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ORIGINAL ARTICLE

Basic Study

Rectification of oxygen transfer through the rat colonic epithelium

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Abstract

AIM
To assess whether higher sensitivity of colonic epithelium to hypoxia at the serosal side is associated with oxygen transfer asymmetry.

METHODS
Rats were fed either with normal chow or a low-sodium diet. Tissues were mounted as flat sheets in a modified, airtight Ussing chamber with oxygen meters in each hemichamber. Mucosal samples from normal diet animals were studied under control conditions, in low-chloride solution and after adding chloride secretion inhibitors and chloride secretagogues. Samples from sodium-deprived rats were studied before and after ouabain addition. In separate experiments, the correlation between short-circuit current and oxygen consumption was analyzed. Finally, hypoxia was induced in one hemichamber to assess the relationship between its oxygen content and the oxygen pressure difference

between both hemichambers.

RESULTS
In all studied conditions, oxygen consumption was larger in the serosal hemichamber than in the mucosal one (P = 0.0025 to P < 0.0001). Short-circuit current showed significant correlation with both total oxygen consumption (r = 0.765; P = 0.009) in normoxia and oxygen consumption in the serosal hemichamber (r = 0.754; P = 0.011) during mucosal hypoxia, but not with oxygen consumption in the mucosal hemichamber. When hypoxia was induced in the mucosal hemichamber, an oxygen pressure difference of 13 kPa with the serosal hemichamber was enough to keep its oxygen content constant. However, when hypoxia was induced in the serosal hemichamber, the oxygen pressure difference with the mucosal hemichamber necessary to keep its oxygen content constant was 40 kPa (P < 0.0001).

CONCLUSION
Serosal oxygen supply is more readily available to support short-circuit current. This may be partly due to a rectifying behavior of transepithelial oxygen transfer.

Key words: Colonic epithelium; Hypoxia; Oxygen diffusion; Short-circuit current; Ussing chamber

Core tip: The physiological dependence of the colonic epithelium on oxygen provided from the serosal side is not only due to the structure of its blood supply and the low oxygen pressure of colonic intraluminal contents, since it is also observed in isolated mucosa preparations. This study demonstrates for the first time that a much larger partial pressure difference is needed for oxygen transfer from the mucosal side to the serosal side of the epithelium than for transfer in the opposite direction, a phenomenon that may be considered a rectifying behavior.

Saraví FD, Carra GE, Matus DA, Ibáñez JE. Rectification of oxygen transfer through the rat colonic epithelium. *World J Gastrointest Pathophysiol* 2017; 8(2): 59-66 Available from: URL: http://www.wjgnet.com/2150-5330/full/v8/i2/59.htm DOI: http://dx.doi.org/10.4291/wjgp.v8.i2.59

INTRODUCTION

Hypoxia is considered the earliest factor causing organ damage in intestinal ischemia[1], caused, for example, by hypoperfusion associated with septic shock[2], general anesthesia[3], or ischemic colitis; the latter condition is the most frequent form of ischemic injury to the gastrointestinal tract[4,5].

The intestinal epithelium is very sensitive to hypoperfusion. Epithelial ion transport is closely coupled to aerobic metabolism[6,7]. However, the intestinal epithelium normally has relatively low oxygen partial pressure (P_{O_2}), a condition characterized as "physiologic hypoxia"[8]. Hypothetically, oxygen might be provided to the epithelium from both the luminal and the serosal side. However, the composition of intraluminal gas is variable and, as a rule, its P_{O_2} is lower than that of either arterial or venous blood[9,10].

While oxygen consumption by intraluminal bacteria may partially account for the differences, it has been reported that intracolonic P_{O_2} was less than 2 mmHg higher in germ-free rats than in control rats[11]. Luminal oxygen is an unlikely source for epithelial consumption, since intraluminal P_{O_2} is lower than mucosal P_{O_2}[12]. In the intact colon *in vivo*, oxygen reaches the epithelial cells through their basolateral membranes by diffusion from the capillary network which surrounds the crypts[8,13].

