Differential Regulation of Basolateral Cl⁻/HCO₃⁻ Exchangers
SLC26A7 and AE1 in Kidney Outer Medullary Collecting Duct

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Abstract. SLC26A7 is a recently identified Cl⁻/HCO₃⁻ exchanger that co-localizes with AE1 on the basolateral membrane of A intercalated cells (A-IC) in outer medullary collecting duct (OMCD). The purpose of these studies was to determine whether AE1 and SLC26A7 are differentially regulated in OMCD in pathophysiologic states. Toward this end, the expression and regulation of AE1 and SLC26A7 was examined in water deprivation, a condition known to increase the osmolality of the medulla. Rats were subjected to water deprivation while having free access to food. Northern hybridizations demonstrated that in the outer medulla, the mRNA expression of SLC26A7 increased by ~300% (versus control; n = 3), whereas the expression of AE1 decreased by ~50% (versus control, n = 3) in water-deprived rats. Immunoblot analysis studies demonstrated that in the outer medulla, SLC26A7 abundance increased by ~3.5-fold (P < 0.02 versus control; n = 3), whereas the AE1 abundance decreased by ~55% (P < 0.05 versus control) in water deprivation. The expression of SLC26A7 remained unchanged in the kidney cortex and stomach in water deprivation, indicating the specificity of SLC26A7 upregulation in outer medulla. In situ hybridization indicated the exclusive expression of SLC26A7 in the outer medulla and double immunofluorescence labeling confirmed the co-localization of AE1 and SLC26A7 on the basolateral membrane of A-IC cells in OMCD. It is concluded that AE1 and SLC26A7 are differentially regulated in OMCD in water deprivation. On the basis of these results and previous functional studies indicating the activation of SLC26A7 activity by high osmolality, it is proposed that SLC26A7 may play an important role in bicarbonate reabsorption and or cell volume regulation in OMCD (specifically under hypertonic conditions).

The outer medullary collecting duct (OMCD) plays an essential role in acid-base homeostasis by acid secretion and bicarbonate reabsorption, which are mediated via H⁺-ATPase (and to some extent H⁺-K⁺-ATPase) on the apical membrane and Cl⁻/HCO₃⁻ exchanger on the basolateral membrane (1). The OMCD has the highest rate of H⁺ secretion and, therefore, HCO₃⁻ absorption in the collecting duct segments (2). As a result, OMCD has been regarded as a major regulator of acid-base homeostasis.

Two major families of Cl⁻/HCO₃⁻ exchangers have been identified and studied. The first one is designated SLC4A and has four well known members (AE1, AE2, AE3, and AE4 or SLC4A1, A2, A3 and A10) (3). AE1, AE3, and AE4 show limited tissue expression pattern, whereas AE2 is more widely distributed. AE1 is predominantly expressed in kidney intercalated cells and osteoblasts with low levels in the lower gastrointestinal tract (3). The AE family belongs to the AE/NBC superfamily, indicating similar ancestral origin between the AE (SLC4A1 to 3) and NBC (the Na⁺:HCO₃⁻ co-transporters or SLC4A4 to 11) families (2–7). The other group of Cl⁻/HCO₃⁻ exchanger belongs to the SLC26A family, which has 11 identified members (8–14), with little homology to AE/NBC superfamily. All members of the SLC26A family have been shown to transport anions. Four closely related members of this family are SLC26A3 (down-regulated in adenoma [DRA]), SLC26A4 (Pendrin [PDS]), SLC26A6 (PAT1 or CFEX), and SLC26A7. These four transporters mediate Cl⁻/HCO₃⁻ exchange (12,15–19). DRA is expressed on the apical membranes of colonocytes (8,9,15), whereas PAT1 or CFEX is expressed on the apical membranes of kidney proximal tubule and duodenum (11,16,20). PDS mRNA expression is detected in proximal tubule and cortical collecting duct (15). However, immunocytochemical studies localize PDS only to the apical membrane of a subpopulation of cortical collecting duct cells distinct from A-IC cells, which are thought to be B-IC cells and non-A, non-B IC cells (15,21–24). A recently
cloned member of the SLC26A family is SLC26A7, which was shown to be expressed in kidney and testis (14). Very recent studies from our laboratory demonstrated that SLC26A7 is abundantly expressed in the stomach and mediates $\text{Cl}^-/\text{HCO}_3^-$ exchange (19,25). SLC26A7 expression in the stomach is limited to the basolateral membrane of gastric parietal cells (25).

