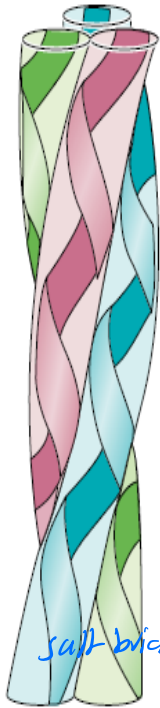


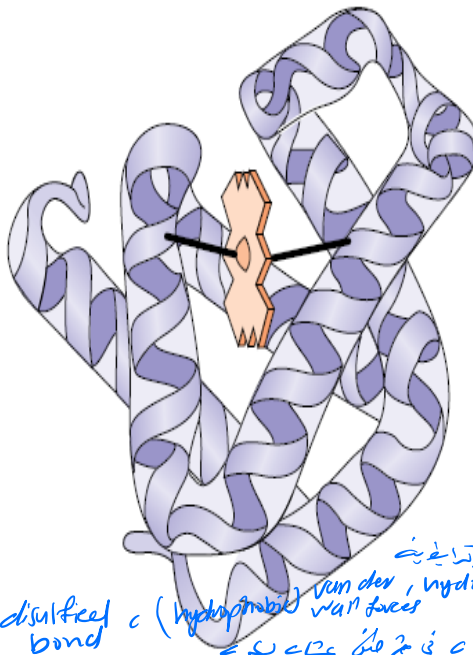
Classification of Proteins

(a)



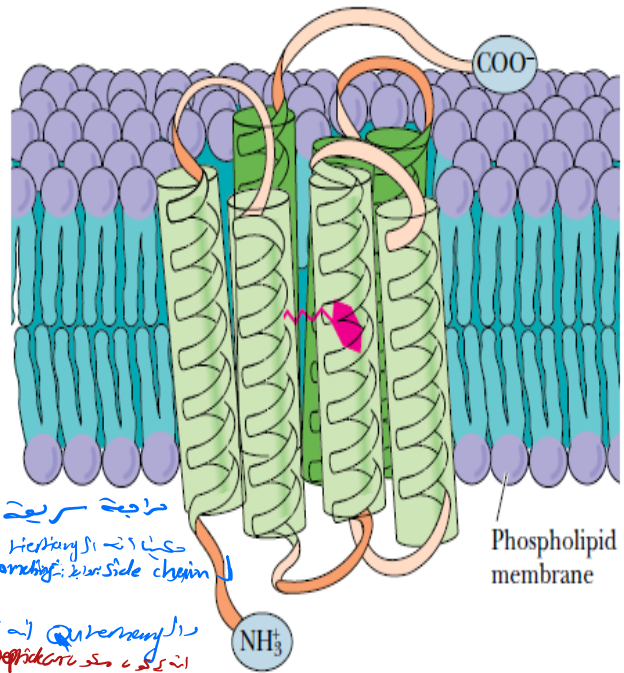
Collagen, a fibrous protein

(b)



Myoglobin, a globular protein

(c)



Bacteriorhodopsin

salt bridges
disulfide bond

(hydrophobic)

van der Waals forces
hydrogen bonding
side chain interactions

more than one polypeptide chain
non-covalent bonding

renaturation
denaturation
degradation
aggregation

لا يمكن فصل
البنية
التي تتكون من
البروتينات

re-formation
denaturation
degradation
aggregation

Classification of Proteins

Proteins can be classified based on their shape and solubility into three groups:

1- **Fibrous proteins**: These proteins have a rod like structure. They are not soluble in water. Collagen is an example these proteins often serve structural roles in cells.

2- **Globular proteins**: Due to their distribution of amino acids (hydrophobic inside, hydrophilic outside) they are very soluble in aqueous solutions (e.g Myoglobin) these proteins serve metabolic functions

3- **Membrane proteins**: Those membrane proteins that are embedded in the lipid bilayer have extensive hydrophobic amino acids that interact with the non-polar environment of the bilayer interior. Membrane proteins are not soluble in aqueous solutions.

e.g: Rhodopsin

Membrane proteins carry out transport activities, receptor functions, and other related processes

ارسطوس
صفا
متحوي

Cell membrane

hydrophilic
موجود في
الجزء
المتحوي

مفرد

Les

الذات

توزيع

شكلها كروي

صفا

Fibrous Proteins

General characteristics

1-Serve structural roles in cells

•Fibrous proteins are often mechanically strong & highly cross-linked

ترتبط بعضها ببعضه أو cross-linked

2-Insoluble in water

3-Secondary structure is simple based on one type only

Fibrous proteins have high alpha-helix or beta-sheet content.

محتوى high من alpha-helix أو beta-sheet أو mix من Fiber protein

4-Functions in structure of the body or cell (tendons, bones, muscle, hair, skin)

Most are structural proteins.

Examples include:

•Collagen

•Elastin

•Keratin

•Fibroin

بعض النسيج المرنة

بعض النسيج

elasticity مرونة

relaxation استرخاء

stretching تمدد
تتمتع بالخاصة كما تتميز به نسيج الجلد
منه تتحرك بمرحله الوضعية الطبيعي

