Mechanism of n-butyrate uptake in the human proximal colonic basolateral membranes

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Tyagi, S., J. Venugopalakrishnan, K. Ramaswamy, and P. K. Dudeja. Mechanism of n-butyrate uptake in the human proximal colonic basolateral membranes. Am J Physiol Gastrointest Liver Physiol 282: G676–G682, 2002; 10.1152/ajpgi.00173.2000.—Current studies were undertaken to characterize the mechanism of short-chain fatty acid (SCFA) transport in isolated human proximal colonic basolateral membrane vesicles (BLMV) utilizing a rapid-filtration n-[14C]butyrate uptake technique. Human colonic tissues were obtained from mucosal scrapings from organ donor proximal colons. Our results, consistent with the existence of a HCO₃⁻/SCFA exchanger in these membranes, are summarized as follows: 1) n-[14C]butyrate influx was significantly stimulated into the vesicles in the presence of an outwardly directed HCO₃⁻ and an inwardly directed pH gradient; 2) n-[14C]butyrate uptake was markedly inhibited (~40%) by anion exchange inhibitor niflumic acid (1 mM), but SITS and DIDS (5 mM) had no effect; 3) structural analogs e.g., acetate and propionate, significantly inhibited uptake of HCO₃⁻ and pH-gradient-driven n-[14C]butyrate; 4) n-[14C]butyrate uptake was saturable with a Kₘ for butyrate of 17.5 ± 4.5 mM and a Vₘₐₓ of 20.9 ± 1.2 nmol·mg protein⁻¹·s⁻¹; 5) n-[14C]butyrate influx into the vesicles demonstrated a transstimulation phenomenon; and 6) intravesicular or extravesicular Cl⁻ did not alter the anion-stimulated n-[14C]butyrate uptake. Our results indicate the presence of a carrier-mediated HCO₃⁻/SCFA exchanger on the human colonic basolateral membrane, which appears to be distinct from the previously described anion exchangers in the membranes of colonic epithelia.

short-chain fatty acids; transport; human large intestine; contraluminal membranes

SHORT-CHAIN FATTY ACIDS (SCFAs; i.e., acetate, propionate, and butyrate) are the major anions in the colonic lumen produced by anaerobic fermentation of dietary fiber by luminal microflora (4, 6, 8–10). SCFAs are a preferred source of energy for the normal colonic epithelial cells (6–8, 10, 11, 32, 33). SCFAs, particularly butyrate, have been shown to regulate colonic fluid and electrolyte absorption (1, 34, 36), induce cell differentiation, and promote growth and proliferation of the colonic mucosa (8, 25, 39). Variations in the usual colonic production and malabsorption of SCFAs have also been shown to be the potentiating factors in the inflammatory bowel diseases in humans (3, 13, 17, 27, 28). Despite the significance of SCFAs in maintaining the human colonic physiology, the mechanism of SCFA absorption and regulation is still not fully understood.

A number of previous studies using in vivo perfusion experiments (18, 24), flux studies with whole epithelial preparations (5, 19, 43), or isolated membrane vesicles (15, 16, 22, 38) have attempted to characterize the mechanisms of SCFA absorption across the colonic luminal membranes. To date, however, the two main mechanisms proposed for SCFA absorption across the colonic apical membranes, protons may be available from the Na⁺/H⁺ exchanger in the apical domains (12) or generated from hydration of CO₂ by carbonic anhydrase activity (35). In this regard, previous perfusion studies have shown SCFA absorption to stimulate Na⁺ uptake (1, 23, 34, 35) and also luminal Na⁺ concentrations to increase SCFA uptake (41). However, at the physiological colonic luminal pH, the predominant members of SCFA (pKa ~4.8) are in the ionized state and not available for simple diffusion and, therefore, may be transported by a possible carrier-mediated process.

Recent studies from our laboratory and others utilizing vesicle transport techniques have clearly demonstrated the presence of a bicarbonate-dependent, carrier-mediated anion exchange mechanism for SCFA uptake in the apical membranes of the human ileum and colon (15, 16), rat distal colon (22), and rabbit intestine (21). In this regard, it has been shown that the absorbed butyrate is not completely metabolized by the colonocytes (31–33) and could be further transported across the colonic basolateral membranes into the blood stream. A recent study by Reynolds et. al. (30) characterized a distinct carrier-mediated HCO₃⁻ and OH⁻-gradient-dependent anion exchange in basolateral membrane vesicles (BLMV) of rat distal colon.