The $\text{Cl}^-/\text{HCO}_3^-$ exchanger AE1, which is a variant of red cell band 3, was shown to be expressed on the basolateral membrane of A-IC of OMCD (2,3). It was presumed that AE1 is the only basolateral $\text{Cl}^-/\text{HCO}_3^-$ exchanger in OMCD A-IC. However, recent studies from our laboratory demonstrate that SLC26A7 mediates $\text{Cl}^-/\text{HCO}_3^-$ exchange and localizes to the basolateral membrane of A-IC in OMCD (19). The presence of two distinct $\text{Cl}^-/\text{HCO}_3^-$ exchangers on the same membrane domain raises the possibility of differential regulation in pathophysiologic states. Accordingly, we tested the effect of increased osmolality of the medullary interstitium on the expression of SLC26A7 and AE1. Toward this end, animals were subjected to water deprivation for 3 d, killed, and examined.

Materials and Methods

Female Sprague-Dawley rats that weighed 100 to 150 g were used for these studies. Animals were subjected to 3 d of water deprivation with free access to food according to approved institutional protocols. Animals were killed with the use of anesthetics (pentobarbital sodium) according to the institutional guidelines and approved protocols. In separate but similar studies from our group, we find elevated urine osmolality and enhanced expression of AQP2 in rats that are subjected to water deprivation for 3 d (26), consistent with dehydration and increased medullary interstitial osmolality.

Reverse Transcription–PCR of SLC26A7 in the Kidney

A mouse Expressed Sequence Tag (EST) (GenBank accession no. BB6666404) that matched the human SLC26A7 sequence (GenBank accession no. AF331521) was identified. The following oligonucleotide primers were designed on the basis of the EST cDNA sequence and used for reverse transcription–PCR (RT-PCR) on RNA isolated from rat stomach and kidney: 5'-CTCACCCACGAACCTTTCAC (sense) and 5'AACTCCGATAAGCCCCAACAC (antisense). An ~550-bp PCR fragment that corresponded to the human nucleotides 8 to 550 was purified and sequenced. The purified fragment was used as probe for Northern hybridization.

RNA Isolation and Northern Blot Hybridization

Total cellular RNA was extracted from various rat kidney zones (cortex, outer medulla, and inner medulla) and stomach according to established methods, quantified spectrophotometrically, and stored at −80°C. Total RNA samples (30 μg/lane) were fractionated on a 1.2% agarose-formaldehyde gel, transferred to Magna NT nylon membranes, cross-linked by ultraviolet light, and baked. Hybridization was performed according to established protocols. The membranes were washed, blotted dry, and exposed to a PhosphorImager screen (Molecular Dynamics, Sunnyvale, CA). For SLC26A7, a $^{32}\text{P}$-labeled cDNA fragment corresponding to nucleotides 8 to 550 of SLC26A7 cDNA (see above) was used for Northern hybridizations. For AE1, a $^{32}\text{P}$-labeled 650-bp cDNA (SacI-BglII fragment) from rat AE-1 cDNA was used as specified.

In Situ Hybridization

The distribution of SLC26A7 within the rat kidney was assessed with in situ hybridization as previously reported (27). In brief, rat kidneys were rapidly dissected, fixed in 4% paraformaldehyde, cryo-protected with 30% sucrose in PBS, and frozen in optimum cutting temperature compound. Cryostat sections (7 μm) were then mounted on silane-coated slides.

For labeling of SLC26A7 in kidney, the following oligonucleotide primers were designed and used for RT-PCR on RNA isolated from mouse kidney: 5'-CTCACCCACGAACCTTTCAC (8) and 5'-AACTCCGATAAGCCCCAACAC (550). The PCR product was purified, ligated into pGEM-T vector, and linearized by SacII, and the antisense cRNA was generated by SP6 DNA-dependent RNA polymerase (Riboprobe Gemini Core System II transcription kit; Promega, Madison, WI). A sense cRNA probe was used as a negative control. The radiolabeled (S35-UTP) probes were hybridized and washed under high-stringency conditions. Hybridization was performed with 0.5 to 1.0 ¥ 106 counts/min labeled probe in a final volume of 30 μl/slide. After overnight incubation at 42°C, the sections were treated with 50 μg/ml RNase A and 100 U/ml RNase T1 for 30 min at 37°C and washed to a final stringency in 0.1% saline-sodium citrate at 50°C. The slides were dipped in NTB2 emulsion (Eastman Kodak) diluted 1:1 with 0.6 M ammonium acetate and exposed for 2 wk. Thereafter, slides were developed with D19 developer (Eastman Kodak) and counterstained with hematoxylin and eosin.

