Globular Proteins

biochemistry433@hotmail.com

Respiratory block

Color index:

Red= important

Purple = addition

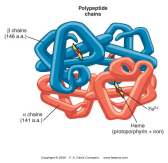
Orange = Explanation

Objectives:

- What are globular proteins.
- Types and functions of globular proteins.
- Hemoglobin (a major globular protein).
- Myoglobin.
- α, β-globulins.
- γ-globulins (immunoglobulins).
- Diseases associated with globular proteins.

Keywords:

- Globular proteins.



Globular proteins

• Formed from amino acid chains that fold into shapes that resemble spheres → that makes them more soluble in water
• Since water is polar, then the polar groups are arranged on the surface and the hydrophobic are arranged interiorly, so they can be soluble in water.
• Fibrous proteins are mainly insoluble structural proteins (found in gum) .

Hemoglobin

- O_2 transport function from lungs to tissue.
- CO_2 transport from tissue to lungs.
- Normal level (g/dL):

Males: 14-16 / Females: 13-15

Myoglobin

- O_2 storage
- supply function in heart & muscles

alpha1, alpha2, beta-globulins

- Various functions.
- Beta is more important than alpha.

gamma-globulins (immunoglobulins)

Immune function

enzymes

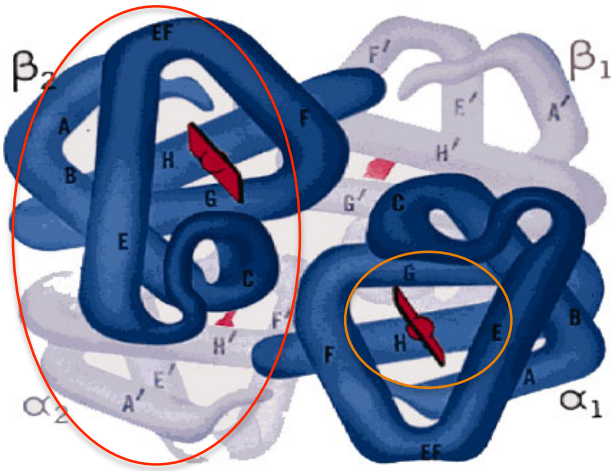
Catalysis of biochemical reactions

hemoglobin

A major globular protein in humans, composed of:

• 4 polypeptide chains: Two alpha and two beta chains.
•Contains two dimers of αβ subunits (a dimer is a macromolecular complex formed by two non-covalently bounded subunits).
• Each chain is a subunit with a heme group (planar structure that contains iron) in the center that carries oxygen, so there are 4 heme groups that carry 4 molecules of O_2, and only two molecules of CO_2.

dime



heme group

hemoglobin

Normal

abnormal

HbA (97%)

• Deoxygenated form: Weak hydrogen and ionic bonds occurs between alpha-beta dimer pairs.
• Oxygenated form: some of the ionic and hydrogen bonds are broken and relaxed to allow oxygen to bind.

HbF (1%)

•Major hemoglobin found in the fetus and newborn
•Tetramer with two α and two γ chains
•Since it has higher affinity to O_2 than HbA , O_2 is transferred from maternal to fetal circulation across placenta.
• function is unknown in adults.

HbA_2 (2%)

•appears ~12 weeks after birth.

•composed of 2 α & 2 δ globin chains.

HbA_{1c}

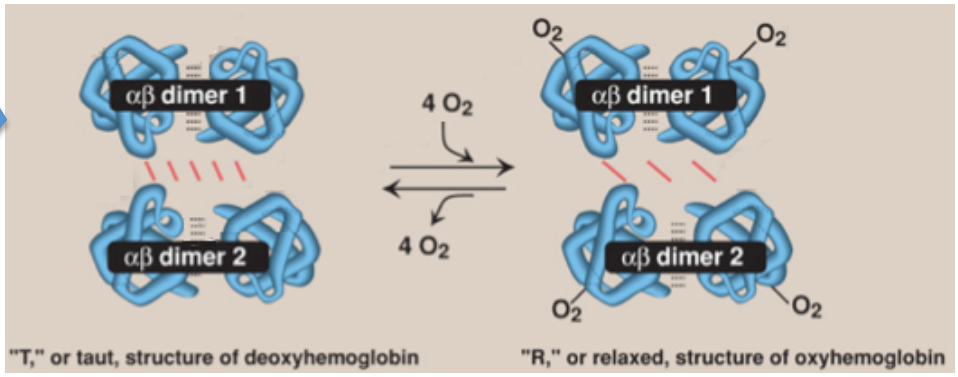
non-enzymatic

•HbA undergoes ~~enzymatic~~ glycosylation spontaneously depending on plasma glucose levels.