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The present basolateral membrane studies were, therefore, undertaken to examine the mechanism of SCFA uptake in isolated BLMVs of the human proximal colon.

Results of our present study provide strong evidence for the existence of a carrier-mediated, HCO$_3^-$-gradient-dependent anion-butyrate exchange system, which appears to be distinct and separate from the apical membrane SCFA and basolateral membrane Cl$^-$/HCO$_3^-$ antiporters.

MATERIALS AND METHODS

Materials. SITS, DIDS, amiloride, niflumic acid, and acetazolamide were obtained from Sigma (St. Louis, MO). All other materials were obtained from either Fisher Scientific (Fairlawn, NJ) or Sigma unless otherwise stated and were of highest purity available. Radionuclide n-[1-$^3$C]butyrate (19.7 mCi/mmol) was obtained from New England Nuclear (Boston, MA).

Isolation of human proximal colonic BLMVs. Approval of the present investigations was obtained from the Institutional Review Board of the University of Illinois at Chicago. Colon from healthy (primarily trauma victims) adult organ donors (which were declared brain dead) were obtained immediately after harvest of transplantation organs. After the donors (which were declared brain dead) were obtained immediately after harvest of transplantation organs. After the donors were obtained, the remaining large intestine was cleaned with an ice-cold 0.9% NaCl and divided into two equal parts, proximal and distal. The mucosa was scraped from the seromuscular layer of the proximal colon and stored at −70°C. The human colonic basolateral plasma membranes were purified utilizing a Percoll density gradient technique recently established in our laboratory (40). The final membrane pellet was suspended in the transport buffer by passing it 10 times through a 25-gauge (1.5 in.) needle. After the final suspension, the vesicles are used for uptake studies either within 1–2 h of purification or frozen at −80°C for later use within a week. Membrane protein was assessed as described by Bradford (2), using bovine plasma gamma globulin as a standard.

Purity of the membrane vesicles and the degree of contamination with intracellular organelles were assessed by appropriate marker enzymes. Enrichment of the basolateral membrane with the marker enzyme activity, Na$^+$-K$^+$-ATPase, was 8–11-fold over that of homogenate. The membranes showed minimal contamination with markers of the apical or microsomal membranes (40).

n-[14C]butyrate uptake. Uptake of n-[14C]butyrate was measured at 25°C by a rapid filtration technique as described previously (15, 16). Unless otherwise stated, the membrane vesicles were preloaded with 150 mM KHCO$_3$ and 50 mM Tris-HEPES (pH 8.2). Experiments were started by the addition of 80 μl of the incubation medium consisting of 0.5 mM n-[14C]butyrate, 147 mM K gluconate (K$_{gluc}$), 3 mM KHCO$_3$, and 50 mM Tris-MES (pH 6.5) to 20 μl of the membrane vesicles (80–100 μg membrane protein). All solutions containing HCO$_3^-$ were gassed with 95% N$_2$:5% CO$_2$ for 10 min. After designated periods of time (see RESULTS), the reaction was terminated by the addition of 5 ml of ice-cold isotonic “stop” solution containing 147 mM K$_{gluc}$, 3 mM KHCO$_3$, and 50 mM Tris-MES (pH 6.5). The diluted sample was immediately filtered through a 0.65-μm Millipore filter (DWP) using a Millipore manifold filtration assembly. Filters were further washed twice with 5 ml of cold stopping solution, dissolved in Filtercount (Packard Instruments, Downers Grove, IL), and the radioactivity was measured in a Packard TR-1600 (Packard Instruments) liquid-scintillation counter. All values were corrected for n-[14C]butyrate binding to filters and/or vesicles by subtracting radioactivity present in zero time vesicle blanks. For studies utilizing transport inhibitors, inhibitors were preincubated with vesicles for 15 min. The uptake studies for most experiments were performed at either a 5- or 10-s time period, that being the linear uptake time for butyrate.

Statistical analysis. All experiments were performed using at least three to four separate membrane preparations from colons of different organ donors. Paired or unpaired Student's t-tests were used in statistical analysis as appropriate. Results are expressed as means ± SE. A P value < 0.05 was considered statistically significant.