In most studies of epithelial biology employing Ussing chambers, both sides of the samples are oxygenated. If unremoved, in the intestinal epithelium both the adherent mucus gel layer and the submucosal tissue restrain oxygen diffusion[14]. Hypoxia induced in the serosal hemichamber while keeping a high oxygen pressure at the mucosal side lowers short-circuit current (I_{sc}) just as effectively and with the same time-course as hypoxia simultaneously induced in both sides. On the other hand, hypoxia induced in the mucosal hemichamber does not reduce I_{sc} as long as the serosal side remained oxygenated[15]. Furthermore, non-everted colonic sacs oxygenated from the serosal side showed a 127% higher I_{sc} than everted sacs oxygenated from the mucosal side[15]. One possible cause of the observed asymmetry is higher serosal than mucosal oxygen consumption (QO_2); another is some kind of barrier, present at the mucosal but not at the serosal side, which hinders oxygen diffusion.

Our working hypotheses were, first, that the observed asymmetries are due to an intrinsic property of the epithelium, and therefore they should be found under different experimental treatments. Second, that the epithelial hindrance to oxygen diffusion may be different for transfer from lumen to interstitium than in the reverse direction. This may be deemed a rectifying behavior by analogy to electrical devices. Rectification is a property of diodes, which are electrical devices that allow current flow in one direction far more easily than in the other. Some membrane ion channels display rectifying behavior, since they show a nonlinear relationship between the driving force (potential difference) and the resulting current[16].

The aims of this paper are, first, to assess the differences in oxygen consumption provided from the apical side of the epithelium and from its serosal side during different experimental treatments and, second, to measure the partial pressure difference needed for oxygen transfer from the mucosal to the serosal side and for oxygen transfer in the opposite direction.

MATERIALS AND METHODS

Animals

Wistar-Hokkaido male rats weighing 250-300 g were housed and managed according to the guidelines for animal care and biosafety of our Medical School. The animals were kept at an environmental temperature of 25 ℃ ± 1 ℃ with a 12-h light-dark cycle.

All animals were given food and drink *ad libitum*. A group of rats drank tap water and ate a standard rat chow containing 1.77 mg of sodium per gram of food (76.9 mEq/kg; Cargill Co.). A second group was given distilled water and a low-sodium diet with 0.161 mg of sodium per gram of food (7 mEq/kg; ICN Flow Catalog # 902902) for 10 d. The low-sodium diet was purchased from ICN, Inc. (Costa Mesa, California, United States). Daily food consumption was recorded in both groups.

All procedures involving the care and use of animals were approved by the Committee for Animal Care and Use of the Faculty of Medical Sciences, National University of Cuyo. This study was reviewed and approved by the Secretaría de Ciencia y Técnica, National University of Cuyo, institutional review board.

Serum aldosterone determination

Blood samples from all rats fed with the sodium-deficient diet and an equal number of rats fed with standard chow were obtained during the surgical procedure. Blood was allowed to clot; serum was extracted and frozen at -70 ℃. Aldosterone concentration in stored sera was afterwards measured with a coated-tube radioimmunoassay (Diagnostic Products Corporation, Los Angeles, California, United States).

Dissection and mounting

Under ether anesthesia, the entire colon was excised. A 3-cm segment was cut from the descending portion just above the pelvic brim and dissected to obtain an isolated mucosa preparation, as previously described[15]. The segment was cut open along its mesenteric border, the adherent mucus gel layer was gently removed with a cotton tip soaked in dissecting solution and the segment was mounted as a flat sheet in a modified Ussing chamber (described below).