Antibodies

For SLC26A7, antibodies against human or mouse sequence were used. For human, SLC26A7-specific antibodies were raised against a synthetic peptide based on human sequence (11). We raised polyclonal antibodies against a synthetic peptide corresponding to the amino acids residues CGAKRRKRSVLWGKMHTP of mouse SLC26A7 in two rabbits. The specificity of these antibodies has been studied in detail (19,25). AE1 antibodies were raised against the N-terminal end of AE1 and were purchased from Chemicon (Temecula, CA). β-Actin monoclonal antibodies were purchased from Alpha Diagnostics (San Antonio, TX).

For aquaporin 2 (AQP2), a polyclonal antibody specific to AQP2 water channel was raised against the rat AQP2 peptide CEVRRRQSVELHPSQLPGRSKA, which corresponds to amino acid residues 250 to 271 of the carboxy-terminal tail of the vasopressin-regulated AQP2 water channel. This antibody is highly specific and labels the apical membrane of principal cells in the collecting duct (28).

Preparation of Membrane Fractions from Various Kidney Zones

Microsomal membrane vesicles from cortex and medulla were prepared as described with minor modifications. Briefly, the tissue samples were homogenized in ice-cold isolation solution (250 mM sucrose and 10 mM triethanolamine [pH 7.6]) containing protease inhibitors (0.1 mg/ml phenazine methyl sulfonyl fluoride, 1 μg/ml leupeptin), using a Polytron homogenizer. The homogenates were centrifuged at low speed (1000 ¥ g) for 10 min at 4°C to remove nuclei and cell debris. After this, the supernatants were spun at 150,000 ¥ g for 90 min at 4°C; the pellets that contained plasma membrane and intracellular vesicles were suspended in isolation solution with protease inhibitors. The total protein concentration was measured, and the membrane fractions were solubilized at 60°C for 20 min in Laemmli sample buffer.
Electrophoresis and Immunoblotting

Electrophoresis and immunoblotting experiments were carried out as described (12,16). Briefly, the solubilized membrane proteins were size-fractionated on 12% polyacrylamide minigels (Novex, San Diego, CA) under denaturing conditions. Using a BioRad transfer apparatus (BioRad Laboratories, Hercules, CA), the separated proteins were electroblotter transferred to nitrocellulose membranes. The membranes were blocked with 5% milk proteins and then probed with affinity-purified anti-SLC26A7 or AE1 immune serum at an IgG concentration of 0.14 μg/ml. The secondary antibody was donkey anti-rabbit IgG conjugated to horseradish peroxidase (0.16 μg/ml; Pierce, Rockford, IL). The sites of antigen-antibody complexation on the nitrocellulose membranes were visualized using chemiluminescence method (SuperSignal Substrate; Pierce) and captured on light-sensitive imaging film (Kodak). Bands corresponding SLC26A7 and AE1 proteins were quantified by densitometric analysis (UNSCAN-IT gel software; Silk Scientific, Orem, UT) and were expressed as a percentage of control.

Immunofluorescence Labeling Studies

Rats were killed with an overdose of sodium pentobarbital and perfused through the left ventricle with 0.9% saline followed by cold 4% paraformaldehyde in 0.1 M sodium phosphate buffer (pH 7.4). Kidneys were removed, cut in tissue blocks, and fixed in formaldehyde solution overnight at 4°C. The tissue was frozen on dry ice, and 6-μm sections were cut with a cryostat and stored at −80°C until used. Single and double immunofluorescence labeling was performed as described using either Alexa Fluor 488 (green) or Alexa Fluros 568 (red) goat anti-rabbit antibody as secondary antibodies (19,25).

