Review

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Ion Channels Involved in Cell Volume Regulation: Effects on Migration, Proliferation, and Programmed Cell Death in Non Adherent EAT Cells and Adherent ELA Cells

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Key Words
VRAC • TMEM16 • TASK-2 • RVD • Osmotic stress • Cell migration • Cell proliferation • Programmed cell death • Apoptosis

Abstract
This mini review outlines studies of cell volume regulation in two closely related mammalian cell lines: nonadherent Ehrlich ascites tumour cells (EATC) and adherent Ehrlich Lettre ascites (ELA) cells. Focus is on the regulatory volume decrease (RVD) that occurs after cell swelling, the volume regulatory ion channels involved, and the mechanisms (cellular signalling pathways) that regulate these channels. Finally, I shall also briefly review current investigations in these two cell lines that focuses on how changes in cell volume can regulate cell functions such as cell migration, proliferation, and programmed cell death.

Introduction

Current knowledge of cell volume homeostasis supports the notion of a pump-leak balance, based on the pump-leak, steady-state concept introduced by Krogh [1] and analysed in detail by Leaf [2], Ussing [3], and Tosteson and Hoffman [4]. Later, many of the classical "leak" pathways were found to be the actual effectors of volume regulation, due to their extreme sensitivity to changes in cell volume. This mini review will discuss two of these effector pathways (the K^+ and Cl^- channels involved in RVD) and their regulation in two model cell types: Ehrlich ascites tumour cells (EATC) and Ehrlich Lettre ascites (ELA) cells. The basic physiology of cell volume regulation has been detailed in previous reviews [5-7].

Regulatory volume decrease (RVD)

In EATCs, the osmotic permeability to water is 10^5 times higher than the permeabilities to K^+ and Na^+ [8] and 10^6 times higher than the permeability to Cl^- [9]. Thus,

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Review

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Life and Death of Lymphocytes: A Volume Regulation Affair

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Key Words
Cell Volume Regulation • Apoptotic Resistance • Osmotic stress • RVI

Abstract
The loss of cell volume, termed apoptotic volume decrease (AVD) has been a hallmark feature of apoptosis. However the role of this characteristic attribute of programmed cell death has always been questioned as to whether it plays an active or passive factor during apoptosis. Here we review studies that suggest that AVD plays an active role during apoptosis and the underlying flux of ions that results in this morphological event regulates the programmed cell death process.

Lymphocyte Apoptosis

Apoptosis is a physiological series of cellular processes initiated by stimuli or signals that ultimately results in the death of individual cells within particular tissues. These apoptotic events permit the selective deletion of cells, leaving neighboring cells intact. This process is complementary, but opposing, to cell proliferation in the regulation of mammalian cell number homeostasis [1]. Apoptosis is characterized by a distinct set of morphological and biochemical characteristics that includes cell shrinkage, nuclear condensation, and internucleosomal DNA fragmentation [1, 2]. Additional features such as externalization of membrane phosphatidylserine, caspase activation, and mitochondrial membrane depolarization, along with the loss of cytochrome c from the mitochondria, have also been used to define and characterize this mode of cell death. During

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Review

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Osmotic Regulation of Bile Acid Transport, Apoptosis and Proliferation in Rat Liver

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Key Words
Integrins • Src • Fyn • EGFR • CD95

Abstract
Changes in mammalian cell volume as induced by either anisoosmolarity, hormones, nutrients or oxidative stress critically contribute to the regulation of metabolism, membrane transport, gene expression and the susceptibility to cellular stress. Osmosensing, *i.e.* the registration of cell volume changes, triggers signal transduction pathways towards effector pathways (osmosignaling) which link alterations of cell volume to changes in cell function. This review summarizes our own work on the understanding of how osmosensing and osmosignaling integrate into the overall context of bile acid transport, growth factor signaling and the execution of apoptotic programs.

Osmotic regulation of bile acid transport

Hepatic bile formation is due to the vectoria trans-hepatocellular transport of solutes and involve the coordinated action of transport proteins at th basolateral (sinusoidal) and the apical (canalicular membrane of the liver parenchymal cell [1-4]. Th hepatocellular hydration state, i.e. hepatocyte volume exerts powerful control on the transcellular transpo of solutes, such as conjugated bile acids, glucuronid and glutathione conjugates [5-9]. Since liver cell hydratio is a dynamic parameter, which changes within minute under the influence of hormones, nutrients an oxidative stress, the functional relevance of th liver hydration state for hepatic bile formation is eviden and of physiological and pathophysiological interest [1 11].

One major mechanism of short-term regulatio of bile formation is regulated transporter insertion int and retrieval from the canalicular membrane [8, 12]. B this mechanism, the number of transporter molecule in the canalicular and sinusoidal membrane can chang

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