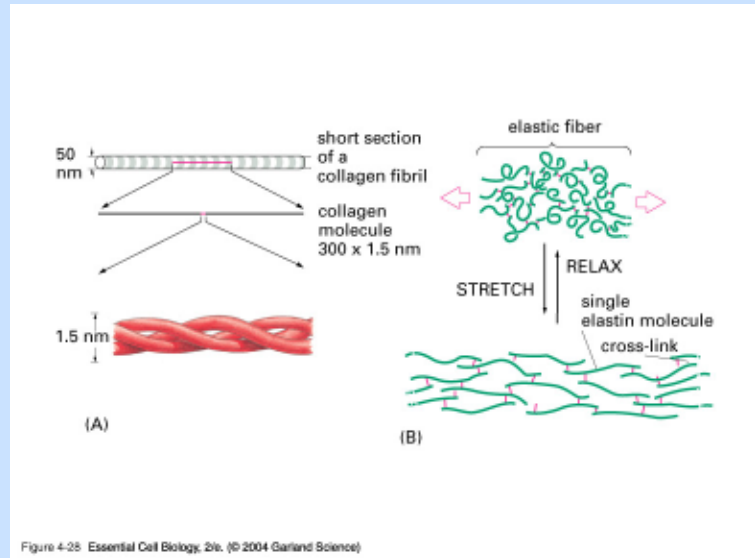
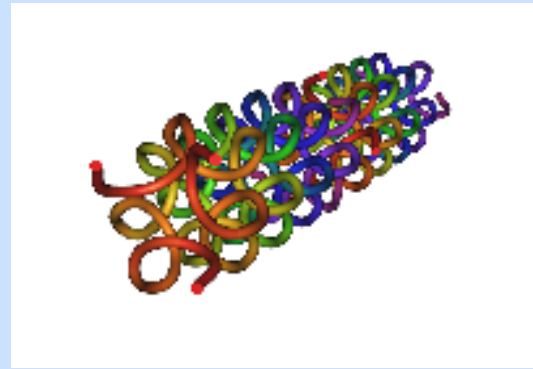


Figure 4-28 Essential Cell Biology, 2/e. © 2004 Garland Science

Collagen

is the main structural protein of the various connective tissues in animals.



The collagens are the most abundant proteins in the body, make up from 25% to 35% of the whole-body protein content

- They occur in connective tissues where tensile strength is needed.
- Examples: skin, tendons, cartilage, bones.

Tensile strength results from the use of:

- The triple helix secondary structure
- The assembly of tropocollagen subunits into a fibre
- Chemical cross linking to strengthen the fibre

الكولاجين مكون من 3 peptides
يكون كل واحد من الـ d-helix
يكون متفعل في بعضه
ويكون triple helix
يعني 3 helices متفاعلات

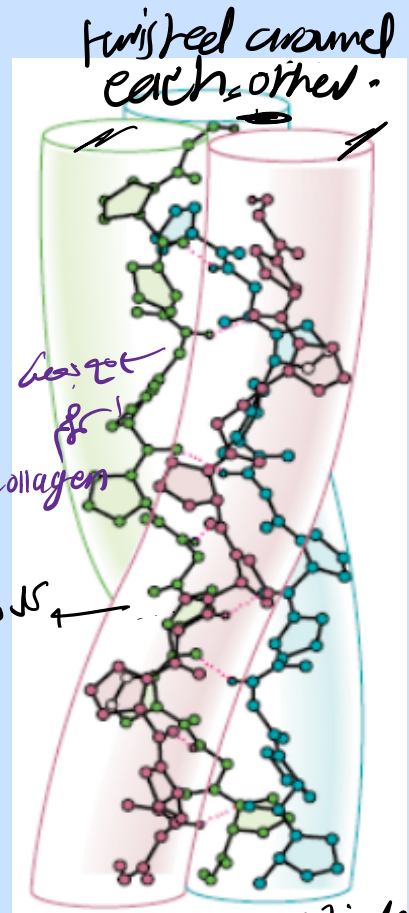
المدا بطول الـ fiber
cross linking

Structure of collagen

amino acid sequence *سلسلة الأحماض الأمينية*
 family (أحد عائلتي الكولاجين) *عائلة الكولاجين*
 19 residues per triple helix *19 بقية لكل حلزوني*
 right handed *يمين يمين*
 left handed *يسار يسار*

Collagen is made up of three polypeptides (referred to as "α-chains") that are twisted around one another (tropocollagen) in a rope-like triple-helix and are held together by hydrogen bonds.

بعين القوة *بعضة القوة* *و موجود بال (connective tissue) ربي و على القوة*
 Collagen is formed from tropocollagen subunits. The triple helix in tropocollagen is highly extended and strong.



tropocollagen *تري بوليكولاجين*
 left handed *يسار يسار*
 right handed *يمين يمين*
 α-chain *ألفا سلسلة*
 tropocollagen *تري بوليكولاجين*

Features:

(1) Three separate polypeptide chains arranged as a left-handed helix (note that an alpha-helix is right-handed).

(2) 3.3 residues per turn *كثافة 3.3 بقية*

(3) Each chain forms hydrogen bonds with the other two

α-helix (secondary structure) *ألفا حلزوني (بنية ثانوية)*
 α-polypeptide *ألفا بوليكولاجين*
 α-polypeptide α-helix *ألفا بوليكولاجين ألفا حلزوني*
 3 α-peptide *3 ألفا بوليكولاجين*
 α-polypeptide α-helix *ألفا بوليكولاجين ألفا حلزوني*
 secondary structure *بنية ثانوية*

Types of collagen

In humans at least there are 19 different collagens. Within these 19 structural types, four major classes are generally identified.

Collagen type I

انظر

- i) The fibers have diameter between 80 to 160nm.
- ii) Found in bone, dentin, skin, tendon, muscles and walls of blood vessels.

Collagen type II

- i) have a diameter < 80nm
- ii) found in intervertebral discs and hyaline cartilage.

Collagen type III

Found in spleen, muscle, and aorta.

سك

Collagen type IV


Found around different types of the basement membranes and muscles.

Collagen type V

من العين العين

It is found in embryonic cell cultures and the basement membranes.

