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CONNECTIVE TISSUE PROTEINS

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Bone tissue is a specialized mineralized type of connective tissue. Being the basis of the musculoskeletal system, it performs the function of mechanical protection of internal organs from external influences. Bone tissue stores up to 95% of inorganic substances, including 99% of calcium reserves, 87% of phosphorus and 58% of magnesium. Bone tissue contains 4 types of cells: osteoblasts, osteocytes, osteoclasts and stem cells.

The main function of osteoblasts is to produce bone matrix, which includes protein synthesis, formation of collagen network, matrix vesicles, cytokines, growth factors, collagenase, glycoproteins, osteonectin, bone sialoprotein, etc. Among other things, osteoblasts have receptors on themselves and produce substances that regulate the remodeling process.

Collagen is a polymorphic protein, and has 28 different types, differing from each other in the primary structure of the polypeptide chain, in function and location. A special formula is used to designate each type of collagen, which uses Roman numerals indicating the type of collagen and Arabic numerals indicating the collagen chain. For example, type 1 collagen is written with the formula [α1(I)2 α2(I)]. The index in parentheses indicates the number of identical chains in the collagen molecule. Due to the polymorphism of the collagen molecule, there are different classifications of collagen proteins. According to the most common classification, there are 5 groups of collagen proteins.

90-95% of the organic matrix of bone tissue is type I collagen, which ensures the strength of bone tissue. Each type I collagen molecule consists of 2 α1 chains and

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1 α2 chains. Each of these chains consists of a helical domain, with C- (carboxytherminal) and N- (aminotherminal) terminal propeptides at the end necessary for the formation of a triple helix of a tropocollagen molecule. In the process of collagen biosynthesis, during the formation of the tropocollagen molecule, the N-terminal (amino terminal) and C-terminal (carboxytherminal) propeptide are cleaved off with the help of specific proteases. These propeptides are necessary for the formation of the triple helix of the collagen molecule and for the further formation of collagen fibrils. When the terminal propeptides are cleaved from the procollagen molecule, they are released into the blood. The detection of these terminal propeptides (C- and N-terminal propeptides) are of important clinical and diagnostic importance, since they reflect the exchange of collagen molecules, i.e. functional activity of osteoblasts. PINP (aminotherminal propeptide of procollagen type I) and PICP (carboxytherminal propeptide of procollagen type I) serve as biochemical markers of bone formation. These markers have proven themselves well in monitoring the effectiveness of anti-osteoporotic treatment. In addition, they are of great value in the diagnosis of diseases such as osteoporosis, Penjet's disease, renal osteodystrophy, as well as in some oncological and rheumatic diseases.

Type II collagen is an important component for the normal development of bones and teeth. It is most present in cartilage, intervertebral discs, as well as in the vitreous body. Its molecule consists of three identical α chains, each of which consists of 1060 amino acid residues with an extended continuous domain and short non-spiral fragments. Collagen fibrils are relatively thinner than type I collagen fibrils. Type III collagen is a homotrimer (α1(III). Each of the α chains contains up to 1029 amino acid residues. It is the predominant protein in the skin and interstitial blood vessels. It is present in bone tissue only in trace amounts. Collagen IV is a key structural component of the basement membranes. Its molecules form hexameric structures formed by the "butt-to-butt" connection of the N-ends of collagen trimers. These hexamers are additionally stabilized by transverse covalent crosslinking between lysine and meteonin residues. The spirals of type IV collagen, connecting with each other, form a "web" characteristic of this type of collagen, which plays an important

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role in regulating the permeability of the basement membranes. Type V collagen is present in the skin, in fetal bone tissue, in the mature cornea and interstitial kidneys. It is considered as a factor in the initiation of the assembly of type I collagen molecules.

The main component of descemet membranes of the corneal endothelium is type VIII collagen. It is also present in large quantities in the subendothelial layer of blood vessels. Type VIII collagen chains (α1 and α2) are structurally similar to type X collagen chains. Type X collagen is secreted by hypertrophied chondrocytes during endochondrial ossification. It is represented by a homotrimer in which each of the α chains contains short spiralized sections of 154 amino acid residues, limited by non-collagen domains from the N- and C-terminus, with a length of 37 and 161 amino acid residues, respectively. Unlike fibrillar collagens, terminal fragments are not cleaved off during posttranslational modification. And the presence of non-collagen domains provides a characteristic structure for collagens of types IV, VIII and X. There are transmembrane collagens, which belong to the class of transmembrane proteins. These collagens have a short cytoplasmic terminal fragment (N-terminus) and, connected to a hydrophobic membrane site, an extracellular long interrupted spiralized domain. The presence of extracellular domains in the molecules of transmembrane collagens ensures their cellular adhesion. Type VIII collagen is mainly found in focal contacts, type XVII collagen in hemidesmosomes, type XXV collagen in neurons, type XXIII collagen is expressed by prostate carcinoma cells.

Collagens XV and XVIII are classified as chondroitin sulfate and heparan sulfate proteinoglycans, respectively. They are mainly localized in the area of the basement membranes. Type XV collagen is most common in skeletal muscles, heart and placenta. They are expressed by the adrenal glands, kidneys and pancreas. Type XVIII collagen pre-mRNA in humans undergoes 2 types of splicing. During translation, 2 isoforms of this protein are formed: short and long. The short chain is expressed in various organs and tissues, but the synthesis of the long isoform is characteristic only of the liver. The biological role of these types of collagen has not been fully studied. But it is assumed that they are involved in the regulation of the

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functions of specialized basement membranes. Thus, in most diseases of the skeleton, the metabolism of bone tissue is disrupted, remodeling processes with predominant bone resorption occur intensively, as a result of which type I collagen degradation products are released into the blood in large quantities, which are widely used in the diagnosis of many diseases of bone tissue, and are also widely used to control treatment.

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