نوف الزندي .

GLOBULAR HEMOPROTEINS

what's the meaning of Globular ?
- كلمة كروي
- have 3 Dimention
- not more than one sub unit.

random note/ remember that hemeprotin in cytochrome can accept and release electrones (so iron in Hemoprotin cytochrome can be in oxdise and reduced state) but not in globular Hemoprotin.

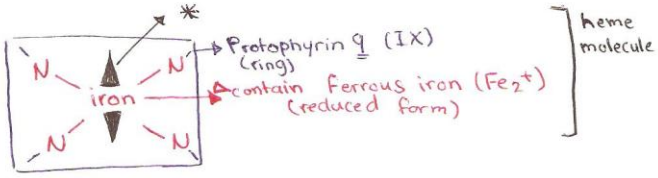
- Hemeproteins are a group of specialized proteins that contain heme as a tightly bound prosthetic group.
- Heme is a complex of protoporphyrin IX and ferrous iron (Fe^{2+}).
- The iron is held in the center of the heme molecule by bonds to the four nitrogens of the porphyrin ring.
- The heme Fe^{2+} can form two additional bonds, one on each side of the planar porphyrin ring.
- In myoglobin and hemoglobin, one of these positions is coordinated to the side chain of a histidine residue of the globin molecule, whereas the other position is available to bind oxygen

hemeprotin (الجزء من البروتين الذي يرتبط مع covalant bond)

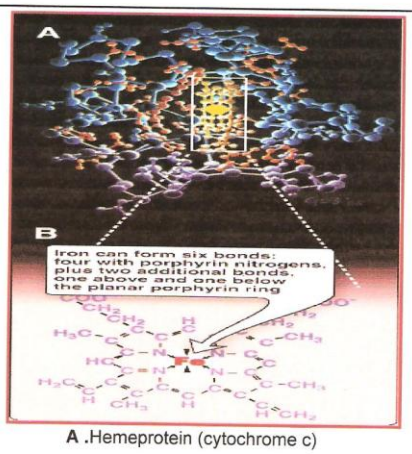
معنى آخر :
Hemoprotin is Protin contain (heme prosthetic ly (covalantly) bond to it)

these 2 additional bonds attach to histidine in myoglobin and hemoglopin

random note / Fe_2^+ is reduced and glopin or protin Part of hemeglopin prevent the oxidation of it.



So heme molecule containing
- iron (in the center) attach to prophyrin ring by 4 Nitrogens bonds
- two additional bonds one of each side of (Planar prophyrin ring)



A .Hemeprotein (cytochrome c)

B .Structure of heme

Myoglopin :- is globular heme-protin containing heme that attached to protin prosthetictly.

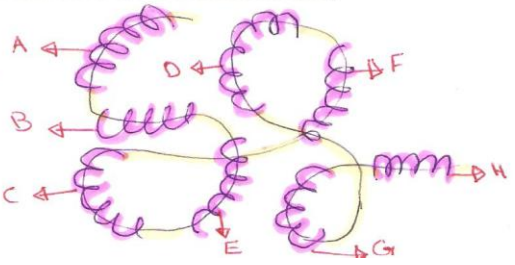
هي مخزن للأكسجين تعطيه للعضلة أثناء الحاجة ***Myoglobin*** ⇒ one subunit = tertiary globular protin

Structure and function:

- Myoglobin, a hemeprotein present in heart and skeletal muscle, functions both as a reservoir for oxygen, and as an oxygen carrier that increases the rate of transport of oxygen within the muscle cell.
- ① Myoglobin consists of a single polypeptide chain that is structurally similar to the individual subunit polypeptide chains of the hemoglobin molecule.
- ② Myoglobin is a compact molecule, with approximately 80 % of its polypeptide chain folded into 8 stretches of α-helix. These α-helical regions, labeled A to H ⇒ most of Myoglopin α-helical structure

- it's one polypeptide chain folded into 8 stretches of α helix (80 %)

this α-helical regions labeled A to H (8)