RESULTS

Effect of HCO$_3^-$ and pH-gradients on n-[14C]butyrate uptake. A HCO$_3^-$-dependent SCFA exchange mechanism has been demonstrated in rat colonic and human ileal and colonic apical membrane vesicles (AMVs) (15, 16, 22). To determine whether SCFA uptake by human proximal colonic BLMV involves a carrier-mediated anion exchange process, the effect of an outwardly directed OH$^-$ and HCO$_3^-$ gradient on n-[14C]butyrate uptake was examined. As shown in Fig. 1, in the presence of an outwardly directed HCO$_3^-$ gradient and inwardly directed pH gradient, n-[14C]butyrate uptake into the BLMVs was markedly stimulated compared with the uptake observed in the absence of bicarbonate and proton gradient (P < 0.05). Results clearly suggest the presence of a pH-dependent carrier-mediated transport process across the colonic basolateral domains.

Effect of transmembrane potential on n-[14C]butyrate uptake. To differentiate whether an HCO$_3^-$ and H$^+$ gradient-stimulated transport is an electroneutral process or an electrogenic process, the effect of an electrogenic gradient was examined. As shown in Fig. 1, in the presence of an inwardly directed pH gradient and outwardly directed HCO$_3^-$ gradient, n-[14C]butyrate uptake into the BLMVs was markedly stimulated compared with the uptake observed in the absence of bicarbonate and proton gradient (P < 0.05). Results clearly suggest the presence of an electrogenic carrier-mediated transport process across the colonic basolateral domains.

Fig. 1. Effect of HCO$_3^-$ and pH gradients on n-[14C]butyrate uptake. n-[14C]butyrate (0.5 mM) uptake was determined at 25°C by diluting the membrane vesicles preloaded with 150 mM KHCO$_3$ and 50 mM Tris-HEPES (pH 8.2) into a reaction medium containing either 150 mM KHCO$_3$, 50 mM Tris-HEPES (pH 8.2), or 147 mM K$_{gluc}$, 3 mM KHCO$_3$, and 50 mM Tris-MES (pH 6.5). All solutions were gassed with 95% N$_2$:5% CO$_2$ for 10 min. Values are means ± SE for 3–5 separate experiments.
cess rather than a membrane potential-dependent mechanism, the effect of K+/valinomycin-induced membrane potential on butyrate uptake was determined. n-[14C]butyrate uptake into the BLMVs was measured after imposition of an intravesicular negative or positive membrane potential or voltage clamping the vesicles. As shown in Table 1, changes in transmembrane potential (with K+/valinomycin) did not influence butyrate uptake in these membranes.

Kinetics of n-[14C]butyrate uptake. To further differentiate the mechanisms contributing to HCO3−gradient-stimulated n-[14C]butyrate uptake into the colonic BLMVs, the kinetics of the n-[14C]butyrate transport process was also determined. The results in Fig. 2, clearly demonstrate that the HCO3−-dependent butyrate uptake exhibited saturability in the presence of increasing concentrations of sodium butyrate (2–50 mM) in the extravesicular media. A Lineweaver-Burk plot of the data (Fig. 2, inset) demonstrated a straight line with an apparent $K_m$ of 17.5 ± 4.5 mM and a $V_{max}$ of 20.9 ± 1.2 nmol·mg protein$^{-1}$·5 s$^{-1}$. These data again support the presence of an anion exchanger in the human colonic basolateral membranes.

Effect of transport inhibitors on n-[14C]butyrate uptake. To further assess the properties of n-[14C]butyrate transport process across the colonic BLMV, effects of various membrane ion transport inhibitors on the initial uptake rates of n-[14C]butyrate were determined. Of the known membrane ion transport inhibitors, the stilbene derivatives DIDS and SITS have been shown to be the potent inhibitors of many anion exchange processes. However, as shown in Fig. 3, incubation of the BLMV with DIDS and SITS (5 mM) had no inhibitory effect on HCO3−gradient-driven n-butyrate uptake. Niflumic acid, another anion exchange inhibitor, was found to be the most effective, significantly inhibiting butyrate uptake by ~50% ($P = 0.05$).

