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Erythrocyte-bioreactors that neutralize ammonium

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Abstract

Erythrocytes (RBCs) with built-in metabolic pathways that are absent in normal RBCs are called erythrocyte-bioreactors (EBRs), and can be produced by encapsulating enzymes catalyzing target reactions into normal erythrocytes. They can be used to treat some diseases by regulation of the concentration of certain metabolites in a person's blood. EBR metabolism is a complex system in which an embedded metabolic pathway interacts with the natural metabolic system of the erythrocyte. Some of these interactions can cause disruptions in the resulting metabolic system, with consequences ranging from decreased EBR efficiency to cell death. To develop an effective EBR, an analysis of the factors limiting the maximum effectiveness of EBR is required. There are two groups of such factors. The first of them includes restrictions caused by the low permeability of the RBC's membrane for substrates or products of the target reaction. If the substrate passes through the membrane slowly, the efficiency of EBR is low, since the maximum rate of the target reaction is limited by the substrate influx. If the product can not be quickly removed from the cell, accumulation of this product can lead to osmotic lysis of the EBR. The second group of limitations is due to the interactions of the embedded metabolic system with the own metabolism of RBCs. In this work, we analyzed these limitations on the example of ammonium-neutralizing EBRs using mathematical models of their metabolic system. The analysis showed that the main limitation is associated with the interaction of the built-in ammonium consumption pathway with the pentose phosphate pathway through the joint NADPH oxidation, which, at certain concentrations of incorporated enzymes, can lead to the loss of the steady state in glycolysis.

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Biography

Evgeniy Protasov was born in Stavropol, Russia in 1991. In 2015, he graduated from the Physics Department of Lomonosov Moscow State University. He is a junior researcher at the Center for Theoretical Problems of Physicochemical Pharmacology, Russian Academy of Sciences, and the Dmitriy Rogachev National Medical Research Center of Pediatric Hematology, Oncology, and Immunology, Moscow, Russia.

Publications

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