Solutions and gas mixtures

The composition of the standard Ringer solution employed was as follows (in mmol/L): Na 132.8; K 4.5; Ca 1.25; Mg 1.0; Cl 114.0; HCO_3 24.0; H_2PO_4 1.0; SO_4 1.0; D (+) glucose 10.0. In the low-chloride solution, most chloride was replaced by sulfate, with the addition of mannitol to compensate for the difference in osmolality[11], as follows (in mmol/L): Na 136.6; K 4.5; Ca 1.25: Mg 1.0; Cl 2.5; HCO_3 24.0; H_2PO_4 2.0; SO_4 58.1; D (+) glucose 10.0; mannitol 93.4. The osmolality 0f both solutions was 280 mOsm/kg H_2O.

Two gas mixtures were used: 950 mL/L O_2 - 50 mL/L CO_2 (normoxic mixture) and 950 mL/L N_2 - 50 mL/L CO_2 (hypoxic mixture). The gas mixtures were purchased from Air Liquide, Inc. (Buenos Aires, Argentina). Their compositions were certified by the company. When gassed with either gas mixture, the pH of both solutions was 7.40.

Drugs

Bumetanide, 3-methyl-1-isobutilxanthine (IBMX), serotonin, and amiloride were purchased from Sigma-Aldrich (St Louis, Missouri, United States), and diphenylamine-2-carboxylate (DPC) from ICN, Inc (Costa Mesa, California, United States). The appropriate drug solutions were prepared just before each experiment. The standard Ringer solution was employed to dissolve serotonin and carbachol; dimethylsulfoxide was used for IBMX and bumetanide, and absolute ethanol was used for amiloride and DPC. As indicated, bumetanide, IBMX and serotonin were added to the serosal hemichamber, while DPC and amiloride were added to the mucosal hemichamber to achieve the following concentrations (in mmol/L): bumetanide 0.1; DPC 0.5; IBMX 0.1; serotonin 0.1, and amiloride 0.1. At the start of each experiment, 91 μg/mL gentamycin (Schering-Plough, Buenos Aires, Argentina) was added to each hemichamber, to prevent bacterial overgrowth.

Oxymetric Ussing chamber and electrophysiological measurements

For this report, a modified Ussing chamber which has already been described and validated was used[17]. The chamber is airtight and it has a 1 cm^2 window between the hemichambers. Polarimetric oxygen meters (CellOx 325, WTW GmbH, Weilheilm, Germany) are attached to each hemichamber. This arrangement allows measurement of the oxygen concentration and its time course in both the hemichamber facing the basolateral (serosal) side of the epithelium and the hemichamber facing its apical (mucosal) side. The chamber content was kept at 37 ℃ with a water jacket fed from a thermostatic reservoir.

The transepithelial potential difference was recorded with calomel electrodes connected to each hemichamber through saline bridges (agar-in-Ringer, 30 g/L). Ag-AgCl electrodes were used to supply current to the chamber from an amplifier, in order to clamp the transepithelial potential difference (TPD) at 0 mV. The output of the amplifier took into account corrections for solution resistance and bridge asymmetry. The short-circuit condition was kept throughout all experiments, except for the brief periods of release needed to measure open circuit TPD. The transepithelial resistivity was calculated, according to Ohm's law, as the quotient between TPD and I_{sc}.

Experimental procedures

Before each experiment, oxygen probes were calibrated according to the user's manual and had their slopes checked and recorded. At the beginning of each experiment, the hemichambers were gassed with the normoxic mixture until a plateau of their oxygen concentration was reached. Afterwards both hemichambers were hermetically closed. QO_2 was measured under baseline conditions for 30-min periods, starting 60 min after the closure of the hemichambers.

Solution replacement was carried out without opening the chamber with a gravity driven system which allowed passing from a water-jacketed reservoir (37 ℃) through the chamber a volume of low-chloride solution 10-fold larger than the chamber volume, with the overflow being drained through siphons. In experiments involving replacement of Ringer with low-chloride solution or addition of chloride secretion blockers, Isc was allowed to stabilize during 20 min before QO_2 was measured for the next 30 min. On the other hand, the 30-min QO_2 measurement was started immediately after addition of IBMX or serotonin.