Table 1. Effect of membrane potential on [14C]butyrate uptake

<table>
<thead>
<tr>
<th>Buffer Conditions</th>
<th>[14C]Butyrate Uptake, nmol·mg protein$^{-1}$·10 s$^{-1}$</th>
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<tbody>
<tr>
<td>-Valinomycin</td>
<td>+Valinomycin</td>
</tr>
<tr>
<td>150 K[OH] /150 K[Gluc]</td>
<td>0.96 ± 0.04 0.99 ± 0.01</td>
</tr>
<tr>
<td>150 K[Gluc] /300 Mannitol</td>
<td>0.17 ± 0.03 0.17 ± 0.02</td>
</tr>
<tr>
<td>300 Mannitol /150 K[Gluc]</td>
<td>0.16 ± 0.01 0.17 ± 0.02</td>
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Values are presented as means ± SE for 6 determinations of 2 separate preparations. n-[14C]-butyrate (1.0 mM) uptake was determined at 25°C by diluting the membrane vesicles preloaded with 150 mM KHCO3 and 50 mM Tris-HEPES (pH 8.2) into a reaction medium containing either 150 mM K[Gluc], 50 mM Tris-MES (pH 6.5), and n-[14C]-butyrate (1.0 mM) ± 20 μM valinomycin; or preloaded with 150 mM K[Gluc] and 50 mM Tris-MES (pH 8.2) and diluted in 300 mM mannitol, 50 mM Tris-MES (pH 6.5), and n-[14C]-butyrate (1.0 mM) ± 20 μM valinomycin; or preloaded with 300 mM mannitol and 50 mM Tris-MES (pH 8.2) and diluted in 150 mM K[Gluc], 50 mM Tris-MES (pH 6.5), and n-[14C]-butyrate (1.0 mM) ± 20 μM valinomycin.

Although, amiloride (Na+/H+ exchange inhibitor) showed slight inhibition of n-[14C]butyrate transport, acetazolamide (carbonic anhydrase inhibitor) failed to alter the butyrate uptake in the presence of an out-

![Fig. 2. Kinetics of n-[14C]butyrate uptake in colonic basolateral membrane vesicles (BLMV). Initial rates of butyrate transport with increasing extravesicular butyrate concentrations over the range 2–50 mM were determined. The vesicles were loaded with 150 mM KHCO3 and 50 mM Tris-HEPES (pH 8.2). Uptake was measured at 5 s at 25°C by incubating the vesicles in reaction medium containing 147 mM K[Gluc], 3 mM KHCO3, 50 mM Tris-MES (pH 6.5) and varying concentrations of sodium butyrate. Isosmolarity was maintained by adjusting K[Gluc] concentrations and all solutions containing HCO3− were gassed with 95% N2-5% CO2 for 10 min. Kinetic parameters calculated from the Lineweaver-Burk plot (representative plot shown in inset) were $K_m = 17.5 ± 4.5$ mM and $V_{max} = 20.9 ± 1.2$ nmol·mg protein$^{-1}$·5 s$^{-1}$. Values are means ± SE for 7 separate preparations.

![Fig. 3. Effect of transport inhibitors on n-[14C]butyrate uptake. Basolateral membrane vesicles preloaded with 150 mM KHCO3 and 50 mM Tris-HEPES (pH 8.2) were incubated in medium containing 147 mM K[Gluc], 3 mM KHCO3, 50 mM Tris-MES (pH 6.5), and 1 or 5 mM of the specific inhibitor. Uptake was measured at 10 s at 25°C with 0.5 mM n-[14C]butyrate and expressed as percentage of control. All solutions containing HCO3− were gassed with 95% N2-5% CO2 for 10 min. Values are means ± SE for 5–7 separate experiments. Control values, 230 ± 36 pmol·mg protein$^{-1}$·10 s$^{-1}$.](http://ajpgi.physiology.org/ by 10.220.33.3 on June 26, 2017)
wardly directed bicarbonate gradient. These observations clearly indicate involvement of a distinct transporter in the uptake of n-butyrate across the BLMV.

Effect of anions on bicarbonate-stimulated n-[14C]butyrate uptake. To determine the anion specificity of the HCO₃⁻-dependent butyrate exchanger, effects of various structural analogs on the initial rate of butyrate uptake were also investigated. In these studies, the addition of 10 mM of potassium salts of acetate, propionate, and unlabeled butyrate in the reaction media resulted in ~50–60% inhibition (P ≤ 0.05) of HCO₃⁻ and pH-gradient-stimulated n-[14C]butyrate uptake (Fig. 4). In contrast, formate produced small inhibition of butyrate transport, whereas oxalate had no effect on the uptake. These findings suggest that the HCO₃⁻ and pH-dependent butyrate transport in colonic BLMV involves a highly SCFA-specific carrier.

