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## Functional characterization of $\text{Cl}^-/\text{HCO}_3^-$ exchange in villous cells of the mouse ileum

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**ABSTRACT**

At least three kinds of  $\text{Cl}^-/\text{HCO}_3^-$  exchangers, SLC26A3, SLC26A6 and AE2, have been demonstrated to be expressed in the intestinal epithelial cell. To examine the functional expression of these exchangers in the native enterocyte, we studied the  $\text{Cl}^-/\text{HCO}_3^-$ -exchange activity in isolated villi from the mouse ileum by microfluorometric intracellular pH ( $\text{pH}_i$ ) measurement. The  $\text{pH}_i$  value increased upon  $\text{Cl}^-$  removal when the villus was superfused with an  $\text{HCO}_3^-/\text{CO}_2$ -buffered solution, while the response was blunted when superfused with an  $\text{HCO}_3^-/\text{CO}_2$ -free, HEPES-buffered solution. The recovery of  $\text{pH}_i$  value induced by  $\text{Cl}^-$  re-addition (after initial  $\text{Cl}^-$  removal) was totally or partially mimicked by the addition of  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{F}^-$ ,  $\text{NO}_3^-$ , or  $\text{SO}_4^{2-}$  (in the absence of  $\text{Cl}^-$ ). The increase in  $\text{pH}_i$  value induced by  $\text{Cl}^-$  removal was partially inhibited in the presence of DIDS (30  $\mu\text{M}$ ), tenidap (10  $\mu\text{M}$ ), niflumic acid (30  $\mu\text{M}$ ) or NPPB (30  $\mu\text{M}$ ). Increasing the  $\text{K}^+$  concentration from 5 mM to 60 mM in the superfusion solution induced a reversible increase in  $\text{pH}_i$  value under the  $\text{HCO}_3^-/\text{CO}_2$ -buffered condition, while it had hardly any effect on  $\text{pH}_i$  under the HEPES-buffered condition. The  $\text{K}^+$ -induced  $\text{pH}_i$  changes were partially suppressed by removing  $\text{Cl}^-$  from the superfusion solution. These results, together with the reported findings of mouse slc26a3, slc26a6 and AE2 in heterologously expressed systems, suggest the possibility that these three exchangers may all be functionally expressed in mouse ileal villous

cells.

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