The change in oxygen concentration in each hemichamber during the measurement period was used to calculate QO_2, as detailed elsewhere[11]. In experiments assessing oxygen transfer between the hemichambers, a baseline QO_2 was obtained after attaining the same oxygen level in both hemichambers. Then hypoxia was induced in one hemichamber by gassing its contents with 950 mL/L N_2 - 50 mL/L CO_2 for various times while bubbling 950 mL/L O_2 - 50 mL/L CO_2 in the other hemichamber, to obtain graded differences in oxygen pressure (ΔP_{O_2}) between the hemichambers. Afterwards the chamber was closed and the rate of change in oxygen concentration (ΔCO_2) in the hypoxic hemichamber was plotted against the ΔP_{O_2} between both sides.

After a 15-min period of reoxygenation of both hemichambers, the procedure described above was repeated for inducing hypoxia in the other hemichamber. The ΔP_{O_2} was calculated as the difference in mean P_{O_2} of each hemichamber during each hypoxic period. The order in which hypoxia was induced in each hemichamber was switched between experiments to avoid a possible effect derived from the hemichamber which was made hypoxic first. Finally, both hemichambers were reoxygenated and a second control QO_2 measurement was performed.

After each experiment, the mucosa was replaced with a polyethylene membrane for a blankrun. The experiment was discarded if the decrease in oxygen concentration was above 5% of that observed with the biological sample.

Statistical analysis

QO_2 in the serosal and mucosal hemichambers and I_{sc} under each tested condition were compared with a paired, two-sided Student's *t* test. An unpaired, two-sided Student's *t* test was employed for analysis of food intake, sodium intake, and serum aldosterone in rats fed with normal sodium diet and in those submitted to the low-sodium diet. During analysis, significant deviations from a Gaussian distribution were ruled out with the Kolmogorov-Smirnov test.

A one-way analysis of variance with Geisser-Greenhouse correction was used to assess differences in the magnitude of the serosal *vs* mucosal difference in QO_2 under all conditions tested. Simple linear regression was used to assess the relationships between I_{sc} and ΔP_{O_2}, and between ΔP_{O_2} and ΔCO_2. Checks for significant deviation from linearity and outliers were performed for all comparisons.

A commercial software was employed for statistical analyses (GraphPad Prism version 5.1 for Windows, GraphPad Software, San Diego, California, Δ). Values are reported as means ± SEM, unless otherwise stated. The significance level was set at $P < 0.05$.

RESULTS

Mean daily food intake of rats fed with the low-sodium diet (80.0 ± 1.4 g per kilogram body weight; $n = 6$) was not significantly different from that of rats given standard chow (82.1 ± 0.9 g per kilogram body weight; $n = 20$). The respective mean daily sodium intakes per kilogram body weight were 12.9 ± 0.3 mg and 145.3 ± 1.6 mg ($P < 0.0001$). As expected, serum aldosterone concentration was significantly higher in rats with low sodium intake (10.49 ± 2.1 nmol/L; $n = 6$) than in controls (1.42 ± 0.26 nmol/L; $n = 6$, $P = 0.0016$).

Values of I_{sc}, total QO_2, serosal QO_2, and mucosal QO_2 for epithelial samples are shown in Table 1. Compared with controls, I_{sc} and QO_2 were higher in the presence of chloride secretagogues and in epithelial samples from sodium-deprived rats. Conversely, I_{sc} and QO_2 were lower in low-chloride solution, in the presence of chloride secretion blockers or, in tissues from sodium-deprived animals, after addition of amiloride. Under all conditions tested, serosal oxygen consumption was higher than mucosal oxygen consumption (Figure 1). The magnitude of this difference was similar for all treatments ($P = 0.0847$ according to one-way analysis of variance).

I_{sc} was correlated with total QO_2 and serosal QO_2 both under baseline condition and during mucosal hypoxia (Figure 2), but those correlations were lost during serosal hypoxia. On the other hand, I_{sc} was not correlated with mucosal QO_2 under any condition (Table 2).