Collagen type VI

It is found in muscle and skin.  it is found in muscle and skin

Collagen Amino Acid Composition

وہی ہے جی جی سے الی (کرنل) (a-helix) 33%

دیکھتے ہیں a-helix

Nearly one residue out of three is Gly

Proline content is unusually high

Proline facilitates the formation of the helical conformation of each α -chain because its ring structure causes "kinks" in the peptide chain.

helix amino acid breathers
 proline Gly
 winding ہلکا ہلکا a-helix

Many modified amino acids are present:

-4-hydroxyproline

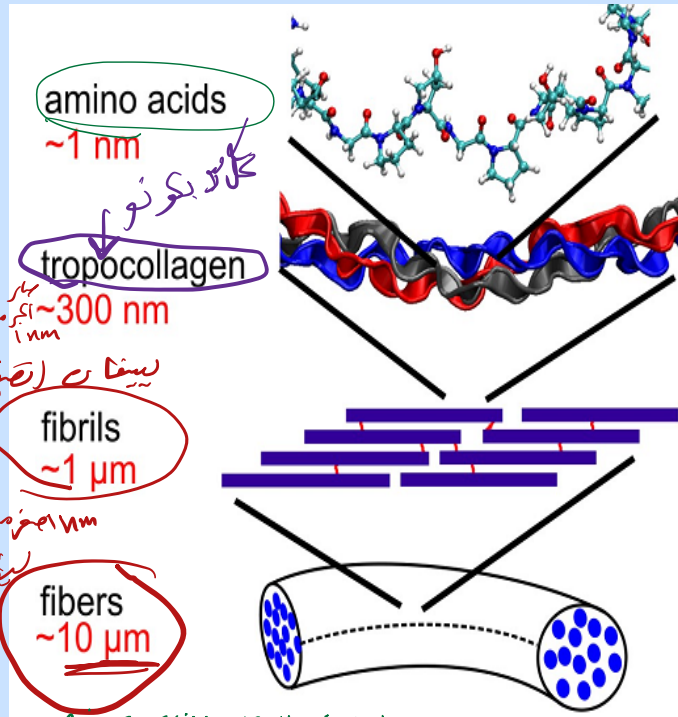
-3-hydroxyproline

-5-hydroxylysine

amino acid
 کد دیکھ جائیں
 وہ کدوں میں
 یہ اس کے لیے

more extended مارے extension

The hierarchical design of collagen.



The structural features of collagen ranges from the amino acid sequence, tropocollagen molecules, collagen fibrils to collagen fibers.

سینا (تصویر)

fibrils ~1 μm

fibers ~10 μm

تالورہ الی بالیون
 الی بعد صاف کرنے
 اسیکا
 amino acid sequence
 a-chain
 b-chain
 triple helix
 collagen fibrils
 collagen fibers

لو جیتے ۲ زنجیر کا تقابلہ ردھلیم
 بیچے باہر قلو ہے لو جیتے ۲ زنجیر کا
 تقابلہ عموماً وہ اد جلمہ بہ قلو
 سان صر عکال الی

یعنی بعد و (winding) کی لڑجیر کا تقابلہ ع
 تقابلہ اد جلمہ قلو (winding around each other)

Ehlers-Danlos syndrome (EDS)

Connective tissues are proteins that support skin, bones, blood vessels and other organs.

EDS usually affects your skin, joints and blood vessel walls.

EDS is a group of inherited connective tissue disorders, caused by a defect in the synthesis of collagen (Type I or III).

There is no cure, and treatment is supportive, including close monitoring of the digestive, excretory and particularly the cardiovascular systems.

The fragile skin and loose joints is often a result of abnormal genes that produce abnormal proteins that confer an inherited frailty of collagen (the normal protein "glue" of our tissues).



inherited

يعني المرض كزيم نقص - تباصا دن يادن دفاعه - كذا رنجا قر بيته منه

تلكه ال tissue تاله
 ت بعده

كودة ع تفر
 البروتين
 the glue of
 our tissue

Collagenopathy

The type II and XI collagenopathies are a group of disorders that affect connective tissues.

These disorders are caused by defects in type II or type XI collagen.

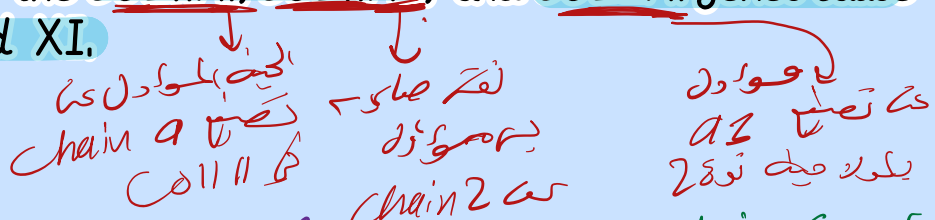
لنفسه جينا 2 و 11

بمقلو اج بعلا في توكية صا كالا سوح

Type II and type XI collagen disorders are grouped together because both types of collagen are components of the cartilage found in joints and the spinal column, the inner ear, and the jelly-like substance that fills the eyeball

Causes

Mutations in the COL11A1, COL11A2, and COL2A1 genes cause collagenopathy, types II and XI.



COL11A1 و COL11A2 و COL2A1 جينات
COL11A1 و COL11A2 جينات COL11A1 و COL11A2
COL2A1 جين COL2A1
COL11A1 و COL11A2 جينات COL11A1 و COL11A2
COL2A1 جين COL2A1

Collagenopathy, type 2 alpha 1

بالامثلة ان انه الجينات التي تصفوا التوكيد واحد منكم بسفل
ناده منكم رة يد فل كونه كية التسمية التي صر COL2A1

refers to a wide range of conditions that can result from problems with cartilage collagen tissue due to a defect in the COL2A1 gene.

المخفاص

Defects in the COL2A1 gene result in defective or reduced collagen production which in turn affects the development of connective tissues including bones.