Transstimulation of n-[14C]butyrate uptake in human colonic BLMV. To further determine whether a carrier-mediated anion exchange process accounts for HCO₃⁻-gradient-driven butyrate uptake in colonic BLMV, a series of experiments was designed to study the transstimulation of n-[14C]butyrate uptake by intravesicular bicarbonate or unlabeled butyrate (100 mM). If a butyrate/anion exchanger exists in these membranes, loading of the vesicles with high concentration of cold butyrate should increase uptake of the extravesicular n-[14C]butyrate due to an increased turnover rate of the transporter functioning as a butyrate/butyrate exchanger. As shown in Fig. 5, imposition of an outwardly directed butyrate or bicarbonate gradient in the presence of an inwardly directed proton gradient resulted in substantial increase in n-[14C]butyrate uptake into the vesicles. This transstimulatory effect seen on n-butyrate preloaded vesicles in the presence of a pH gradient strongly suggests the existence of a pH-sensitive anion exchanger in colonic BLMV.

Effect of intravesicular and extravesicular Cl⁻ on n-[14C]butyrate uptake. Previous membrane vesicle studies have identified distinct electroneutral Cl⁻/HCO₃⁻ and SCFA/HCO₃⁻ exchangers in the human proximal colonic AMVs. To demonstrate the existence of a Cl⁻-independent pathway for HCO₃⁻-gradient-stimulated n-butyrate uptake in the human colonic BLMV the effects of Cl⁻ in the intravesicular and extravesicular reaction media on butyrate transport were also determined. As shown in Fig. 6, in these experiments, the uptake of n-butyrate into the vesicles in the presence of an outward- as well as inward-directed chloride gradient was similar to that observed in the absence of a Cl⁻ gradient (P > 0.05). Lack of inhibition of HCO₃⁻-dependent n-[14C]butyrate uptake in the presence of chloride strongly indicates that n-butyrate transport is independent of Cl⁻ uptake across the colonic basolateral epithelia.

DISCUSSION

SCFAs (acetate, propionate, and butyrate) are mainly produced as a result of microbial fermentation of dietary fiber in the lumen of the mammalian colon (4, 8–10). Although SCFAs have been shown to play a vital role in maintaining colonic health and in preventing colonic diseases (3, 13, 17, 27, 28), a clear understanding of the mechanisms of SCFA absorption across
the colonic epithelial membrane domains and their further metabolism inside the colonocytes has not yet been well established. A number of previous in vivo (18, 24) and in vitro studies (5, 15, 19, 22, 38, 43) have suggested that the SCFAs absorption across the intestinal apical domain involves either the nonionic diffusion of protonated SCFAs and/or a carrier-mediated anion exchange system. However, the contribution of the simple diffusion (5) versus anion exchange pathway (15, 16) under in vivo conditions is not entirely clear. Additionally, the mechanism of transport of the unmetabolized SCFA, across the human colonic basolateral domains is not well understood. Studies have shown extensive metabolic use of SCFAs by liver (26) and other peripheral tissues, thereby suggesting a possible existence of a transport mechanism for SCFA movement across the basolateral membrane of the colonocytes.

Recent studies from our laboratory and others utilizing vesicle techniques have demonstrated the existence of a distinct carrier-mediated HCO₃⁻ and pH-gradient-dependent anion exchange mechanism for SCFA absorption in the apical membranes of human ileum and colon (15, 16) and rat distal colon (22). In the present investigation, our results for the first time provide evidence for the existence of a distinct electroneutral HCO₃⁻-butyrate exchanger in the human proximal colonic BLMVs. With respect to the inhibition characteristics of this transporter, niflumic acid (1 mM) markedly inhibited the butyrate uptake into BLMVs, whereas the stilbene derivatives, SITS and DIDS, and acetazolamide had no effect. Insensitivity of HCO₃⁻-gradient-stimulated butyrate uptake to SITS and DIDS has also been observed for the previously described SCFA-HCO₃⁻ exchanger in the human ileum and colon (15, 16) and rat colon AMVs (22). However, in contrast, Reynolds et al. (30) observed a significant inhibition of the butyrate uptake by DIDS (1 mM) and acetazolamide (1 mM) in BLMVs of rat distal colon. These differences in DIDS sensitivity of the SCFA transporter may be possibly due to either species differences or the possible involvement of distinct monocarboxylate transporter (MCT) isoforms (which are known to be DIDS insensitive) in this transport process (14).