When different oxygen tension differences were imposed between both hemichambers, the oxygen content of the hypoxic hemichamber increased with time when ΔP_{O_2} was high but decreased when it was low (Figure 3). The relationship was linear when hypoxia was induced in either hemichamber. The slope for hypoxia induced in the mucosal hemichamber was 0.0535 ± 0.009 $\mu mol \times cm^{-2} \times h^{-1}$ per kPa. The slope for hypoxia induced in the serosal hemichamber was 0.0494 ± 0.014 $\mu mol \times cm^{-2} \times h^{-1}$ per kPa ($P = 0.8244$ for the comparison of both slopes). However, the calculated ΔP_{O_2} at which

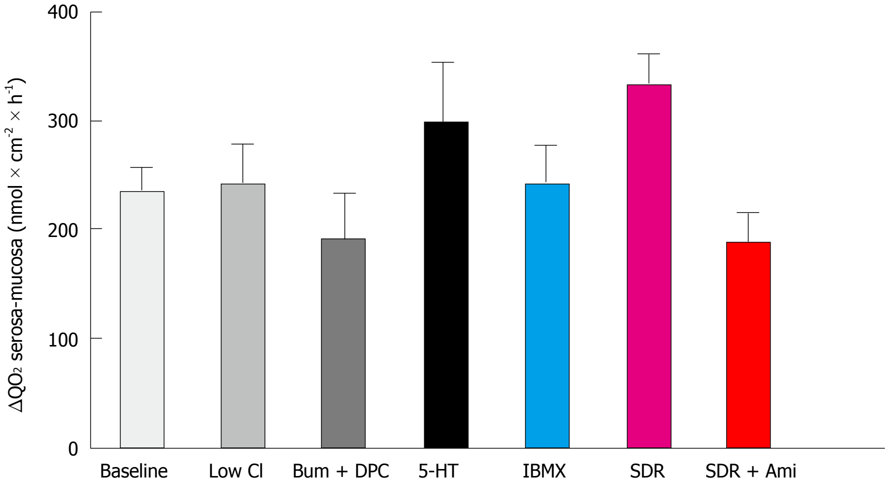

Figure 1 Differences in serosal *vs* mucosal oxygen consumption of rat sigmoid colon epithelium under several conditions. No significant difference between groups was found, as assessed by one-way analysis of variance (P = 0.0849). ΔQO_2: Serosa-mucosa, difference between serosal and mucosal oxygen consumption; Bum: Bumetanide; DPC: Diphenylamine-2-carboxylate; IBMX: 3-methyl-1-isobutilxanthine; SDR: Sodium-deprived rats; Ami: Amiloride.

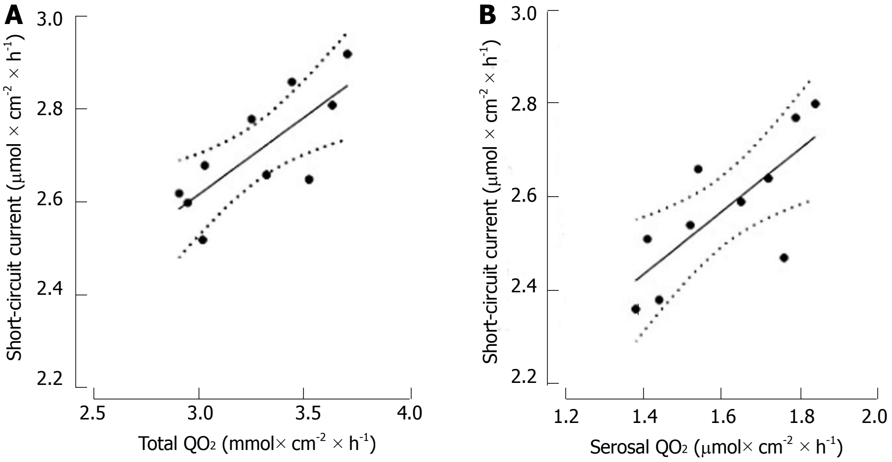

Figure 2 Linear regression of short-circuit current *vs* total oxygen consumption during normoxia (A), and *vs* serosal oxygen consumption during mucosal hypoxia (B). Regression coefficients were 0.765 for A (P = 0.009) and 0.754 for B (P = 0.011). No outliers were detected.

