5. MOLECULAR BIOLOGY
FIRST MYOGLOBIN-LIKE HEME-CONTAINING PROTEIN IN ARCHAEA

All biological cells require energy, both to drive the chemical reactions involved in building cell components, and to power the activities of these components. In many biological systems, the major source of energy involves the utilization of molecular oxygen in specific chemical processes, with such utilization dependent on the recognition and uptake of oxygen by specific biochemical entities.

In general, the term "heme" (ferroprotoporphyrin) refers to any iron-porphyrin complex irrespective of the valence state of the iron atom, and the term "heme protein" (hemoprotein) refers to any protein to which an iron-porphyrin compound is linked in a stoichiometric manner [*Note #1]. The heme proteins include hemoglobin, myoglobin, various cytochromes, catalase, and some peroxidases. The term "hemoglobin" refers to any of a group of red, iron-containing, oxygen-carrying pigments of the blood of vertebrates and some invertebrates; the substance also occurs in the root nodules of leguminous plants. All vertebrate (including human) hemoglobins consist of two pairs of associated protein polypeptide chains ("*globins"), each polypeptide chain carrying a heme *prosthetic group in non-covalent bonding, the iron atom of which is in the ferrous state and forms a coordination complex with the pyrrole nitrogens. Myoglobin is a similar macromolecule, occurring in muscle fibers, and consisting of a single polypeptide chain of 153 amino-acid residues to which a single ferroheme prosthetic group is non-covalently bound. (In a vertebrate physiological context, in muscle fibers, hemoglobin essentially transports oxygen via the blood to cellular myoglobin, and myoglobin then stores the oxygen for subsequent release to intracellular enzymes when the local oxygen supply becomes limiting.)

The archaebacteria (also called the Archaea) are considered to be ancient compared to other kingdoms, and are possibly the most ancient life forms. They typically exist in extreme environments, and include the methane-producing bacteria (methanogens), the "salt-loving" bacteria (halophilic bacteria), and the sulfur-acid tolerant thermoacidophilic bacteria. There is presently a controversy concerning whether the Archaea should be classified as a kingdom separate from the Bacteria. If such a distinction is made, then the three primary kingdoms of life forms are Archaea, Bacteria, and Eukarya, the first two (prokaryotes) without internal membrane-bound organelles such as a nucleus, while Eukarya (eukaryotes) do have such internal organelles.

The term "aerotaxis" refers to the movement of an organism, especially bacteria, with reference to a directed gradient of oxygen or air.

Comparisons of the amino acid sequences of globins from Bacteria and Eukarya suggests that they share an early common ancestor, but until now no members of the globin family have been found in Archaea. Also, recent studies of biological signaling in the Bacteria and Eukarya have revealed a new class of heme-containing proteins that serve as oxygen sensors, but no heme-based sensor has been described in the Archaea.

... ... S. Hou et al (8 authors at 3 installations, US) now report the first myoglobin-like heme-containing protein in the Archaea, and the first heme-based aerotactic transducer in the Bacteria. The authors report these proteins exhibit spectral properties similar to those of myoglobin and trigger aerotactic responses.

S. Hou et al: Myoglobin-like aerotaxis transducers in Archaea and

Bacteria.
(Nature 3 Feb 00 403:540)
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Text Notes:
... ... *Note #1: The porphyrins are cyclic organic molecules that form the basis for many important biochemical compounds. They form complexes with metal ions, iron in the case of hemoglobin and magnesium in the case of chlorophylls, and this property is essential to their function.
... ... *globins: The term "globin" refers to the globular protein that complexes with the heme group in oxygen-carrying proteins such as hemoglobin and myoglobin. (This term must be distinguished from "globulins", which refers to a class of globular proteins of importance in the immune system).
... ... *prosthetic group: The non-protein group of a *conjugated protein. It may be another organic molecule or an inorganic metal ion.
... ... *conjugated protein: A protein to which a non-protein component (prosthetic group) is attached. This should not be confused with "conjugated" as a term referring to alternating single and double bonds in a chemical structure.