Symptoms of Collagenopathy, type 2 alpha 1

Abnormal bone development

Short stature ^{قاسم}

Enlarged joints ^{مرفق}

Curved spine ^{منحنى / قوس}

Premature arthritis ^{التهاب مفاصل}

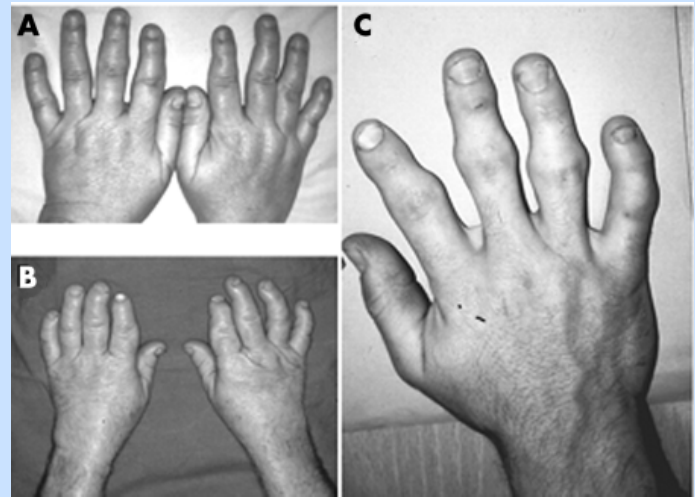
Vision problems

Hearing problems

Cleft palate ^{فتحة}

Small lower jaw

Various facial anomalies ^{مشردر}



Keratin

Keratin is the key structural material making up the outer layer of human skin.

يكون الطبقة الخارجية للجلد

- Tough and insoluble in water
- Main constituent of hair, nails and tooth enamel
- Two major conformational groups
 - (a) alpha-keratin whose peptide backbone forms a α -helix
 - (b) β -keratin whose backbone forms a β -sheet structure.

α -Keratin

سلسلة α -chain
دimer of α -helices
يسمى بروتين
disulfide bond

Made up of α -helix

alpha-keratin is found in hair, nails, outer layer of skin. It forms almost the entire dry weight of these materials.

The entire secondary structure is a dimer of two alpha-helices.

It is rich in amino acids that favours alpha-helix formation

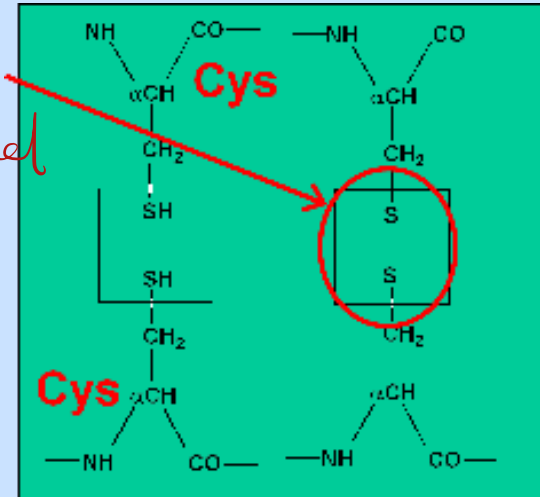
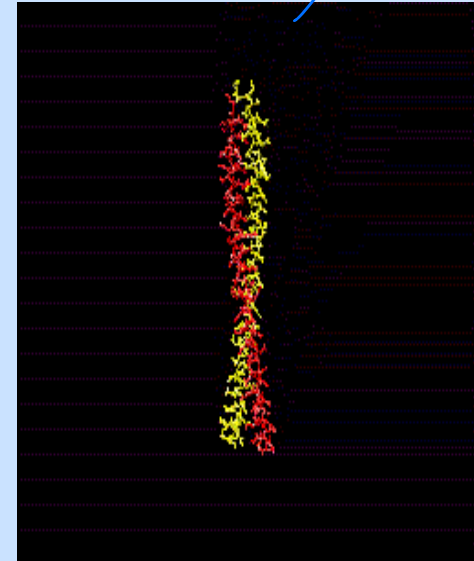
These hydrophobic side chains are on the alpha-helix surface-explaining its insolubility.

It is also rich in Cys residues. \rightarrow disulfide bond

Two Cys residues form disulphide bridges in alpha-keratin, and link the alpha-helices together.

The more disulphides, the stronger the alpha-keratin.

كلما كان فيه اكثر بروتين
disulfide اكثر ويكون البروتين اقوى

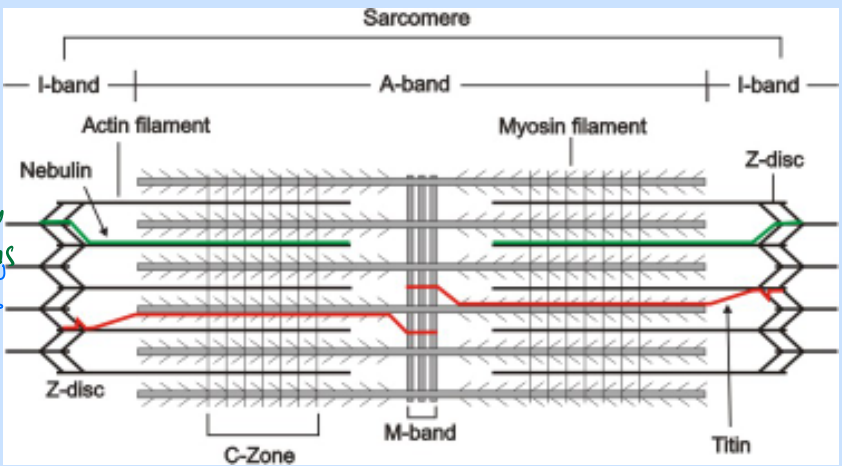


Motor Proteins

المركبات التي تسمى بالبروتينات
 muscle relaxation
 muscle contraction
 العضلات
 انقباضها وانفلاتها

- The most prominent example of a motor protein is the muscle protein myosin and actin which performs the contraction of muscle fibers in animals.

regulatory proteins
 البروتينات التنظيمية
 regulatory proteins
 البروتينات التنظيمية
 regulatory proteins
 البروتينات التنظيمية
 regulatory proteins
 البروتينات التنظيمية



- Sarcomere is the smallest functional structure of the muscle.
- Sarcomere is made up of three different filament:
 - 1- Myosin the thick filaments
 - 2- Actin the thin filaments.
 - 3- Proteins that stabilize the positions of the thick and thin filaments, and proteins that regulate the interactions between thick and thin filaments.
- = The myosin head attaches to an actin filament within the sarcomere of a myofibril then pull towards the centre of the sarcomere. In the process, the sarcomere length shortens and the muscle contracts.

regulatory protein
 البروتينات التنظيمية

Myosin structure

و هي بنية أساسية تتصلب
 حيث يسبب عليه انقباض العضلة بوجود الكالسيوم حيث يتشبه بوجود (ATP) كما تسمى في الأكتين

Myosins are motor proteins that interact with actin thin filament and hydrolyse ATP to generate movement.

