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Capacity of Bioregulators of Stem and Progenitor Cells to Strongly Affect Liver Redox-Dependent Processes

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Abstract

Effects of stem and progenitor cells or their compounds on recipient cells are investigated intensively today. In spite of this, their ability to interact with native cells and the final targets affected by them, particularly biochemical parameters that characterize cell redox-dependent processes, remain little studied. We have studied how bioregulators of stem and progenitor cells affect these processes in freshly isolated liver after animal pretreatment *in vivo*. Cytosol of human fetal mesenchymal–mesodermal tissues (8–10 weeks gestation) was administered intravenously; the control group was treated with Hanks' solution. After 4 hr, rats were sacrificed and their livers were isolated. To evaluate liver redox-dependent state, mitochondrial respiratory activity and nitroxyl radical and Alamar Blue™ reduction rates, mitochondrial and cytosolic glycerol kinase and nicotinamide adenine dinucleotide (NADH)-dependent malate dehydrogenase activities were studied. The results obtained demonstrate that bioregulators strongly affect liver redox-dependent processes, increasing mitochondrial respiration in state III and spin probe reduction rate and enhancing Alamar Blue™ reduction by glycolytic and nonglycolytic postmitochondrial enzymes. In addition, mitochondrial glycerol kinase and both isoforms of NADH-dependent malate dehydrogenase were inhibited. These data bring us closer to understanding stem and progenitor cell effects via directed regulation of metabolic redox-dependent processes.

Introduction

At present, the study of stem and progenitor cells of various origin is a rapidly developing area of cellular biology and medicine. These *in vivo* and *in vitro* studies deal with both the properties of these cells and their effects realized during transplantation in animals and human. Among the most important participants in these effects are the biologically active substances produced by stem and progenitor cells. In particular, signal cascades from transplanted cells to recipient cells and vice versa have been discovered. These cascades include growth factors, cytokines, their receptors and transcription factors, protein kinases, and so forth. However, the specific biochemical indices that represent the final targets affected by bioregulators remain almost unstudied.

Another side of this problem is the widening of commercial propositions to rejuvenate and to revitalize the human organism by various stem or/and progenitor cell preparations, and extracts. These programs often result in improvement of the psycho-physical state of aged recipients. Some of these programs are controversial because they are of doubtful reputation and the mechanisms and pathways responsible for their effects are unknown.

It is well known that developing tissues are characterized by the highest content of stem and progenitor cells at early stages of embryogenesis. Thus, we decided to use fetal tissue cytosol (FTC) of mesenchymal–mesodermal origin consisting of protein and peptide bioregulators for animal pretreatment before stress influence or for support of experimental pathology. It has been shown that FTC administration to animals *in vivo* for 4 hr before acute toxic hepatitis induction[1] or liver isolation for hypothermic storage[2] led to a significant decrease in organ injury degree and supported liver prooxidant/antioxidant balance during 3 days in the first case and 24 hr in the second one. In models of experimental cirrhosis[3] and chronic alcohol poisoning,[4] FTC was introduced to animals with generated pathology and the observation term was prolonged to 2 weeks. In these cases, FTC efficacy was also shown, especially its capacity to stimulate liver reparative processes and partially restore injured organ functional state. Thus, the community of observed effects was almost independent on experimental model and this fact undoubtedly, closely with universality of targets for FTC action.

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