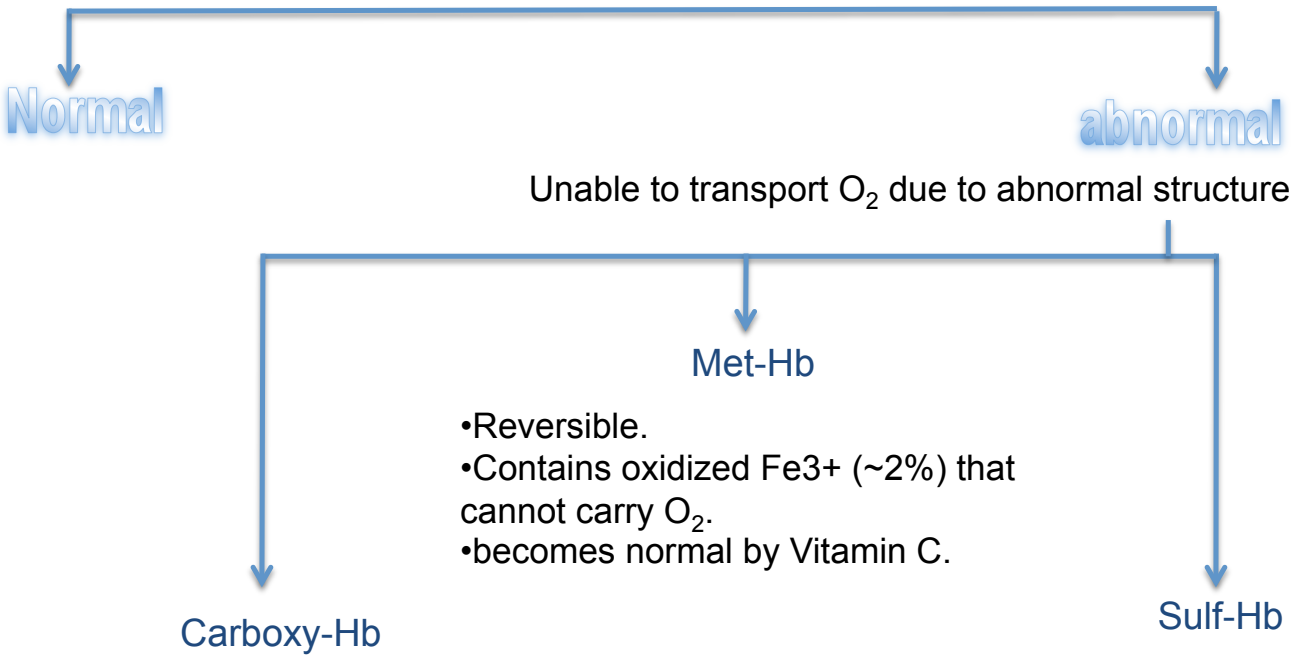
•**HbA + glucose = HbA_{1c}**

•high in patients with Diabetes Mellitus.

•Sensitive and specific marker for sugar level in blood.



hemoglobin


Normal
abnormal
Unable to transport O_2 due to abnormal structure
Met-Hb
•Reversible.
•Contains oxidized Fe3+ (~2%) that cannot carry O_2.
•becomes normal by Vitamin C.
Carboxy-Hb
•Reversible.
•CO replaces O_2 & binds 200X tighter than O_2 (happens in smokers).
Sulf-Hb
•Irreversible.
•Forms due to high sulfur levels in blood.

Hemoglobinopathies

caused by:

- Synthesis of structurally abnormal Hb (qualitative).
- Synthesis of insufficient quantities of normal Hb (quantitatve).
- Combination of both.

1 Sickle cell (HbS) disease

- Caused by a single mutation in β-globin gene which then causes the Glutamic acid at position 6 in HbA to be replaced by valine.
- The mutant HbS contains β^s chain.
- The shape of RBCs become sickled.
- Causes sickle cell anemia.

2 Hemoglobin C disease

- Caused by a single mutation in β-globin gene which then causes the Glutamic acid at position 6 in HbA to be replaced by lysine.
- Causes a mild form of hemolytic anemia.

3 Methemoglobinemia

- Caused by oxidation of Hb from ferrous to ferric (Fe3+) state.
- could be congenital.
- Methemoglobin cannot bind to oxygen.
- Caused by certain drugs, reactive oxygen species and NADH-cytochrome b5 reductase deficiency
- Chocolate cyanosis: brownish-blue color of the skin and blood.

Hemoglobinopathies

4 Thalassemia

Defective synthesis of either α or β-globin chain due to gene mutation

α-thalassemia

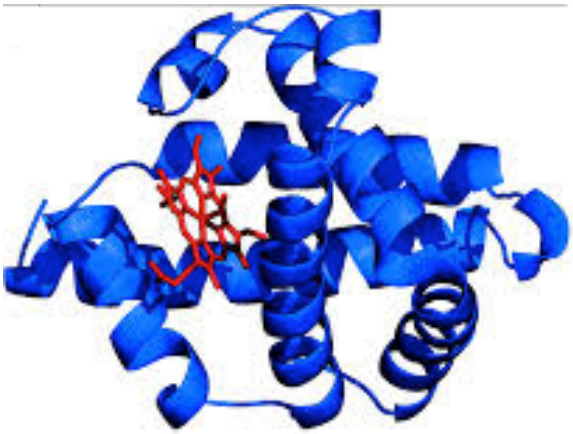
- Synthesis of α-globin chain is decreased or absent.
- Causes mild to moderate hemolytic anemia.