Myosin is a hexamer that consists of two heavy chains (220 kDa), and four light chains (~ 20 kDa each) paired into two regulatory light chains and two essential light chains.

The heavy chain consists of three proteolytically defined domains:

- 1- subfragment 1 (S1)
- 2- subfragment 2 (S2)
- 3- light meromyosin (LMM).

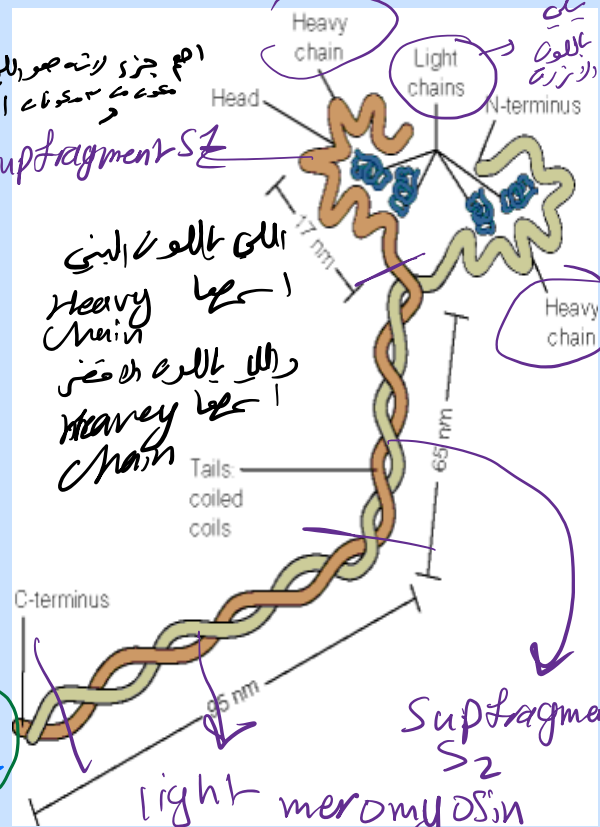
The globular head (S1) forms the actin binding site and the ATPase site and can be further divided into 3 subdomains:

- 1- the N-terminal 25 kDa nucleotide binding domain
- 2- the central 50 kDa actin binding domain
- 3- C-terminal 20 kDa actin binding domain

كل وحدة من (تحتلوزون الجبرني)

لانه مكون من 6 اجزاء

الجزء اثنى عشر من الـ 220 كيلو
 مكون من 20 كيلو
 و 20 كيلو
 و 20 كيلو
 و 20 كيلو



التي باللو الالبي
 Heavy chain
 واللي بالور الالبي
 Heavy chain

Supfragment S2
 light meromyosin

بعض الكتلين يرتبط بمنطقة الـ 25 كيلو
 nucleotide binding site - ATP binding site

الجزء الـ 20 كيلو يرتبط مع الـ (actin)

Actin

بجزيء الذي يرتبط به
رؤوسه متوسعة
ميوعة انقباضية
muscle contraction

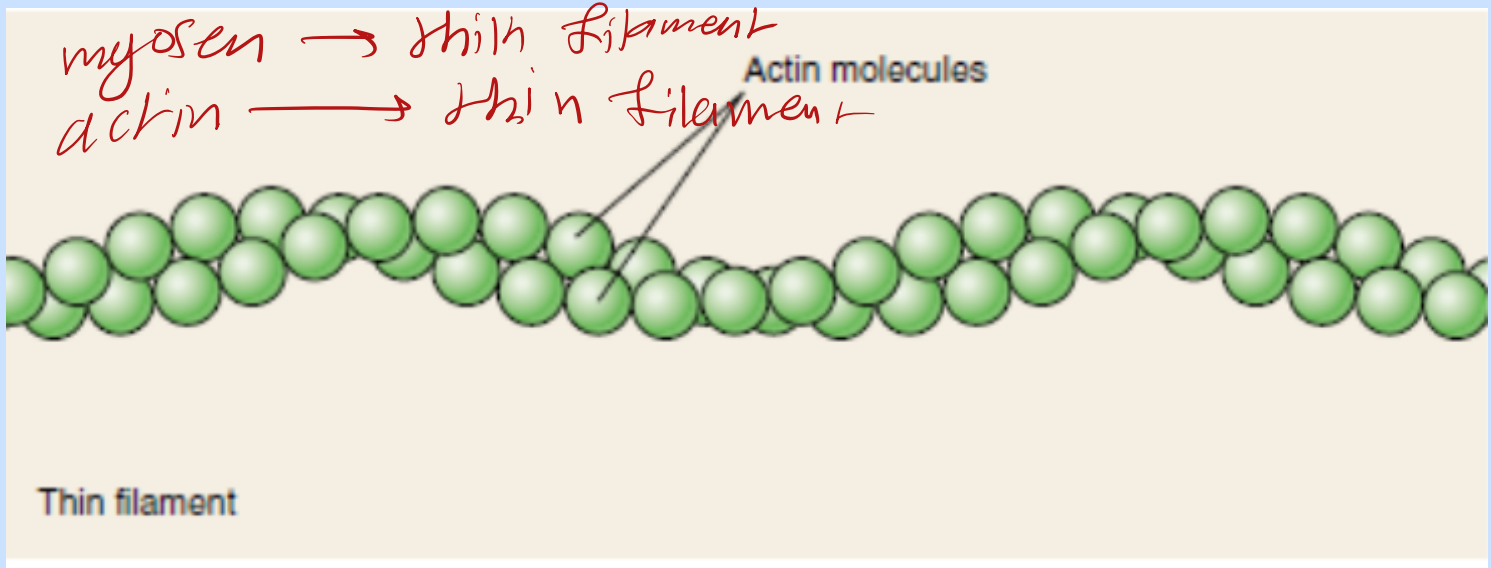
Actin is a 42 kDa adenine nucleotide-binding protein that made of 375 amino acids, and it is essential for so many cell functions.

