ANION EXCHANGER OF ERYTHROCYTES MEMBRANE (REVIEW)

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Erythrocytes membrane representations as fiber lipid complex are well-known, they have been included into school textbooks. Now the basic tendency of molecular membraneology and cellular physiology is to disclosing separate components of a cellular membrane and providing of normal functioning of a cell in its interrelations with an environment. In the review the modern condition of question on structure and functions of one of integrated fibers of a cellular membrane identified as fiber of strip 3 (f.s.3) with the help of electrophores is considered. In erythrocytes of f.s.3 carrying out anion exchange, mediates carry H^+ inside of cell and serves as the active participant of transport CO_2 in blood of the person and animals.

Structure of anionexchanger

Human f.s.3 is a part to the multigenic family of related fibers including three isoforms F.s.3 of erythrocyte membrane membranes relates to isoforms AE1, functioning. AE2 – anionexchanger presents in tissues. AE3 is expressed with the cells of heart, brain and retina tissues [5,13].

AE1 of person erythrocytes is glychosilire membrane fiber with molecular weight 110 consisting of 911 amino acids [21]. There are two 2 functionally differing domains in it: C-terminal, penetrating into membrane, and N-terminal, M=40, exhibited on its surface [3, 27, 33].

The analysis of cloned AE1 has shown significant homology of its trance membrane domains at various kinds of animals. The all consist of 10 waterproof regions penetrating membrane at least in 12 times. The N-terminal domain, on the contrary, showed divergence during evolution. Only responsible for linkage of ankirin the fragment of this domain is homologues among AE1 of different kinds [20].

In particular, transmembran domain of erythrocyte anion exchanger of chicken is more than in 70 % homologues to domains of f.s.3 of other kinds [7]. The waterproof part of molecule penetrates the membrane in 12-14 times. The majority of the amino acids directly participating in carry anions are conservative. On the other hand in N-terminal domain about 90 amino acids of human and rat f.s.3 are absent, as a result there is no site of linkage gliceraldehyde -3-phosphatdegidrogenase. The other part of cytoplasm domain is only in 40 % similar to N-domains of other kinds though the ankirin connecting region is conservative [7].

By means of antibodies to various sites citoplasmatic domain f.s. 3 it is shown [20], which sites of linkage of ankirin are localized at cistein cluster 21-317 and in N-terminal area citoplazsmatic domain that specifies presence of 2 various sites citoplazsmatic domain AE1, on primary sequence is far from each other [34].

The famous aspect, concerning structures of this fiber is its oligomer condition. AE1 can be covalent connected in diameters and actually in a membrane, presented as a mix of homodimers and homotetrametres [27]. Only after denaturation by dimetilmalein angidrin or SDS anionexchanger of membranes passes in the monomeasured form. Ankirin is connected, basically, with teramers AE1 [30]. This conclusion follows from data on anisotropy of fluorescence in which existence of 2 populations AE1 - is proved to one with smaller molecular weight, more mobile, another - with greater, immobilized [30].

Functions of anion exchanger

Each of two domains AE1 carries out strictly certain functions. For transport of anions is responsible C-terminal penetrating membrane area. Process of carry of ions is electrically neutral, owing to it transport CO2 by blood and stabilization pH plasmas is carried out [7, 15, 34]. In actually anion transport is involved a fragment of molecule P5, change of which causes proteolitic degradation of erythrocyte shadows. Here join all

known inhibitors of anion exchange (in particular at pH 7.3 – inhibitor of anion transport of phenilisotiocinat) [29].

AE1 transports small molecules of anions, including Cl-, HCO3-, H2PO4-, SO42- and others. Speed of exchange Cl- is constant at pH 7 11, hence, univalent anions are communicated under the transfer with guanidine group of the rest of arginin since only this amino acid has high value of pK and remains thus pH positively charged. For measurement of activity of ino exchange SO42 is often used which is transported in 104 times more slowly, than Cl-[31]. It is assumed, that with bivalent anions (SO42-, HPO42-) contransport H^+, unconnected from - ε-amino groups near to the rest of lisin [2, 20].

