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Role of Crystalloids in the Perioperative Setting: From Basics to Clinical Applications and Enhanced Recovery Protocols. Lorente JV, Hahn RG, Jover JL, Del Cojo E, Hervas M, Jimnez I, Ua R, Clau-Terr F, Monge MI, Llau JV, Colomina MJ, Ripolls-Melchor J, Lorente JV, et al. J Clin Med. 2023 Sep 12;12(18):5930. doi: 10.3390/jcm12185930. J Clin Med. 2023. PMID: 37762871 Free PMC article. Review. Levy, Amir[1]; de Souza, J. Pedro[2]; Bazant, Martin Z.[3] Massachusetts Inst. of Technology (MIT), Cambridge, MA (United States). Dept. of Physics; Massachusetts Inst. of Technology (MIT), Cambridge, MA (United States) Massachusetts Inst. of Technology (MIT), Cambridge, MA (United States). Dept. of Chemical Engineering Massachusetts Inst. of Technology (MIT), Cambridge, MA (United States). Dept. of Chemical Engineering; Massachusetts Inst. of Technology (MIT), Cambridge, MA (United States). 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Thorie de la permabilit ionique journal January 1936 Direct Observation of Charge Inversion in Divalent Nanofluidic Devices journal June 2015 Analysis of electrolyte transport through charged nanopores journal May 2016 Analysis of ionic conductance of carbon nanotubes journal November 2016 Deionization shocks in microstructures journal December 2011 The effect of protein dielectric coefficient on the ionic selectivity of a calcium channel journal July 2006 Electrostatics of ions inside the nanopores and trans-membrane channels journal October 2006 Transport in one-dimensional Coulomb gases: From ion channels to nanopores journal January 2006 159 Comparison of gene Expression Profiles between Normal and Sclerosis Regions of Human Osteoarthritic Subchondral bone journal October 2010 Tough Electrodes: Carbon Nanotube Fibers as the Ultimate Current Collectors/Active Material for Energy Management Devices journal October 2015 Anomalous ion transport in 2-nm hydrophilic nanochannels journal November 2010 Electrolyte osmosis through capillaries journal August 1981 Electrochemomechanical Energy Conversion in Nanofluidic Channels journal December 2004 Exact Statistical Mechanics of a OneDimensional System with Coulomb Forces journal September 1961 Multicomponent Gas Diffusion in Porous Electrodes journal January 2015 As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn more: PMC Disclaimer | PMC Copyright Notice Renal type IIa Na+-coupled inorganic phosphate (Pi) cotransporters (NaPi-IIa) mediate divalent Pi transport in an electrogenic manner, whereas the renal type IIc isoform (NaPi-IIc) is electroneutral, yet it shows high sequence identity with NaPi-IIa. Dual uptake (32Pi/22Na) assays confirmed that NaPi-IIc displayed Na+-coupled Pi cotransport with a 2:1 (Na+:-Pi) stoichiometry compared with 3:1 established for NaPi-IIa. This finding suggested that the electrogenicity of NaPi-IIa arises from the interaction of an additional Na+ ion compared with NaPi-IIc. To identify the molecular elements responsible for the functional difference between isoforms, we used chimera and amino acid replacement approaches. Transport activity of chimeras constructed with NaPi-IIa and NaPi-IIc indicated that residues within the first six transmembrane domains were essential for the electrogenicity of NaPi-IIa. Sequence comparison between electrogenic and electroneutral isoforms revealed differences in the charge and polarity of residues clustered in three areas, one of which included part of the predicted third transmembrane domain. Here, substitution of three residues with their NaPi-IIa equivalents in NaPi-IIc (S189A, S191A, and C195D) resulted in a transporter that displayed a 1:1 charge/Pi coupling, a 3:1 Na+-Pi stoichiometry, and transient currents that resembled pre-steady-state relaxations. The mutant's weaker voltage dependency and 10-fold lower apparent Pi affinity compared with NaPi-IIa indicated that other residues imported to the NaPi-IIa kinetic fingerprint exist. Our findings demonstrate that, through a minimal number of side chain substitutions, we can effect a switch from electroneutral to electrogenic cotransporter function, concomitant with the appearance of a cosubstrate interaction site.Secondary-active transporter proteins mediate uphill transport of a solute by tapping into the free energy provided by the concentration gradient of a coupled ion that is specific to the transporter protein (e.g., H+, K+, or Na+). The coupling between driving and driven species confers a strict stoichiometric ratio on cotransport function. When