Chapter 31

Overview: Potassium Channels in Vascular Endothelial Cells

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1. INTRODUCTION

Vascular endothelium appears to be a unique organ that not only responds to numerous hormonal and chemical signals but also senses changes in physical parameters, such as changes in blood flow through shear stress and changes in blood pressure through stretch. The endothelium integrates these signals and responds to them by regulating the production and release of vasoactive substances that play a role in blood pressure regulation and vascular growth. These regulatory substances include prostaglandins, endothelium-derived relaxing factor (EDRF or NO) and endothelium-derived hyperpolarizing factor (EDHF), endothelin, natriuretic peptides, small signaling molecules, such as substance P, ATP, growth factors, steroids, and even larger proteins, such as receptors and proteins involved in the blood clotting cascade (for reviews, see Inagami et al., 1995; Nilius and Casteels, 1996). In addition to this endocrine function, endothelial cells either prevent or trigger blood clotting in response to various signals and exert thrombolytic as well as thrombogenic activity. As antigen-presenting cells, they are also involved in immune responses. Their ability to modulate cell–cell contacts controls the permeability of the blood–tissue interface. Finally, they initiate angiogenesis and vessel repair.

2. K^+ CHANNELS OF ENDOTHELIUM

2.1. Inward Rectifier K^+ Channels

The most prominent K^+ channel in resting endothelial cells is the inward rectifier K^+ channel (Kir), which conducts inward currents at potentials more negative than the
Figure 1. Whole-cell and single-channel Kir currents in calf pulmonary artery endothelial (CPAE) cells. (A) and (B) Current traces recorded in CPAE under control conditions (A) and after application of 1 mM Ba²⁺ (B) at various potentials applied from a holding potential of 0 mV. Large inward currents are present at negative potentials, and a rapid inactivation is prominent at the most negative potentials. (C) I–V curves corresponding to the recordings in panels A (○) and B (■) and the Ba²⁺-blocked difference current measured at the end of the applied voltage step (●). Notice the pronounced inward rectification of the current reversing near -80 mV. (D) Single-channel recordings in cell-attached mode at symmetrical K⁺ concentrations. (E) Corresponding I–V curve reconstructed from the amplitudes of the measured single-channel currents. (Reproduced, with permission, from Kamouchi et al., 1997b.)

K⁺ equilibrium potential but permits much smaller currents at potentials positive to that potential (Fig. 1). The channel appears to be more abundant in cultured than in intact endothelial cells. In intact endocardial endothelial cells, it is mainly confined to the luminal side of the endothelium (Manabe et al., 1995b). However, in monolayers of cultured bovine aortic endothelial cells, it appears to be randomly distributed (Colden-Stanfield et al., 1992).

The conductance of Kir channels, together with the basal activity of the volume-regulated anion channel and a background nonselective cation current, determines the resting membrane potential of endothelial cells (Campbell et al., 1991; Fransen and Sys, 1997; Voets et al., 1996), which ranges between -10 and -70 mV, depending on the cell type. The resting potential seems to be more negative in macrovascular than in microvascular cells (Daut et al., 1994; Vargas et al., 1994; Zunkler et al., 1995) and also in electrically coupled confluent cells (Vargas et al., 1994; Zunkler et al., 1995). In bovine pulmonary endothelial cells, blocking the Kir channel by micromolar concentrations of Ba²⁺ results in a depolarization of cells with a negative resting potential but