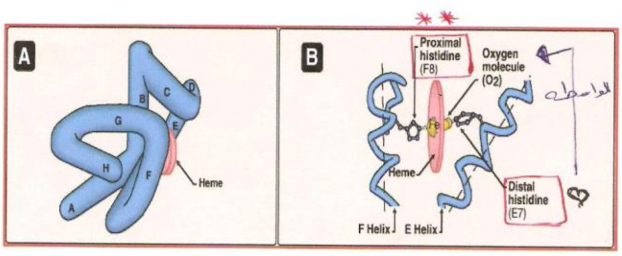


Amino acids → Polar → surface of molecule
قاعدة عامة
→ non polar → داخل (anterior of myoglopin)

ولكل قاعدة شواذ ⇒ except for histidine (inside the cervice) but they are polar

- The interior of the myoglobin molecule is composed almost entirely of nonpolar amino acids.
- In contrast, polar amino acids are located almost exclusively on the surface of the molecule.
- The heme group of myoglobin is located in a crevice in the molecule between helix E and helix F, which is lined with nonpolar amino acids. Notable exceptions are two histidine residues.

cervice
عبارة عن جرح أو شق صغير يوجد فيها الـ heme



A. Model of myoglobin showing helices A to H.
B. Schematic diagram of the oxygen-binding site of myoglobin

remember :- heme is complex of protoporphyrin 9 and ferrous iron (Fe_2^+)

Fe_2^+ have 2 additional bonds (one on each side of palanar porphyrine ring) attach to histedine

** one bond which is proximal histidine F8 (in F helix) ⇐ لاتحتاج لواسطة للارتباط بال (Fe_2^+)

♡ the other bond which is Distal histidine (E7) تحتاج لواسطة وهي (O_2) حتى ترتبط بـ (Fe_2^+)

For You: F8 → الكبيرين → directly =)
E7 → لصغيرين → indirectly

- One, the proximal histidine (F8), binds directly to the iron of heme.

- The second, or distal histidine (E7), does not directly interact with the heme group, but helps stabilize the binding of oxygen to the ferrous iron. ← الوظيفة

random note ⇒

- The protein, or globin, portion of myoglobin prevents the oxidation of iron of heme.

Hemoglobin

⇒ more than one = Quatarnary

sub unit = 4 subunit

more than one sub-unit.

Structure and function:

- Hemoglobin is found exclusively in red blood cells, where its main function is to transport oxygen from the lungs to the capillaries of the tissues.

- Hemoglobin A, the major hemoglobin in adults, is composed of four polypeptide chains - two α chains and two β chains - held together by noncovalent interactions.

- Each subunit has stretches of α-helical structure, and a heme-binding pocket similar to that described for myoglobin.

- However, the tetrameric hemoglobin molecule is structurally and functionally more complex than myoglobin.
- For example, hemoglobin can transport H^+ and CO_2 from the tissues to the lungs, and can carry four molecules of O_2 from the lungs to the cells of the body.
- Physiology → Furthermore, the oxygen-binding properties of hemoglobin are regulated by interaction with allosteric effectors .

مهم
هي عبارة عن مواد تتحكم بالخروج ودخول الـ O_2 مثل H^+ ، CO_2 ، 2,3 BPG

Form	Chain composition	Fraction of total hemoglobin
HbA (Adult)	$\alpha_2\beta_2$	90%
HbF (Fetal)	$\alpha_2\gamma_2$ (gama 2)	<2% in adult
HbA_2	$\alpha_2\delta_2$ (delta 2)	2–5%
HbA_{1c}	$\alpha_2\beta_2$-glucose	**3–6 %** ← normal

Normal adult human hemoglobins.