Speed of work of AE1 depends from pH and concentration of endocellular Ca^{2+}. Optimum for exchange oxalate/chloride value extracellular pH makes at 5.5. At alkaline values pH environments transport of anions are inhibited because of deproton of groups with pK 11.3 [20]. Ionophor AE23187, causing increase in concentration of endocellular Ca2 +, inhibits anion exchange [32].

AE1 mammals plays a critical role in system of transport CO2. In system capillaries CO2 on a gradient of paracial pressure diffunds in erythrocytes where turns in HCO3- which in turn leaves from erythrocytes in exchange for extracellular Cl-owing to work of AE1. Speed of such exchange is very high - the order 5*104 anion/s with - on this parameter this fiber is one of the fastest fibers-conveyors [1]. As quantity AE1 in a membrane is very great (1.2*106 spears/cells) [12], speed anion exchange for some orders exceeds speed of all other reactions participating in transport CO2.

Because of high permeability of membrane for anions, membrane potential of erythrocytes is according to transmembrane distribution of Cl.. Transport H^+ in эритроцит is carried out by reactions of cycle of Jacobs-Stewart [10]: in reply to extracellular loading acid H + incorporates to bicarbonate. H2CO3 is formed a coal acid which dehydrates up to CO2, quickly diffunding in erythrocyte inside of a cell. CO2 again hydrates up to HCO3 and H^+. Most part of H^+ is neutralized, and bicarbonate leaves the cell in exchange for Cl^- which acts inside of erythrocyte through anionexchanger. This phenomenon (хлоридный shift, by Hamburger), finishes the cycle.

N-terminal segment AE1 is not involved in transport of anions. Its removal does not break transport activity [20]. This region cooperates with ankirin, f.s. 4.1 and f.s. 4.2 [7, 13, 14, 34], forming sites of an attachment of a membrane to cytoskeleton. Owing to it the biconcave form erythrocyte [34] is supported. Hemoglobin, enzymes and glicolis also are attached to N-segment [16, 19], hemihromes which can cause aggregation of AE1 or change of the form of cells [4]. C-area of N-segment is connected with karboangidrase, forming methabolone, mediating carry of HCO3.[4, 31].

In old erythrocytes AE1 serves as an antigene, signal for their removal from blood channel [22]. It is also a receptor for invasion of *Plasmodium falciparum*. The mutation or deletion of a gene AE1 leads to occurrence of various variants of erythrocyte morphology and such diseases, as south Asian ovalocitose and erythrocyte spherocitose. Mice with insufficiency of AE1 have hemolytic anemia, growth and development is late, the percent if neonatale destructions [26] strongly raises.

AE1 also is responsible for group specificity of blood. Antigenes of Diego connected with dot mutations in its molecule (Di^a, Di^b, Rb^a, WARR, Wd^a). The changes of amino acids connected with last three antigens makes accordingly 548 Pro - Ley, 552 Thr - Ile, 557 Val - met [18].

If functioning of this fiber in denuclearized erythrocytes is investigated in details [8,9,10, 17] data about AE1 in nuclear erythrocytes of the invertebrates are not numerous [25].

In the membrane of nuclear erythrocytes all vertebrates except for Agnata also there is plenty of AE1, carrying out eletroneutral exchange Cl^- on ^{HCO3}.[23, 28].

Limiting step of transport of H^+ is non-catalised extracellular stage of dehydration of coal acid up to CO2. In comparison with a speed of anion exchange $t_{1.2}$ this reaction is in 100 times has less than exchange, than speed of anion exchange [28]. All steps of Jacob-Stewart 's cycle are passive. H^+ is distributed on both sides of erythrocyte membranes in conformity with value of membrane potential created by chloride.

Other mechanisms of carry H^+ in erythrocyte work only under special conditions. In [9] it is shown, that after degazing of environments reduction of concentration of H^+ occurs due to movement through membrane of H^+ or OH^-, kinetic characteristics of both types of transport are equivalent. Probably, stream of H^+, carried out on mechanism of N^+, Cl^- cotransport, dominates under sour values of pH, OH^-/Cl^- an exchange at alkaline.

Thus, successes in understanding of features of anion exchange between erythrocyte cell and the extracellular environment are rather significant. At the same time there is a big layer of problems which development depends not only the base of modern membranology, but also a lot of the practical problems connected first of all with clinic.

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