



Colonic Epithelium Oxygen Utilization and Transfer



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Mini Review

Epithelial ion transport is critically dependent on an adequate oxygen supply. In recent years, it has become increasingly apparent that oxygen availability plays an important role in regulating ion transport [1] and that normally the intestinal epithelium in situ operates under low oxygen pressure, a condition that has been dubbed “physiological hypoxia” [2]. This minireview summarizes some contributions from our laboratory on this issue. We have developed a method for the simultaneous measurement of short-circuit current (a measure of electrogenic ion transport) and oxygen consumption rate of epithelial samples mounted as flat sheets in a hermetically closed Ussing chamber provided with polarimetric oxygen probes in both sides [3].

Electrogenic ion transport demands a large fraction of epithelial oxygen consumption (about 25%) under baseline conditions both in the rat [3] and in the human colonic epithelium [4, 5]. This fraction is increased (up to 40%) under stimulation of electrogenic ion transport. This is true both for secretagogues that increase chloride secretion [6] and for stimuli that increase sodium absorption, like feeding the animals on a sodium-free diet or in vitro incubation with aldosterone [7]. In all cases, there is a significant linear relationship between the magnitude of the short-circuit current and the oxygen consumption rate [3-7].

Furthermore, electrogenic ion transport in the colonic epithelium is very sensitive to acute hypoxia in the rat [8] and even more in humans [4,9]. On the other hand, chronic hypobaric hypoxia induces an adaptation in electrogenic transport, as indicated by higher baseline short-circuit current in epithelial samples from hypoxic rats than in controls [10]. This adaptation is not associated with increased oxygen consumption under conditions of normal oxygenation and, remarkably, the linear relationship between the magnitude of the short-circuit current and the oxygen consumption rate is preserved [11]. Moreover, chronic

hypoxia affects neither the short-circuit current response to acute hypoxia [10], nor the acute effect of aldosterone of this tissue [12].

Under normal conditions in vivo, the oxygen supply to the colonic epithelium depends on the blood flow, with oxygen diffusing from the capillaries to the epithelium due to a partial pressure gradient [1,2,13]. Little or no luminal contribution to the oxygen supply is expected, since the lumen is an essentially anaerobic environment [14]. We measured oxygen transfer rates of the submucosa, the mucosa and the mucus gel layer in samples from rat descending colon and calculated their oxygen permeability coefficients and oxygen diffusion coefficients [15]. While the mucus gel layer and submucosal tissue limited oxygen diffusion, the epithelium itself represents a significant hindrance to it. Interestingly, the inhibition of cellular respiration with potassium cyanide did not change mucosal oxygen transfer coefficients [15].

In another study, we induced different oxygen concentration differences between the mucosal and serosal sides of the oxymetric Ussing chamber to determine the partial pressure difference above which there was net oxygen transfer from one side to the other. The relationship between the change in oxygen concentration and the oxygen pressure difference between the chambers was linear for both serosal to mucosal transfer and for mucosal to serosal transfer [16]. However, net transfer from the serosal to the mucosal side was detected when the oxygen pressure difference was above 100 mmHg, while net oxygen transfer from the mucosa to the serosa was apparent only when the oxygen pressure difference was above 300mmHg [16]. We interpret this large difference as a rectifying behavior, since transfer in one direction demands a larger oxygen pressure difference than transfer in the opposite direction.

As already noted, in vivo the oxygen diffuses to the mucosa from the serosal side, while when the tissue is mounted in an Ussing chamber, both sides may be simultaneously oxygenated. However, this does not necessarily mean that the mucosal and serosal sides of the chamber make an equal contribution to oxygen delivery to the epithelium. When hypoxia is induced at the serosal side only (keeping the oxygen supply to the mucosal side), the depression of short-circuit current is as large as, and follows the same time course, as when hypoxia is induced simultaneously at both sides. On the other hand, hypoxia induced at the mucosal side only (keeping the oxygen supply to the serosal side) has little, if any, effect on short-circuit current [17]. These findings suggest that there is an asymmetry in the oxygen availability to the epithelium, with serosal supply playing a predominant role. This was corroborated by experiments in everted sacs of rat colonic epithelium.

The everted sac preparation, in which oxygen is delivered to the epithelium from the mucosal side, was introduced to improve oxygenation of the small intestinal epithelium in 1954 [18], and since then it has been extensively used [19]. However, counterintuitively, everted sacs from the colonic epithelium had less than half the short-circuit current than non-everted sacs, in which oxygen is supplied from the serosal side [17]. The larger role of serosal oxygen supply to electrogenic ion transport might be a characteristic feature of the colonic epithelium, as we also demonstrated it in samples from human sigmoid colon [4,5,9].

In addition to the different effect of selective mucosal and serosal hypoxia, we have shown that for the rat colon, the contribution of the serosal side to epithelial oxygen consumption is consistently larger than the contribution of the mucosal side under a variety of experimental stimuli [16]. A higher oxygen supply from the serosal than from the mucosal side has also been shown in the human colon in vitro [4]. Two questions remain to be addressed by future research. The first concerns the structural and molecular basis of the reported asymmetries in oxygen transfer and availability. The second is whether similar asymmetries exist for gases other than oxygen.

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Conflict of Interest

None

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