For double immunofluorescence labeling, both AQP2 and SLC26A7 antibodies (or AE1 and SLC26A7) were used at the 1:40 dilution. SLC26A7 antibody was labeled directly by using Zenon Alexa Fluor 488 Rabbit IgG labeling kit, and AQP2 was labeled by Zenon Alexa Fluor 488 Rabbit IgG Labeling kit (Molecular Probes, Eugene, OR) according to the manufacturer’s instructions. Briefly, SLC26A7 or AQP2 antibody was incubated with a fluorophore-labeled, Fc-specific anti-rabbit IgG Fab fragment. Fab fragment/primary antibody molar ratio was 6:1. The Fab fragment binds to the Fc portion of the rabbit primary antibody, rendering fluorophore-labeled primary antibody ready to be applied to the kidney sections. Sections were examined, and images were acquired on the Nikon PCM 2000 laser confocal scanning microscope as 0.5 to 1 μm “optical sections” of the stained cell membrane. A ×20 objective and a ×60 oil-immersion objective was used. The 543.5-nm single-line output of the HeNe laser was used for the red dye excitation, and the standard red channel long-pass 565-nm filter was used as an emission filter. The standard Argon laser 488-nm line and the 515/30-nm emission filter were used for the green-emitting dye. Black level, gain, and integration time (i.e., pixel dwell time) were kept the same when sections from control and water-deprived animals were compared. In addition, all sections from control and water-deprived animals were processed the same day and with the same dilutions of primary and secondary antibodies. More than 20 sections from four separate animals were examined in each group of control or water deprivation.

Materials

32P-dCTP was purchased from New England Nuclear (Boston, MA). Nitrocellulose filters and other chemicals were purchased from Sigma Chemical Co. (St. Louis, MO). RadPrime DNA labeling kit was purchased from Life Technologies BRL. BCECF was from Molecular Probes. mMESSAGE mMACHINE Kit was purchased from Ambion (Austin, TX). The human multiple tissue blot was purchased from Clontech (Palo Alto, CA.)
Cl\(^{-}/\)HCO\(_3^{-}\) exchangers (SLC26A7 and AE1) on the basolateral membrane of an intercalated cell in OMCD (Figure 3B).

Water Deprivation in Rats

Table 1 summarizes the serum electrolyte and renal function parameters (serum sodium, bicarbonate, potassium, blood urea nitrogen, creatinine, etc.) in normal and water-deprived rats. As indicated, rats that were subjected to water deprivation had increased serum sodium, chloride, and albumin, consistent with hemoconcentration. Blood urea nitrogen level was elevated, indicating kidney hypoperfusion in water-deprived rats. An unexpected but intriguing finding was a significant reduc-
tion in serum bicarbonate and an elevation in anion gap in water-deprived rats, consistent with the generation of anion gap metabolic acidosis. Water-deprived rats eat very little despite full access to food, presumably because of suppressed appetite. It is very likely that metabolic acidosis in these animals is due to increased generation of ketoacids, which has been well documented in mammals with voluntary or nonvoluntary food abstinence. The increment in anion gap (from 21 mEq/L in normal rats to 29 mEq/L in water-deprived rats) parallels the reduction in serum bicarbonate, indicating that generation of ketoacidosis is likely responsible for serum bicarbonate reduction.

Expression of SLC26A7 in Water Deprivation

The presence of two Cl⁻/HCO₃⁻ exchangers on the basolateral membrane of A-IC cells in OMCD raises the question of differential regulation in disease states. SLC26A7 is activated by increased osmolality (19), raising the possibility that it can adapt to hypertonic environment. The outer medulla has the capability to increase its tonicity in several conditions by
upregulating osmolyte transporters. We asked the question of whether increasing the osmolality of the medulla alters the expressions of SLC26A7 (or AE1). Rats were subjected to 3 d of water deprivation with access to food and killed, and their kidneys were processed for expression studies.

In the first series of studies, we examined the mRNA ex-

Figure 3. (A) Double immunofluorescence labeling of SLC26A7 and aquaporin 2 (AQP2) in outer medulla. SLC26A7 and AQP2 localize to two distinct cell types in OMCD, with AQP2 expression on the apical membrane of principal cells and SLC26A7 expression limited to the basolateral membrane of intercalated cells (merged images). (B) Double immunofluorescence labeling of SLC26A7 and AE1 in outer medulla. SLC26A7 (red) and AE1 (green) co-localize on the basolateral membrane of the same cells in OMCD. We conclude that both transporters are located on the basolateral membrane of A intercalated (A-IC) cells in OMCD.