Further evidence supporting the involvement of a distinct carrier in HCO₃⁻ and pH gradient-driven butyrate transport across the human colonic BLMVs was provided by the kinetic analyses. In the presence of increasing concentrations of extravesicular butyrate (2–50 mM), the HCO₃⁻-gradient-stimulated butyrate uptake exhibited saturation with a Kₘ of 17.5 ± 4.5 mM and a Vₘₐₓ of 20.9 ± 1.2 nmol·mg protein⁻¹·s⁻¹. Although, the Kₘ value (17.5 ± 4.5 mM) for butyrate in the human colonic BLMVs is comparable to the Kₘ (26.9 mM) of butyrate for the previously characterized exchanger in rat BLMVs (30), it appears to be significantly higher than Kₘ for butyrate exchanger in AMVs in both the human (1.5 ± 0.2 mM) (15) and rat colon (6.9 mM) (22). Also, the present data of the anion-specificity of the HCO₃⁻-dependent butyrate exchanger strongly support the existence of a distinct anion-butyrate antiport system in the colonic BLMVs. Of the various structural analogs, acetate and propionate were found to significantly inhibit the HCO₃⁻ and pH-gradient-driven butyrate uptake, thereby indicating a possible competition of the carrier by the alternative SCFA substrates. The HCO₃⁻-gradient-stimulated n-[¹⁴C]butyrate uptake was not inhibited by chloride. Existence of a distinct carrier-mediated anion-butyrate exchange system in colonic BLMVs was further confirmed by transstimulation experiments. In this regard, imposition of an outward-directed butyrate or HCO₃⁻ gradient in the presence of an inwardly directed proton gradient was observed to cause a tremendous transstimulatory increase in butyrate uptake into the vesicles, thereby supporting the presence of a pH-sensitive anion butyrate exchanger in colonic BLMVs.

Recent membrane vesicle studies from our laboratory have identified distinct electroneutral Cl⁻/HCO₃⁻ (20) and SCFA/HCO₃⁻ (15) exchangers in the human proximal colonic AMVs. Similar to the above findings, our results of the present studies strongly confirm that HCO₃⁻-gradient-stimulated butyrate uptake across the colonic BLMVs is independent of Cl⁻ uptake. In the presence of high concentrations of extravesicular as well as intravesicular Cl⁻ no inhibition was observed in the butyrate uptake into the BLMV compared with the uptake in the absence of a Cl⁻ gradient. However, these results are not in agreement with the observations of Rajendran and Binder (29), who demonstrated a Cl⁻-dependent SCFA uptake system in rat colonic AMVs. The observed discrepancy in n-butyrate uptake across the colonic epithelia in relation to the effect of
chloride may be due to species differences. Species differences with respect to chloride dependence as well as DIDS sensitivity (described above) could also be due to diverse dietary habits in different species. In this regard, differences in transport patterns of electrolytes in various regions of the intestine in different species have also been observed (12, 20, 29, 36).

The HCO$_3^-$ and pH-gradient-stimulated butyrate exchange in human proximal colonic BLMVs apparently appears to possess transport characteristics identical to the previously demonstrated anion exchange for butyrate in human colonic AMVs. However, our data of the present report clearly reflect significant differences in the kinetic parameters of these two anion exchangers, strongly supporting that two separate and distinct anion exchange systems exist for butyrate transport in the apical and basolateral membrane domains of the colonic epithelia and that the BLMVs were not contaminated by AMVs or vice versa. For example, a Lineweaver-Burk plot analysis of the butyrate uptake in human colonic BLMVs yielded a $K_m$ of 17.5, which is significantly higher and different from the $K_m$ (1.5 ± 0.2 mM) of colonic AMVs butyrate transporter.

In summary, our results provide a clear evidence for the existence of a distinct SCFA/anion exchanger on the basolateral membranes of the human proximal colonic epithelial cells, which appears to be distinct and separate from other previously characterized anion exchangers in the membranes of colonic epithelia. Further molecular identification and characterization of the anion-butyrate carrier in the human colonic basolateral membranes will be of great significance for understanding its role in SCFA absorption across the colonic epithelia and their relationship to the other colonic transporters.

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