HEMOGLOBIN – BILLIONS YEARS OF EVOLUTION

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The lecture is dedicated to the problem of origin and evolution of hemoglobins as protein superfamily. Hemoglobins were found in all kingdoms of living organisms.

After the discovery of bacterial Hb in 1986 it was supposed that the prokaryotic and eukaryotic Hb have a common origin. The main point of view now is that all Hb lineages have evolved from bacterial proteins. Proposed stages of early hemoglobin evolution are: (1) Emergence of ancestral Hb and its initial evolution (~4100–3500 Ma) - the ancestral Hb with a 3/3 α-helical folding finally emerged ~3500 Ma; (2) Divergence of 2/2 and sensor 3/3 hemoglobins; subsequent attachment of nonhemoglobin domains to the C-terminus, yielding chimeric Fgb and GCS (~1600–1000 Ma); and (3) Horizontal gene transfer from some globin lineages to certain groups of archaebacteria and unicellular eukaryotes before the origin of multicellular organisms (~900–650 Ma).

The evolution of Hb structure is tightly connected with the evolution of their functions. The primary functions of ancestral Hb were transformation of NO into a less toxic form; and O_2 detection, isolation, and detoxication, because they functioned in bacteria under predominantly oxygenless conditions. And even now the main function of 3/3 Fgb and 2/2 Hb is NO detoxication; and GCS play the role of O_2 sensors and regulators of gene activity. During the evolution, the changes in conditions of Hb functioning induced changes in the heme region and other regions involved in ligand binding, which led to the loss of several properties by ancestral proteins. For instance the majority of extant Hb lack cysteine E19, involved in H_2S binding in annelid Hb; this is result of adaptation to O_2 conditions and the absence of H_2S in the environment. Thus almost every serious evolution innovation led to appearance of new Hb with modified properties and functions which sometimes can be presented in the same organism..

Presumably, the ancestral Hb had a hexacoordinated iron. Then, on the emergence of a pentacoordinated heme iron, the existing hemoglobin functions were supplemented with new ones. The evolution of functions was directed not only to the modification of the heme pocket, but also to a change in the length of the polypeptide chain, fusion with other proteins, and the formation of oligomers. All these changes assisted the emergence of a wide range of functions: transport and storage of O_2, H_2S, NO, and CO and peroxidase activity. Appearance of oligomeric structures for Hb molecule resuled in allosteric effect in it. The invertebrate Hb provide an illustrative example of multifunctionality, because they are involved in the transport and storage of oxygen and sulfides and can act as enzymes with oxidase, peroxidase, and superoxide dismutase activities. All other functions for the oxygen-carrying Hb are the traces of enzymatic functions that were dominating in the past.

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