Actin is found in two major forms:

Globular which is the monomeric form (G-actin) that can spontaneously polymerise into the filamentous form (F-actin) at physiological salt concentration.

كحبات التي تتجمع بالانقباض

البروتين
المتجمع
المنفرد



Actin monomers are arranged in a two-strand helix.

Tropomyosin (Tm) \rightarrow *بروتين رابط العضلات* *regulatory proteins*

Tropomyosin (Tm) is a right-handed helical protein which forms a coiled dimer that cooperatively binds with actin thin filament.

Each Tm chain is composed of 284 amino acids, and a tight hydrophobic interaction between two chains holds them together

Tropomyosin is always found associated with actin.

Each tropomyosin spans the length of seven actin monomers.

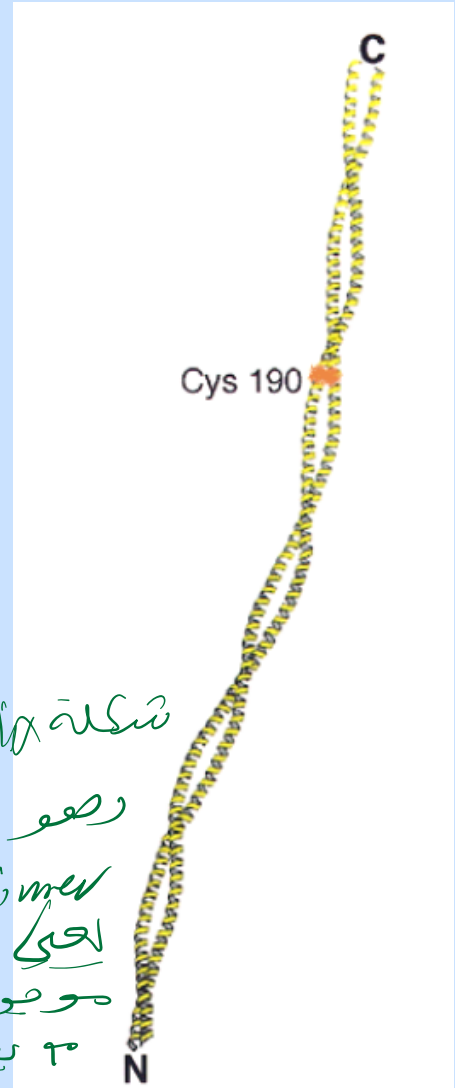
*كل بروتين كل وحدة من الأكتين
one tropomyosin
بشكل متكرر موجود
تربطها
as dimer يكون موجود*

شكله α helix

موجود

as dimer

*موجود على شكل
tropomyosin يرتبط
dimer*



Troponin complex (Tn)

Subunit من اكثر من 1

ثلاث وحدات
 myosin head ← thick filament
 Actin ← thin filament
 regulatory proteins

Troponin is the calcium-based regulator of striated muscle contraction.

على متجانسة

Troponin is a heterotrimeric complex that is composed of three interacting subunits: Troponin C, which is the calcium sensor subunit (18 kDa), Troponin I which is the inhibitory subunit (24 kDa) and Troponin T which is the tropomyosin binding subunit (37 kDa).

اما في حالة وجود الكالسيوم يرتبط الكالسيوم مع Troponin C
 Troponin C يغير شكله واذن يسهل بغيره ارتباط myosin head بجزء Actin
 Troponin I يمنع ارتباط myosin head بجزء Actin
 Troponin T يربط مع Troponin I و Troponin C
 ATP يتوقف بعد ذلك



دوران الحزمة
 Inhibitory Subunit
 Troponin I

تحتوي على
 Troponin I
 Troponin C

يوجد هناك
 وجود الكالسيوم
 الذي يرتبط مع Troponin C

A schematic representation of the interaction between the troponin complex and the rest of the thin filament. The black arrows indicate the interaction between actin-tropomyosin and troponin in the presence and absence of calcium

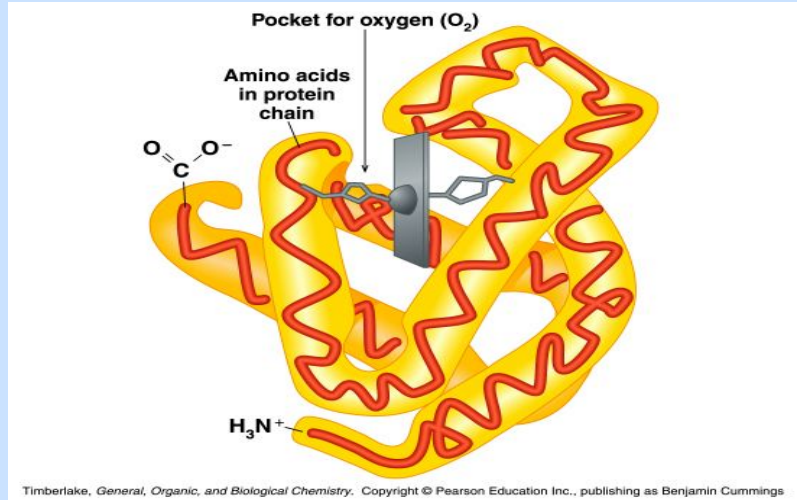
Globular Proteins → ^{كروية} كروية

hydrophilic → on surface & hydrophobic → ^{في الداخل} في الداخل

Hemoglobin و myoglobin (في الدم و في العضلات)

Globular proteins, also known as **sphero-proteins**, are proteins formed by compacted amino acid chains, which are folded into intricate shapes that often roughly resemble spheres.

