of the periodontal ligament are types I, III and XII, with individual fibrils having a relatively smaller average diameter than tendon collagen fibrils.

The vast majority of collagen fibrils in the periodont alligament are arranged in definite and distinct fiber bundles and these are termed as principal fibers. The periodontal ligament has also the capacity to adapt to functional changes. When the functional demand increases, the width of the periodontal ligament can increase by as much as 50 % and the fiber bundles also increase markedly in thickness.[14]

e. Basement membrane: The epithelial basement membrane and adjacent area is termed the epithelial basement membrane zone. The lamina densa consisting of type IV collagen that is coated by heparan sulfate, a glycosamino glycan and anchoring fibrils, that are composed of type VII collagen and extend from the lamina densa to the connective tissue.[15]

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