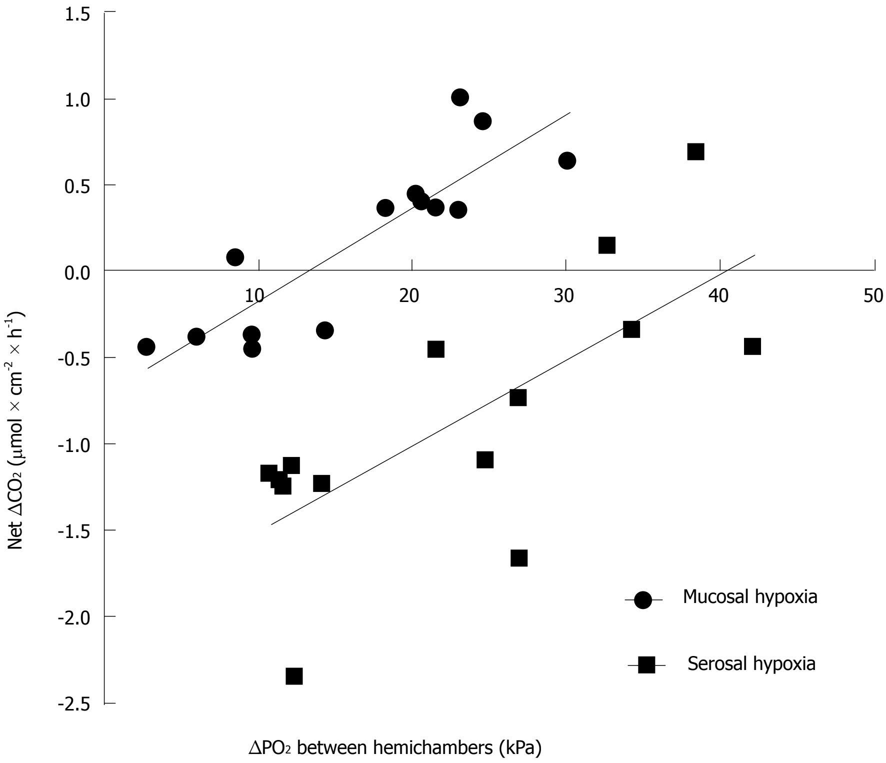

Figure 3 Rate of change in oxygen content of the hypoxic hemichamber as a function of the difference in oxygen partial pressure between hemichambers. Various degrees of hypoxia were induced in either the serosal or the mucosal hemichamber while keeping the opposite hemichamber fully oxigenated, and the change in oxygen content was plotted as a function of the mean difference in oxygen pressure between both hemichambers during a 30-min observation period. The slope of the relationships was the same when either the serosal or the mucosal hemichamber was hypoxic (P = 0.8244), but the oxygen pressure difference at which there was no net change in oxygen content in the hypoxic hemichamber was larger when hypoxia was induced in the serosal hemichamber (P < 0.0001). ΔCO_2: Change in oxygen content of the hypoxic hemichamber; ΔPO_2: Oxygen pressure difference between hemichambers.

Table 1 Short-circuit current and oxygen consumption of the isolated mucosa of rat sigmoid colon