stoichiometrically coupled movement of net charge accompanies cotransport, an additional driving force is available, derived from the free energy established by the transmembrane electric field. For such electrogenic cotransporters, it follows that membrane voltage also becomes a kinetic determinant of the transport mechanism; moreover, under physiological conditions, it can serve to enhance the concentrating ability of the transport protein.One of the many physiologically important transport processes that rely on a secondary active mechanism is reabsorption of inorganic phosphate (Pi) in the renal proximal tubule. Two isoforms of type II Na+-coupled Pi cotransporters (NaPi-II), both localized at the proximal tubule apical brush border membrane, have been identified. Both cotransporters mediate inward transport of Pi by using the inwardly directed Na+ gradient (1, 2). Type IIa cotransporters (SLC34A1 or NaPi-IIa) couple three Na+ ions to the cotransport of one divalent Pi ion, and each transport cycle is accompanied by the inward translocation of one net positive charge (3, 4). The NaPi-IIa cotransport rate is strongly dependent on transmembrane potential. This dependency is hypothesized to result from voltage-dependent transitions between favored conformational states of the protein that include the interaction of one Na+ ion with intrinsic mobile charges of the NaPi-IIa protein (4-9).In contrast, renal type IIc cotransporters (SLC34A3 or NaPi-IIc) (2, 10) mediate electroneutral Na+-coupled Pi cotransport yet, with respect to other steady-state transport parameters (e.g., apparent substrate affinities and pH dependency), resemble NaPi-IIa. Consistent with electroneutral cotransport of divalent Pi, it has been proposed that NaPi-IIc cotransports with a 2:1 stoichiometry (2, 10). It follows that NaPi-IIc may lack one of the three Na+ binding sites postulated for NaPi-IIa. So far, neither the absence of a Na+ binding site nor the stoichiometry have been experimentally established. Topological prediction algorithms indicate no significant differences between NaPi-IIa and NaPi-IIc (4), which suggests that their respective transmembrane topologies are most likely identical. Moreover, a sequence comparison of NaPi-IIa and NaPi-IIc indicates a high degree of similarity (10), particularly in the predicted transmembrane domain (TMD) regions. These findings imply that only small changes in the amino acid sequence may be required to perform a functional switch between the electrogenic and electroneutral behavior, together with a concomitant change in the stoichiometry.To identify the molecular elements responsible and gain insight into the underlying mechanism that confers electrogenicity to NaPi-IIa, we took advantage of the functional difference between the NaPi-IIa and NaPi-IIc isoforms by engineering complementary chimeras between each isoform and expressing these in Xenopus oocytes. We then refined the localization procedure by using a bioinformatic approach. This approach led to the identification of three residues in the predicted third TMD (TMD-3) that are conserved in all electrogenic NaPi-II transporters so far identified. By substituting the equivalent NaPi-IIa amino acids at these sites in the NaPi-IIc sequence, functional expression of this transport protein in Xenopus oocytes displayed Na+-dependent Pi-induced steady-state currents and voltage step-induced transient currents, neither of which were observed in oocytes that expressed the WT NaPi-IIc. Our findings document that TMD-3 mutations transformed the electroneutral NaPi-IIc into an electrogenic cotransporter, and we propose that the electrogenicity results from an increase in the number of Na+ ion binding sites from two to three.Molecular Biology. Chimeras were based on mouse NaPi-IIa (in pSport) and mouse NaPi-IIc (in pT7T3D-Pac, a kind gift from K.-I. Miyamoto, Tokushima University, Tokushima, Japan). To obtain the NaPi-IIa and NaPi-IIc fragments, we introduced new restriction sites at the junctions. The necessary amino acid substitutions were located in predicted TMD linkers, where substitutions are usually well tolerated (11). Mutagenesis and cRNA preparation were performed as described in ref. 9. Oocytes were injected with 50 nl of water or with 50 nl of water containing 10 ng of cRNA.Reagents and Solutions. The solution compositions were as follows. Control superfusate (ND100): 100 mM NaCl/2 mM KCl/1.8 mM CaCl2/1 mM MgCl2/10 mM Hepes-Tris, pH 7.4, unless otherwise stated. For pH

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