[Note: The α-chains in these hemo-globins are identical]

HbA1c could be used as a monitor for the control of the blood glucose level during the last 2 months for diabetic patients

اذا شك للمريض بالسكر لا تأكل Carbohydrate وأكل وهيب اكتشفه عن طريق HbA1c

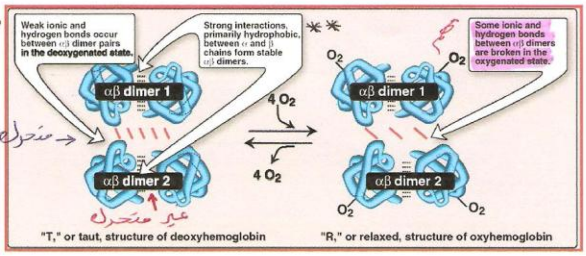
note/ $a_1 B_1$ → diamer 1
$a_2 B_2$ → diamer 2

** between the members of each diamar there's hydrophopic bond (non covalant bond) ← أقوى منه فهو أضعف منه

covalant bond لأنه ① أقوى للضعيفين ??
② ولكن الـ non covalant bond بين diamer 1 و diamer 2 أضعف منه (فلذلك هو أقوى للضعيفين)

♡ non covalant bond between diamer 1 and diamer 2
So it's movable متحرك
وهو أضعف الضعيفين

So the diamer is not movable ليس متحرك
work as one unit.



Schematic diagram showing structural changes resulting from oxygenation and deoxygenation of hemoglobin .

Quaternary structure of hemoglobin:

- The hemoglobin tetramer can be envisioned as being composed of two identical dimers, (αβ)1 and (αβ)2, in which the numbers refer to dimers one and two.
- The two polypeptide chains within each dimer are held tightly together, primarily by hydrophobic interactions
- In contrast, the two dimers are able to move with respect to each other, being held together primarily by polar bonds.
- The weaker interactions between these mobile dimers result in the two dimers occupying different relative positions in deoxyhemoglobin as compared with oxyhemoglobin

Tense form :-
because low affenity of O_2 to bind with Hb

right - shift of O_2-Hb curve
good at tissue level.

- rupture form :-
because of O_2 high affenity binding to Hb

Lift - Shift of O_2-Hb curve
good at lung level.

- **T form:** The deoxy form of hemoglobin is called the "**T**," or taut (tense) form.

diamer I diamer II

•In the **T** form, the two **αβ** dimers interact through a network of ionic bonds that constrain the movement of the polypeptide chains. The **T** form is the low-oxygen-affinity form of hemoglobin.

- **R form:** The binding of oxygen to hemoglobin causes the rupture of some of the ionic bonds between the **αβ** dimers. 1 αb_1 2 αb_2

•This leads to a structure called the "**R**," or relaxed form, in which the polypeptide chains have more freedom of movement . The R form is the high- oxygen-affinity form of hemoglobin.

Binding of oxygen to myoglobin and hemoglobin

- Myoglobin can bind only one molecule of oxygen (O2), because it contains only one heme group.
- In contrast, hemoglobin can bind four oxygen molecules—one at each of its four heme groups.

Physio

- The degree of saturation (Y) of these oxygen-binding sites on all myoglobin or hemoglobin molecules can vary between zero (all sites are empty) and 100% (all sites are full

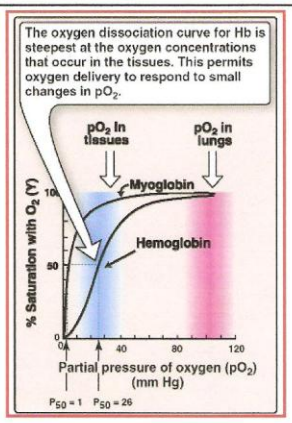
Y

the curve of myoglopin-O_2 → hyperbolic curve

the O_2-Hb curve → Sigmoid Curve

P_{O_2} at tissue level (in venous end) = 40 mmHg

Y = 75 (low)



Oxygen dissociation curves for myoglobin and hemoglobin

P_{O_2} at lung level (arterial end)

P_{O_2} = 104

Y = 97 (high)

Oxygen dissociation curve:

- A plot of **Y** measured at different partial pressures of oxygen (pO2) is called the oxygen dissociation curve.
- The curves for myoglobin and hemoglobin show important differences.
- This graph illustrates that myoglobin has a higher oxygen affinity at all pO2 values than does hemoglobin