Treatment	*n*	Isc μmol × cm^{-2} × h^{-1}	Total QO_2 μmol × cm^{-2} × h^{-1}	Serosal QO_2 μmol × cm^{-2} × h^{-1}	Mucosal QO_2 μmol × cm^{-2} × h^{-1}
None	20	3.33 ± 0.21	2.79 ± 0.06	1.52 ± 0.04	1.28 ± 0.08^b
Low Cl	6	0.66 ± 0.07	2.56 ± 0.13	1.41 ± 0.08	1.14 ± 0.06^d
Bum + DPC	6	0.63 ± 0.08	2.47 ± 0.15	1.35 ± 0.07	1.15 ± 0.08^d
Serotonin	6	5.30 ± 0.29	3.64 ± 0.13	1.97 ± 0.08	1.67 ± 0.06^d
IBMX	6	3.98 ± 0.24	3.22 ± 0.09	1.75 ± 0.07	1.47 ± 0.06^d
SDR	6	8.50 ± 0.45	3.71 ± 0.35	2.02 ± 0.15	1.68 ± 0.12^b
SDR + Ami	6	0.33 ± 0.05	2.88 ± 0.12	1.53 ± 0.07	1.35 ± 0.08^d

$^bP < 0.0001$ and $^dP < 0.01$ for the difference between serosal and mucosal oxygen consumption. I_{sc}: Short-circuit current; QO_2: Oxygen consumption; Bum: Bumetanide; DPC: Diphenylamine-2-carboxylate; IBMX: 3-methyl-1-isobutilxanthine; SDR: Sodium-deprived rats; Ami: Amiloride.

Table 2 Relationship between short-circuit current and epithelial oxygen consumption of the isolated mucosa of rat sigmoid colon

Condition	Comparison	R^2
Baseline	I_{sc} *vs* total QO_2	0.586^b
	I_{sc} *vs* serosal QO_2	0.620^c
	I_{sc} *vs* mucosal QO_2	0.299
Mucosal hypoxia	I_{sc} *vs* total QO_2	0.633^d
	I_{sc} *vs* serosal QO_2	0.569^g
	I_{sc} *vs* mucosal QO_2	0.388
Serosal hypoxia	I_{sc} *vs* total QO_2	0.164
	I_{sc} *vs* serosal QO_2	0.315
	I_{sc} *vs* mucosal QO_2	0.361

$^bP = 0.009$; $^cP = 0.018$; $^dP = 0.006$; $^gP = 0.011$; $n = 10$. I_{sc}: Short-circuit current; QO_2: Oxygen consumption.

there was no change in oxygen content of the hypoxic hemichamber ($\Delta CO_2 = 0$) was three times higher for serosal hypoxia (ΔP_{O_2} = 40 kPa) than for mucosal hypoxia (ΔP_{O_2} = 13 kPa): $P < 0.0001$.

DISCUSSION

Present results show that, when oxygen is available from both the serosal and the mucosal sides to distal colonic epithelium, the tissue consumes more oxygen supplied from the serosal than from the mucosal side. Since blood supply plays no role in oxygen availability under present *in vitro* conditions, the observed preference may not be explained by the path through which oxygen is normally provided to the epithelium. Furthermore, the higher serosal QO_2 was observed under a variety of conditions, including those in which chloride secretion is the major electrogenic phenomenon and those in which the major electrogenic phenomenon is sodium absorption. This suggests that the asymmetry is also not due to the specific ion being transported but represents a physiological characteristic of the colonic epithelium. It should be noted that this asymmetry has also been demonstrated in epithelial samples from human sigmoid colon[18].

The importance of oxygen supply from the serosal side to sustain electrogenic transport was further corroborated by the correlation between I_{sc} and serosal QO_2 under baseline condition and during hypoxia induced in the mucosal hemichamber, while no such correlation was present during hypoxia induced in the serosal hemichamber. On the other hand, no correlation was found between I_{sc} and mucosal QO_2 in any condition tested.