A key difference between globular proteins and fibrous proteins is that the former type of protein is usually soluble in water, while the latter type is not.



- Globular proteins comprise the most varied type of proteins. Globular proteins are soluble in aqueous solution. To achieve this, globular proteins generally have polar residues on the surface and hydrophobic residues on the interior. [↓] hydrophilic
- Globular proteins include enzymes, transport proteins, regulatory proteins, proteins with many other functions.

Classification of Globular Proteins According to Secondary Structure

All alpha: Proteins that contain only alpha helical secondary structure. Myoglobin is an example of an all alpha protein.

دالة هيموگلوبین

All beta: Protein that contain only beta-sheet secondary structure. Tenascin is an example of an all beta protein.

Alpha/beta: Proteins that contain alternating alpha-helical and beta-sheet secondary structure elements. Triose Phosphate Isomerase is an example of an alpha/beta protein.

یعنی فی α -helix و β -sheet pattern

دو سول سول

Alpha + Beta: In these proteins the alpha helical and beta sheet regions occur in independent regions of the molecule. Ribonuclease A is an example of an alpha+beta protein.

اذا انا يتكون من α و β اما يتكون بشكل منفصل
ad مستقل غير متداخل independent pattern

Oxygen-binding proteins

Globular protein ← من الكروية

- Myoglobin and Hemoglobin are the two oxygen-binding proteins present in large multicellular organisms.

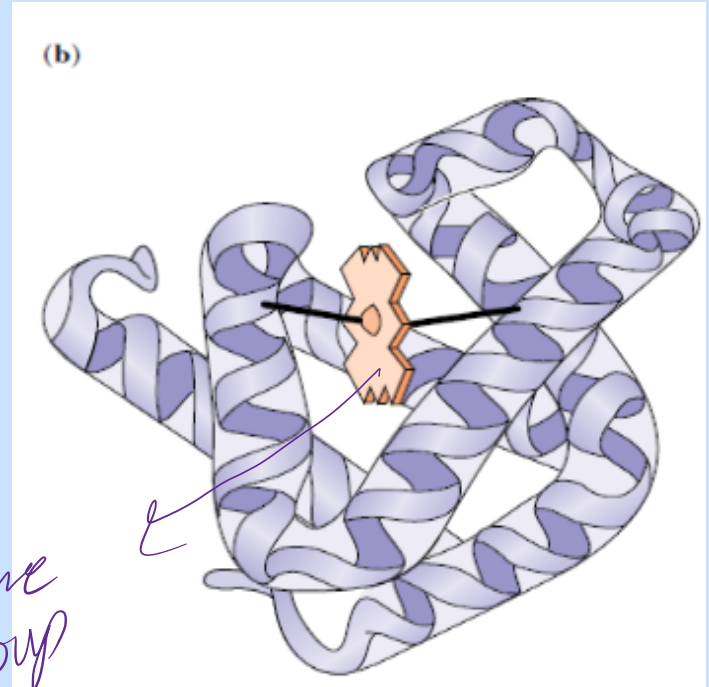
Myoglobin stores the oxygen in the muscles.

تخزن في العضلات

Hemoglobin transports oxygen in the blood and is located in the red blood cells

يُنقل في الدم
في العضلات

Heme group



Myoglobin (Mb)

75% of structure is α -helix in 8 regions, these are termed helices A, B, C, D, E, F, G, and H.

75% of structure is α -helix in 8 regions, these are termed helices A, B, C, D, E, F, G, and H.

- Myoglobin consists of a single polypeptide chain of 153 amino acids attached to a single heme group

Myoglobin interior almost entirely nonpolar residues

hydrophobic
Iron



- Mb Stores and facilitates oxygen diffusion in muscles especially in heart and skeletal muscle.

- The eight α helical segments are folded into a globular structure, creating a cradle (box) and within this cradle lies a single heme group and the binding site of O_2 .