β-thalassemia

- Synthesis of β-globin chain is decreased or absent.
- Causes severe anemia
- Patients need regular blood transfusions.

myoglobin

• A globular hemeprotein in heart and muscle.
•Stores and supplies oxygen to the heart and muscle only.
•Contains a single polypeptide chain forming a single subunit with eight α-helix structures.
•The interior of the subunit is composed of nonpolar amino acids and charged amino acids are located on the surface.
• The heme group is present at the center of the molecule.
• Myoglobin gives red color to skeletal muscles.
•Supplies oxygen during aerobic exercise.
•Binds to 1 o_2 molecule only.



Myoglobin in disease

•Myoglobinuria: Myoglobin is excreted in urine due to muscle damage (rhabdomyolysis).

•May cause acute renal failure because the heme part which contains iron is oxidized and that leads to the oxidation of renal cells.

•Specific marker for muscle injury.

•Less specific marker for heart attack.

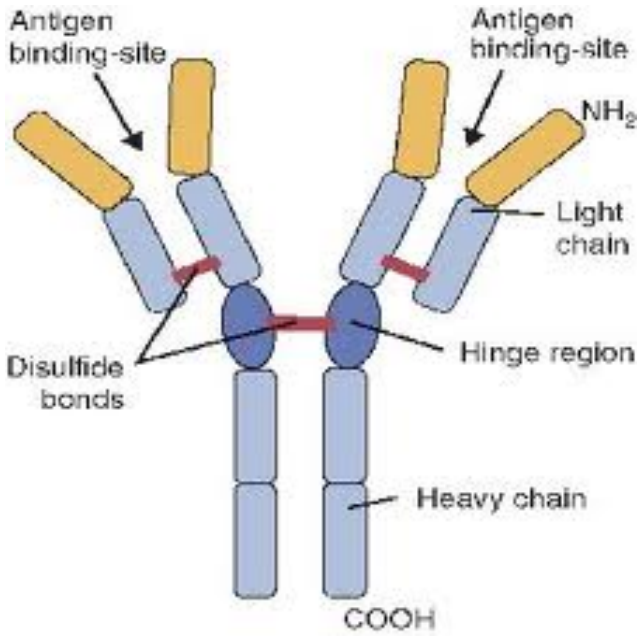
Immunogloulins

•Defensive proteins produced by the B-cells of the immune system.

•Y-shaped structure with 2 heavy and 2 light polypeptide chains.

•Neutralize bacteria and viruses → antibodies bind to antigens to make it bigger and more recognizable to macrophages to engulf them.

•Types: IgA, IgD, IgE, IgG, IgM.



Summary

•Amino acid chains that fold into shapes that resemble spheres are called globular proteins .

•Hemoglobin is the major globular protein in humans .

•Hemoglobin function Carries oxygen from the lungs to tissues and Carries carbon dioxide from tissues back to the lungs .

•Normal level (g/dL): Males: 14-16 and in females 13-15 .

•Types of normal hemoglobin are HbA , Fetal hemoglobin (HbF) that has Higher affinity for bind to oxygen than HbA , HbA_2 and HbA_{1c} that is found in high levels in patients with diabetes mellitus .

•Types of abnormal hemoglobin are Carboxy-Hb, Met-Hb and Sulf-HB .

•Sickle cell (HbS) disease and Hemoglobin C disease are caused by a single mutation in b-globin gene and cause sickle cell anemia and mild form of hemolytic anemia respectively .

•Methemoglobinemia is caused by oxidation of Hb to ferric (Fe^{3+}) state results in Chocolate cyanosis: brownish-blue color of the skin and

• .Myoglobin is A globular hemeprotein in heart and muscle and it supplies oxygen during aerobic exercise.

•Myoglobinuria : Myoglobin is excreted in urine.

•Immunoglobulins Neutralize bacteria and viruses.

Quiz yourself

1- Which of the following is the hemoglobin that is found in fetus and newborn:

A) Hb-F
B) Hb-A
C) Hb-A_{1c}
D) Met-HB

2- Which of the following are the normal levels of hemoglobin (g/dL) in females:

A) 9-11 g/dL
B) 13-15 g/dL
C) 14-16 g/dL
D) 11-13 g/dL

3- Type HbA2 of hemoglobin appears at:

A) ~14 weeks after birth.
B) ~6 weeks after birth.
C) ~8 weeks after birth.
D) ~12 weeks after birth.

4- Sickle cell (HbS) disease is caused by which of the following:

A) A single mutation in β-globin gene.
B) A double mutation in β-globin gene.
C) A single mutation in γ-globin gene.
D) A double mutation in γ-globin gene.

ANSWERS:

1-A 3-D
2-B 4-A

From our team members :

Sara alDokhayel
Maha AlRajhi
Layan AlTaweel
Maram AlAqil
Amjad AlBatili
Lamees alMezaini
Ghada AlHindi

Ahmed Alhussien
Ahmed AlQhtani
Mojahed Otef
Ahmed Alzoman
Meshal AlOhali
Abdullah AlDurihim

You can contact us at:
Biochemistry433@hotmail.com