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Ion channels in the RPE

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Abstract

In close interaction with photoreceptors, the retinal pigment epithelium (RPE) plays an essential role for visual function. The analysis of RPE functions, specifically ion channel functions, provides a basis to understand many degenerative diseases of the retina. The invention of the patch-clamp technique significantly improved the knowledge of ion channel structure and function, which enabled a new understanding of cell physiology and patho-physiology of many diseases. In this review, ion channels identified in the RPE will be described in terms of their specific functional role in RPE physiology. The RPE expresses voltage- and ligand-gated K^+, Cl^-, and Ca^{2+}-conducting channels. K^+ and Cl^- channels are involved in transepithelial ion transport and volume regulation. Voltage-dependent Ca^{2+} channels act as regulators of secretory activity, and ligand-gated cation channels contribute to RPE function by providing driving forces for ion transport or by influencing intracellular Ca^{2+} homoeostasis. Collectively, activity of these ion channels determines the physiology of the RPE and its interaction with photoreceptors. Furthermore, changes in ion channel function, such as mutations in ion channel genes or a changed regulation of ion channel activity, have been shown to lead to degenerative diseases of the retina. Increasing knowledge about the properties of RPE ion channels has not only provided a new understanding of RPE function but has also provided greater understanding of RPE function in health and disease.

Contents

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1. Introduction

With the invention of the patch-clamp technique, understanding of the structure and function of ion channels substantially improved and changed (Ackerman and Clapham, 1997; Colquhoun, 1991; Hamill et al., 1981; Jurkat-Rott and Lehmann-Horn, 2004; Neher and Sakmann, 1976, 1992; Sakmann and Neher, 1984; Sigworth, 1986). General ion channel characteristics were described in detail and the understanding of their cell-specific behaviour in different tissues improved. This knowledge shed new light on many different cell functions and also opened new doors toward an understanding of patho-physiologic changes in cell behaviour. The latter studies coined the term "channelopathies" for ion channel-related diseases (Ackerman and Clapham, 1997; Lehmann-Horn and Jurkat-Rott, 1999).

The retinal pigment epithelium (RPE) fulfills many tasks, which are essential for visual function (Bok, 1993; Steinberg, 1985; Strauss, 2005). The characterization of ion channels in the RPE is, therefore, a necessity to understand these important functions in retinal health and disease. The first patch-clamp study using cells of RPE was published in 1988 by Fox et al. (1988). Since then, the investigation of RPE ion channels has been undertaken by several different research groups who have now described a large number of different ion channels in the RPE. In this review we have endeavoured to summarize existing knowledge about ion channels of the RPE in relation to RPE function and its patho-physiology.

2. The function of the RPE

The RPE is a monolayer of pigmented cells covering the inner wall of the eye bulb (Bok, 1993). The apical membrane of the RPE faces the light-sensitive outer-segments of photoreceptors and the basolateral membrane of the RPE is enface with the fenestrated capillaries of the choroid (Bok, 1993; Boulton and Dayhaw-Barker, 2001; Marmorstein, 2001; Marmorstein et al., 1998). The interaction with the adjacent tissues relies on extracellular matrices on both sides of the RPE. For a close interaction with photoreceptors, the RPE has long apical microvilli that surround the outer-segments of photoreceptors (Boulton, 1991). The space in-between the RPE and photoreceptors is filled with the interphotoreceptor matrix (IPM). The IPM is essential for the interaction between RPE and photoreceptors (Acharya et al., 1998; Gonzales-Fernandez, 2003; Hageman and Johnson, 1991; Hollyfield, 1999; Pepperberg et al., 1993; Uehara et al., 1990). In the differentiated eye, the IPM facilitates the interaction between RPE and photoreceptors enabling the exchange of nutrients, signalling molecules, and metabolic end products (Acharya et al., 1998; Gonzales-Fernandez, 2003; Hageman and Johnson, 1991; Hollyfield, 1999; Pepperberg et al., 1993; Uehara et al., 1990). At the basolateral side, the RPE is separated from the choriocapillaris by Bruch's membrane, a multilayered extracellular matrix structure (Garron, 1963; Guymer et al., 1999; Lerche, 1963; Marshall et al., 1998; Sumita, 1961). Bruch's membrane represents an interface for exchange of nutrients and signalling molecules, in this case between RPE and the