Summary & Notes by SCIENCE-WEEK [http://scienceweek.com] 24Mar00
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Related Background:
THE EVOLUTION OF HEMOGLOBIN
Heme is an iron-containing porphyrin acting as the prosthetic group of several biological pigments, including hemoglobin, *myoglobin, and several *cytochromes. Hemoglobin is the chief transport protein involved in carrying oxygen within red blood cells (erythrocytes). The heme *prosthetic group is similar in a variety of hemoglobins, but the globular *apoenzyme has fluctuated considerably in the course of evolution. Hemoglobin is a tetrameric molecule, consisting of two pairs of nonidentical polypeptides associated in a quaternary structure, each of the 4 heme groups containing an iron atom that binds oxygen reversibly. The molecule occurs intracellularly in vertebrate erythrocytes, but in invertebrates hemoglobin is usually found in simple solution in the blood. It is also found in certain *nitrogen-fixating plants. A variety of hemoglobin types are especially evident in mammals, and in some cases specific polypeptide chains are different for the fetus than for the adult. The molecule produces a red color when oxygenated and a bluish-red color when deoxygenated. The ability of the hemoglobin molecule to pick up and unload oxygen depends on its shape in solution, and this shape varies *allosterically with local pH, which in turn is a function of the partial pressure of blood carbon dioxide. Carbon dioxide combines with hemoglobin at its amino groups. Carbon monoxide (CO) is highly poisonous because it binds to hemoglobin irreversibly, causing suffocation at the cellular level. Human hemoglobin consists of 574 amino acids, and has a globular shape with a diameter of approximately 6 nanometers. The hemoglobin concentration in normal human erythrocytes is extremely high: in the erythrocyte, the hemoglobin molecules are only 1 nanometer apart, but they apparently can rotate and flow past one another without hindrance. ... ... Ross Hardison (Pennsylvania State University, US) presents a review of current research concerning the molecular biology and evolution of hemoglobin, the author making the following points concerning the evolution of the molecule:
1) The 3-dimensional structure of hemoglobin -- its shape, folds, pockets, and surfaces -- have been well conserved over the

folds, pockets, and surfaces -- have been well conserved over the evolutionary history of the protein. But some of the most rapid and dramatic changes in hemoglobin proteins have occurred in the ways these molecules are regulated -- the when and how of their manufacture inside the cell.

2) The active core of hemoglobin, the porphyrin ring, which is responsible for the basic chemistry of the molecule in which it is located, eventually came to be embedded, via evolution, in larger organic structures. The structure of these organic molecules imparts to the molecule its specific function, determining, for example, whether that basic chemistry was used in connection with respiratory reaction chains, oxygen transport, or oxygen sequestration. Thus, structural changes in these organic molecules have been translated into functional changes.

3) Structurally similar molecules can become further differentiated functionally by being expressed at different times in the development of an organism, as is the case for fetal and adult *globins, or under different circumstances, such as the scarcity or abundance of oxygen. These distinctions are not attributable to differences in the overall structures of the proteins themselves, but to the differences in *expression profiles achieved through differences in regulatory segments of genes. It has become apparent that in many cases regulatory regions of genes are changing more rapidly via evolution than are the structures of proteins themselves.

4) This idea is relatively new in the study of molecular evolution, which has concentrated on comparisons between protein structures to determine evolutionary relationships between species. But molecular evolutionists are beginning to recognize the value of looking at relations between regulatory regions.

Ross Hardison: The evolution of hemoglobin.
(American Scientist Mar-Apr 1999 87:126)
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Text Notes:

... ... *myoglobin: See main report.

... ... *cytochromes: The cytochromes are a system of electron-transfer proteins with iron- or copper-porphyrin as a prosthetic group. They are found in both animal and plant cells.

... ... *prosthetic group: See main report.

... ... *apoenzyme: In general, this refers to the protein component of an enzyme-cofactor complex (holoenzyme). The apoenzyme is usually catalytically inactive by itself.

... ... *nitrogen-fixating plants: In general, the incorporation of atmospheric nitrogen to form nitrogenous organic compounds.

... ... *allosterically: In general, an "allosteric" molecule is a molecule whose 3-dimensional conformation alters in response to a change in its environment, the alteration resulting in a change in molecular function. So, for example, the hemoglobin molecule is allosteric under different blood pH values.

... ... *globins: See main report.

... ... *expression profiles: The "expression profile" of a genome or a group of genes in a genome refers to the set of genes that have been "switched on" to express their proteins. Various types of cells have different expression profiles, and within a single type of cell, the expression profile may change during the life history of the cell.

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