When graded hypoxia is induced in one hemichamber, while the other is saturated with oxygen, theoretically the oxygen content of the hypoxic hemichamber could decrease, remain constant, or increase with time. It would decrease if the hypoxic chamber still provides part of the oxygen consumed by the epithelium. It would remain constant if all oxygen consumed by the epithelium is provided by the oxygenated chamber and there is no net oxygen transfer between the hemichambers. Finally, it would actually increase if the oxygenated hemichamber, apart from providing all the oxygen that the epithelium consumes, transfers part of its oxygen to the hypoxic hemichamber. The relationship between ΔCO_2 in the hypoxic hemichamber and ΔP_{O_2} between the hemichambers was linear and showed the same slope for serosal-to-mucosal transfer than for mucosal-to serosal transfer. Remarkably, however, the ΔP_{O_2} at which there was no net oxygen transfer between the hemichambers was three-fold higher for mucosal-to-serosal transfer than for transfer in the reverse direction, indicating that a larger ΔP_{O_2} between hemichambers is needed for mucosal-to-serosal transfer than for serosal-to-mucosal transfer. This may be characterized as a rectifying behavior of oxygen transfer.

One explanation for the larger contribution of oxygen supply from the serosal side may be that the oxygen permeability of the basolateral membrane to oxygen is larger than the oxygen permeability of the apical membrane. While it is classically accepted that biological membranes are very permeable to gases, low permeability of some membranes to gases such as ammonia or carbon dioxide has been reported, for example in gastric glands[19] and colonic epithelium[20]. This issue has been recently reviewed, and the existence of gas channels has been postulated[21,22]. There are few reports on membrane oxygen permeability[21] and the results are contradictory[22].

Even if apical and basolateral epithelial membranes had different oxygen permeability, this would not explain *per se* the apparent rectifying behavior of oxygen transfer. We are not aware of reports on this topic for oxygen, or for any other gas. Since gases generated in the colon as products of bacterial fermentation are partly transferred into the bloodstream[10], it is of physiological and clinical interest to assess whether their rate of transfer from the lumen to the interstitium is selectively limited, as it seems to be the case for oxygen.

In conclusion, the sigmoid colon epithelium *in vitro* in a rat model preferentially consumes oxygen supplied from the serosal side. I_{sc} correlates with serosal oxygen consumption, but not mucosal oxygen consumption. The ΔP_{O_2} for inducing net mucosal-to-serosal transfer is higher than the ΔP_{O_2} for inducing serosal-to mucosal transfer, therefore indicating a rectifying behavior for transepithelial oxygen transfer.

COMMENTS

Background

The colonic epithelium has a high oxygen consumption, a large part of which is needed to sustain electrogenic ion transport. *In vivo*, oxygen is mostly supplied from the serosal side, since the luminal environment has a very low oxygen partial pressure. When the epithelium is placed in an Ussing chamber, oxygen is usually available from both sides of the epithelium, but even then, the serosal supply is more important to sustain electrogenic ion transport than the mucosal supply.

Research frontiers

The intestinal epithelium is normally submitted to a relatively low oxygen pressure when compared with other tissues, a condition known as physiological hypoxia. This makes the epithelium susceptible to hypoxic injury when the oxygen supply is further compromised by disease.

Innovations and breakthroughs

In this paper, it is shown that serosal supply provides more oxygen than mucosal supply to the colonic epithelium under several different conditions, suggesting that the difference is an intrinsic property of the tissue. For the first time, evidence is provided suggesting that transepithelial oxygen diffusion from serosa to mucosa needs a lower gradient of oxygen pressure than diffusion from mucosa to serosa.

Applications

Since epithelial hypoxia seems to be an important cause of injury and dysfunction in several conditions affecting the intestinal epithelium, a deeper knowledge of the factors influencing epithelial oxygen supply may help to understand their pathophysiology and to devise better management strategies.

Terminology

Rectification: A term borrowed from electronics, referring to devices such as diodes, which allow electric current to flow more easily in one direction than in the opposite one. In the present context, it is applied to the observation that oxygen diffuses more easily from the serosal to the mucosal side of the epithelium than in the opposite direction. Short-circuit current: The electrical current passing through the epithelium needed to keep the transepithelial potential difference at 0 mV. It is a measure of electrogenic ion transport.

Peer-review

The aim of this study was to assess whether higher sensitivity of colonic epithelium to hypoxia at the serosal side is associated with oxygen transfer asymmetry. It is a very well design study and the issue is elegantly developed.

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