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expression of SLC26A7. As demonstrated in Figure 4A, the expression of SLC26A7 increased by approximately threefold in outer medulla of water-deprived rats \((P < 0.01; n = 3)\). To determine whether the upregulation of SLC26A7 in water deprivation is specific to outer medulla or can also occur in kidney cortex or stomach, we performed Northern hybridization of SLC26A7 in these latter two tissues. As demonstrated in Figure 4B, SLC26A7 expression remained unchanged in kidney cortex and stomach. In the next series of experiments, we examined the protein abundance of SLC26A7 in outer medulla in water deprivation. As demonstrated in Western blot analysis in Figure 5, SLC26A7 abundance increased by ~3.5-fold in outer medulla of water-deprived rats \((P < 0.02; n = 3)\).

**Expression of AE1 in Water Deprivation**

The results of the experiments in Figures 4 and 5 demonstrate that SLC26A7 is upregulated in OMCD in water-deprived rats. The purpose of the next series of experiments was to examine the expression of AE1 in water deprivation in outer medulla. Figure 6 is a Northern hybridization experiment and demonstrates that the expression of AE1 is actually reduced in water-deprived rats, with mRNA levels decreasing by ~50% versus control animals \((P < 0.05; n = 3)\). To determine the protein abundance of AE1 in water deprivation, we performed Western blot analysis. As shown in Figure 7, AE1 abundance

**Table 1.** Blood composition of control rat (food + water) and rats deprived of water for 72 hours (food present)\(^a\)

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<tr>
<th></th>
<th>BUN (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Na(^+) (mEq/L)</th>
<th>K(^+) (mEq/L)</th>
<th>Cl(^-) (mEq/L)</th>
<th>HCO3(^-) (mEq/L)</th>
<th>Albumin (g/dl)</th>
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<td>Control</td>
<td>18 ± 0.48</td>
<td>0.35 ± 0.03</td>
<td>141 ± 0.58</td>
<td>5.3 ± 0.17</td>
<td>98 ± 0.48</td>
<td>22 ± 1.19</td>
<td>3.18 ± 0.06</td>
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<tr>
<td>Water deprivation</td>
<td>29 ± 1.7</td>
<td>0.4 ± 0.04</td>
<td>154 ± 1.65</td>
<td>5.9 ± 0.27</td>
<td>112 ± 1.49</td>
<td>13 ± 0.48</td>
<td>3.98 ± 0.25</td>
</tr>
<tr>
<td>(P)</td>
<td>&lt;0.002</td>
<td>NS</td>
<td>&lt;0.0004</td>
<td>NS</td>
<td>&lt;0.0002</td>
<td>&lt;0.0007</td>
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\(\text{a}\) \(n = 4\) rats in each group. BUN, blood urea nitrogen.

**Figure 4.** SLC26A7 mRNA expression in outer medulla in water-deprived rats. (A) SLC26A7 expression increased by approximately threefold in outer medulla of water-deprived rats. (B) SLC26A7 expression in the kidney cortex and stomach remained unchanged in water deprivation.

**Figure 5.** Western blot analysis of SLC26A7 in outer medulla in water-deprived rats. SLC26A7 abundance increased significantly in outer medulla of water-deprived rats.

**Figure 6.** AE1 mRNA expression decreased by ~50% in outer medulla of water-deprived rats.
The OMCD expresses two distinct \( \text{Cl}^-/\text{HCO}_3^- \) exchangers, SLC26A7 and AE1, on the basolateral membrane of its A-IC cells. The above studies demonstrate differential regulation of SLC26A7 and AE1 in OMCD in water deprivation, a condition associated with increased tonicity in the medulla. SLC26A7 expression is increased (Figures 4 and 5) whereas AE1 expression is decreased (Figures 6 and 7) in water deprivation, despite the generation of metabolic acidosis (Table 1). The results further confirm the exclusive expression of SLC26A7 in OMCD (Figures 1 through 3) and its co-localization with AE1 on the basolateral membrane of A-IC cells in OMCD (Figure 3).