كوتة في الهيمو جروب
Heme group

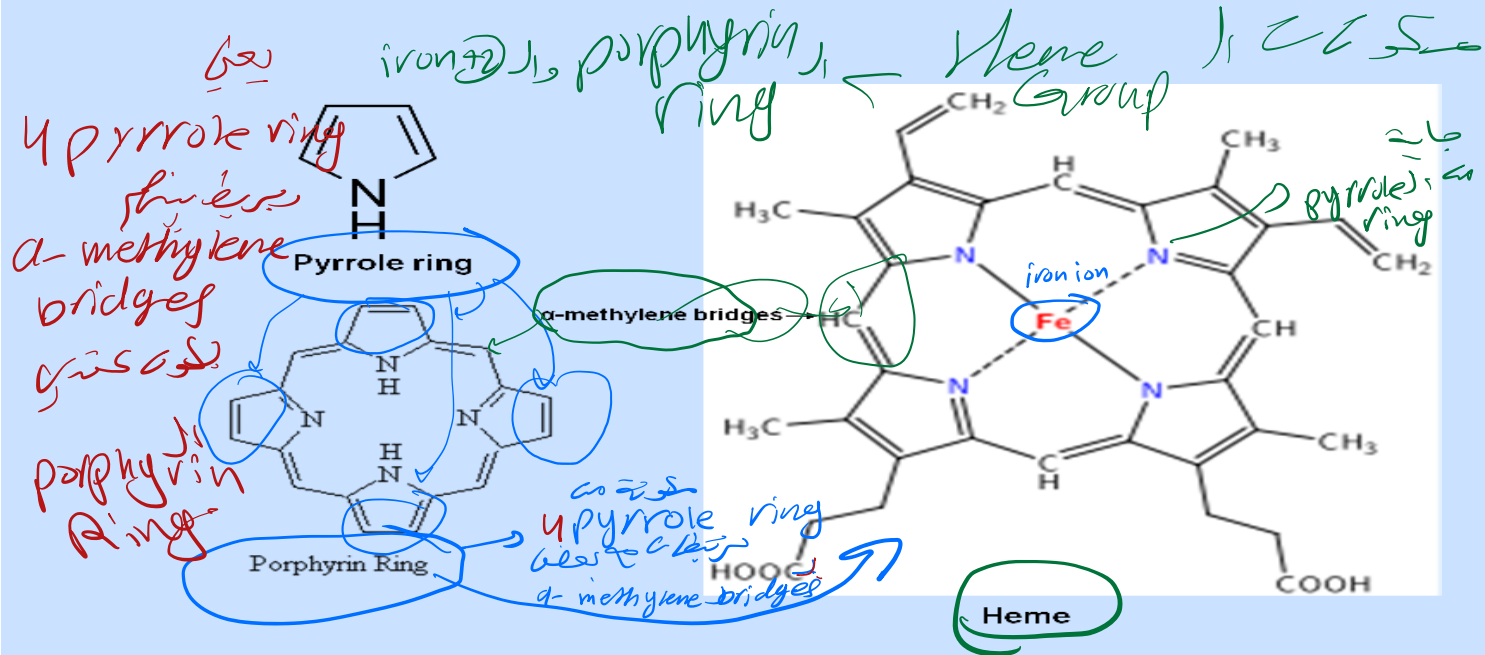
The heme of myoglobin lies between helices E and F.

• Three critical functions for Mb: 1- it holds the heme group, 2- it protects the heme iron atom from oxidation, and 3- it provides a pocket into which the O_2 can fit.

Hydrophilic
Iron
قدرته في تحييد الالوكسجين المتفرقة
Store as myoglobin
pocket
muscle

Structure of heme in myoglobin

- Heme is a complex of porphyrin and ferrous iron (Fe^{2+}).
- Porphyrins are a group of organic compound that have four pyrrole subunits interconnected via α -methylene bridges ($=CH-$)



The hydrophobic environment in the interior of myoglobin or hemoglobin prevents the oxidation of iron.

Heme structure

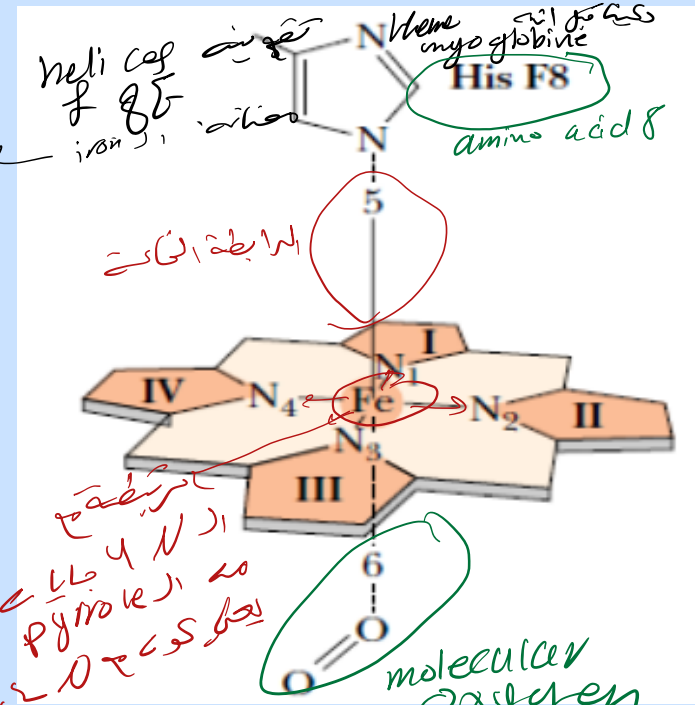
طبيعة الحديد (iron +2) دالةً بحيث يرتبط بالليجاندات 6

- The iron is held in the center of the porphyrin ring.
- Iron ions prefer to interact with six ligands.
- Four of the ligands to this iron ion are provided by nitrogen atoms in the pyrrole ring system.

myoglobin
 بعض شواهد على وجود ال heme group
 لازمة تكون مرتبطة بالبروتين نفسه

5 helix و 8 amino acid ترتبط بالبروتين

-The fifth ligand is provided by a nitrogen atom from the imidazole group of His 93 (proximal histidine) (also known as His F8 the eighth residue of the 'F helix' of myoglobin).



The sixth ligand to iron is provided by molecular oxygen, which binds to the heme group in a pocket formed by Mb.

دالةً الحديد (iron +2) يرتبط بالليجاندات 6
 روابط جالسة مع ال porphyrin ring
 والرابطة الخامسة جالسة مع ال heme group
 لأن ال heme group يرتبط بالبروتين نفسه
 لأنه لا يوجد على ال heme group

الرابطة السادسة
 ال N 4 جالسة مع ال heme group
 يعطى الرابطة
 molecular oxygen
 ال heme group يرتبط بالبروتين نفسه
 لأنه لا يوجد على ال heme group

مترجمه
والترجمة العامة من
molecular oxygen

طبعاً المرة الأولى بدت تعرفي انه اذا الاكسجين يرتبط جزيئاته
كل شكل البروتين اذا كان جزيئاته على شكل البروتين
وهذا يعني انه غير جزيئاته الا ان الاكسجين
في بعض الاكسجين او iron عليه وكما يجب
ال iron معناها هي البروتين
بجوه rubchiving شكل الصخر والبروتين

تم شكر الله

صلى الله عليه وسلم