The presence of two acid-base transporters with similar functional modes in the same epithelial membrane domain has been well established. For example, two \( \text{Na}^+ / \text{H}^+ \) exchanger isoforms (NHE3 and NHE2) have been detected on the apical membrane of intestinal villi, and two \( \text{Na}^+ :\text{HCO}_3^- \) co-transporter isoforms (NBC1 and NBC2) have been localized to the basolateral membrane of small intestinal villi (3,30). However, less is known about the regulation of these transporters in pathophysiologic states. Whether the presence of two acid-base transporters with identical function on the same membrane domain reflects an evolutionary defensive mechanism designed to ensure functional continuity in that epithelium (by compensatory adaptive regulation of one transporter in case of maladaptive regulation of the other transporter) remains speculative. Alternatively, it is plausible that functionally identical acid-base transporters expressed on the same membrane may be differentially regulated in pathophysiologic states.

The present studies report the intriguing observation of differential regulation of two distinct renal basolateral \( \text{Cl}^-/\text{HCO}_3^- \) exchangers in water deprivation. They further demonstrate that SLC26A7 upregulation in water deprivation is specific to outer medulla and does not involve kidney cortex and stomach, two organs with no alteration in their interstitial osmolality in response to water deprivation. AE1 mediates vectorial transport of bicarbonate in the collecting duct. Humans with inactivating AE1 mutation develop distal renal tubular acidosis secondary to bicarbonate wasting as a result of mistargeting of AE1 to the apical side of type A-IC cells (31–33), indicating an essential role for AE1 in bicarbonate reabsorption in the collecting duct. Whether SLC26A7 shows compensatory upregulation in OMCD intercalated cells in humans with inactivating AE1 mutation remains unknown. It is possible that the bicarbonate wasting in these patients originates predominantly from cortical collecting duct, which does not express SLC26A7, or is mitigated by SLC26A7 upregulation in OMCD. Studies in cortical and medullary collecting ducts in AE1 null mice, in case they display distal renal tubular acidosis, should answer these questions. Similarly, whether the absence of SLC26A7 alters the expression of AE1 in OMCD cells will be best answered by studying SLC26A7 knockout mouse.

The downregulation of AE1 in water deprivation (Figures 6 and 7) is intriguing as it occurs in the context of anion gap metabolic acidosis. It is worth mentioning that metabolic acidosis, as caused by \( \text{NH}_4\text{Cl} \) loading, is actually associated with the upregulation of AE1 (1–3). The downregulation of AE1 is presumably a maladaptive process as it can contribute to the worsening of metabolic acidosis by causing bicarbonate wasting in OMCD. That would have been the case if AE1 were the sole bicarbonate extruding mechanism in OMCD A-IC cells. It is plausible that the upregulation of SLC26A7 in OMCD in water deprivation may compensate for the downregulation of AE1 and prevent bicarbonate loss and worsening of metabolic acidosis, which otherwise would have resulted from AE1 downregulation.

The activity of SLC26A7 is enhanced by hypertonicity (19), and its expression in the outer medulla is increased in water deprivation (Figures 4 and 5), a condition known to increase the tonicity of medulla (34). The activation of SLC26A7 by hypertonicity is consistent with increased entry of peritubular chloride in exchange for intracellular bicarbonate in OMCD A-IC cells. This process could be coupled to the upregulation of the basolateral \( \text{Na}^+ / \text{H}^+ \) exchanger NHE1 in OMCD A-IC cells in water deprivation. The expression of \( \text{Na}^+ / \text{H}^+ \) exchanger NHE1 in basolateral membrane of OMCD (35) and its upregulation by hypertonicity (36–38) have been well documented. On the basis of these results and the current studies, we propose that hypertonicity causes parallel activation of SLC26A7 and NHE1, which in turn results in enhanced entry of \( \text{Na}^+ \) and \( \text{Cl}^- \) into A-IC of OMCD with subsequent regulation of cell volume. As such, SLC26A7 may be essential for cell volume regulation in A-IC cells in OMCD, which otherwise are poorly equipped for regulatory cell volume increase in hypertonic environment.

In conclusion, SLC26A7 and AE1 co-localize on the basolateral membrane of A-IC cells in OMCD and are differentially regulated in water deprivation. On the basis of functional studies demonstrating mediation of \( \text{Cl}^-/\text{HCO}_3^- \) exchange, we propose that SLC26A7 plays an important role in bicarbonate transport in OMCD. Further studies are needed to elucidate the molecular basis of differential regulation of these transporters, and whether SLC26A7 can replace AE1 in bicarbonate reabsorption in OMCD.
reabsorption and/or cell volume regulation in OMCD A-IC cells (specifically in conditions associated with increased medullary toxicity).

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