

## Supplementary Data

An extracellular acidic cleft confers profound H<sup>+</sup>-sensitivity to epithelial sodium channels containing the  $\delta$ -subunit in *Xenopus laevis*

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Supplementary Table S1 (+ corrected  $\alpha$ - and  $\delta$ -ENaC polypeptide sequences)

**Table S1:** The table lists the accession numbers to sequences used in order to construct Figure 9 and indicates which alterations were made to sequences as currently present in databases (highlighted in yellow). The fully reconstructed polypeptide sequences with additions highlighted in yellow are provided below the table.

	UniProtKB/ Swiss-Prot	Accession number (NCBI)	Gene ID (NCBI)	Notes
<b><math>\alpha</math>-like ENaC</b>				
<i>E. burgeri</i>		FYBX02010221.1		The sequence is named $\delta$ -ENaC in the database but the exon structure resembles $\alpha$ -like ENaC in lamprey and is generally more similar to $\alpha$ -ENaC
<i>P. marinus</i>	S4RTA3			Addition of 15 amino acids to N-terminus and addition of 142 amino acids to C-terminus
<b><math>\alpha</math>-ENaC</b>				
<i>L. chalumnae</i>	H3AJ42		102356070	Addition of 117 amino acids to C-terminus
<i>P. annectens</i>	W0SAC9	BAO27802.1		Addition of 67 amino acids to C-terminus
<i>N. forsteri</i>	H1AFJ5			
<i>X. laevis</i>	P51167			
<i>N. parkeri</i>		XP_018422874.1	108796007	
<i>P. sinensis</i>		XP_006124236.1	102458615	
<i>P. bivittatus</i>		XP_007429678.2	103050561	

<i>A. mississippiensis</i>		XP_019332028.1	102566743	
<i>G. gallus</i>		NP_990476.2	396050	
<i>O. anatinus</i>		XP_001512591.3	100081848	Addition of 68 amino acids to C-terminus
<i>O. aries</i>		XP_027823781.1	443488	
<i>P. troglodytes</i>	H2Q5A1		451776	
<i>H. sapiens</i>		NP_001029.1	6337	
<i>C. porcellus</i>		NP_001166483.1	100135613	
<i>H. glaber</i>		XP_021103803.1	101700410	
<i>R. norvegicus</i>		NP_113736.1	25122	

## δ-ENaC

<i>L. chalumnae</i>	H3BHF6		102354011	Removal of 6 amino acids at N-terminus, addition of 81 amino acids to C-terminus
<i>X. laevis</i>	Q7SZG4		398622	
<i>N. parkeri</i>		XP_018424177.1	108797105	
<i>P. sinensis</i>		XP_014431009.1	102445975	Exon 8 needed to be reconstructed from genomic DNA
<i>P. bivittatus</i>		XP_025021199.1	103049479	
<i>A. mississippiensis</i>		XP_019349363.1	102571530	
<i>G. gallus</i>		XP_425742.3	428184	
<i>O. anatinus</i>		XP_028921777.1	100084383	
<i>O. aries</i>		XP_027831921.1	101105267	
<i>P. troglodytes</i>	O46547		450189	
<i>H. sapiens</i>	P51172		6339	
<i>C. porcellus</i>		XP_003461599.2	100714892	
<i>H. glaber</i>		XP_004863993.1	101714354	

## Polypeptide sequences

### α-like ENaC

#### *E. burgeri*

MDGVEERGGTSEKTHNVFQFYKGRLWDFYQSYGEMFQFFCDNTTVHGTIRLVASKHNKLTQVFWALLFIGSIVLFY  
VTCGSVLGAYYSYMKVSVSVTFQQTSTPAVTVCSLNSNRESEHKRPLEELDRLAEEVLHKLYNHSSTTDSASNGRN  
GIGQNGQLLNNVNLAWVNDLGFMTCDATGQNCLHNTYSSGVNLTREWYRLHYMDLMARAPNTSRTGNLSIW  
DFVLSCEFNGVPCQSESEYKYVHHPIYENCYTFNGKSMNTNWQSSKPGREHGLSVIMRTDRHNRLPFLSTVAGARIII  
HQQNFTPYLEEGGLDIRPGTETAVVNMKQVSRLEPYGNCTVDGSDVNMTNIYSSSYTLQACVRSRFQHLMVKT  
CGCGYFYPLPSKGYCRQDEFPTWPCYYQLYQRFVSGDLGFIEQCPVLCHSTQYQLIAGYKWPAAQTSNLIQFL  
LSTESAYGNTTSRNDLAKLKVYFGEINLKSYEETPAVTLVWFLSSMGSQFSLWFGSSVLSAIEVVELLIDCIIMAAILA  
WQWIRRQQGSQTKSMADKAIAYETNSFQAQADAILTQGTAAVKHSVTRRSLLIPAHGQVCVVAVISSPSPNDAL  
YEPQVPPDMEASSTGIIHHQEGNTNVLSDQTETGFTSPV

#### *P. marinus*

MGEPAGTGDVAPERRPPTVLEFWRGSVTDFYDSYDEMFEFFCDNTTIHGTIRLVCSKRKLTAFWSLLFTVTVILF

YYTSALVFLQYYSYTVAVTMGLMFQQSTFPAITVCSLNPYRYEVVQSSLSQLDSMTGQALQQLYGYQPATKAAGT  
AAAPGIRLDTGVVLERLTPDVTGFKLCNATGGDCFYQSYGSGVQAVTEWYTFQYVNIMSQVPSYIKQSDDANIEDF  
IFSCMFSGMPCSDSEYSRFHHPTYGNCYTFNSANSSKLWQASKPGRDYGLSLILRTEQNDYIPFLSTVAGARIMVHD  
QESPPFMEEGGDMRPGFETSLGIRMLEATRMPDPYGNCTEDGNSVPVLNLYSSAYTVQACVRSCFQLALVEACG  
CGYFYPLPPNASYCSYNNTAWGHCCYKLYRQFISDELGCVDKCAQPCCTTKRFAVTPGYAAWPDSSSEKWFNLLSL  
QNNYSVTTVRNDVAKLNVYFRELNMKTISESAATNVIWLLSNIGSQWLSLWFGSSVLSWLEVGELGIDCCIMVFLA  
YRRRRSRAERRRARGTGDSEAAPPPPSFREALGCANAAYVGGNDDGGGGVAIGGPTERPPPWRRGSLTRNACSF  
SVVADIRCPAAAAKPTLLGSRDAAAAEARPLDYGSLRRGPEGNVAVSPDPGGPPRGGAGAPLLSPRVSALVASGR  
EVLRRRSASLTVVSVFAVEEA

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## **$\alpha$ -ENaC**

### ***L. chalumnae***

MSEKKEEKSKGLIEFYSSYDLFQFFCSTTTIHGAIRLVCTERNKMKTAFWWSMLFVASFGLMYWQFGIIFGHYFSYPV  
SMSLTLEHKLLFPAVTVCTLNPNRYKEVESELKELDSLADTLFELYRYNTSQHGTSDDSMQSDIRRSNRIISAPDRV  
PLQVLDEPAAEHARTENQMAGTDINNPALYKGEFRKIGFKLCNASGLSCFYQAYSSGMDAVREWYMFHYVNIMV  
QVPMVTNPLQETHIRDFVFSCKFNHASCNQGNITYFNHPVYGNCTYFNGGSTGNLWSSTKPGRENGLSLLLRTQ  
NDYIPFLSTVAGARVMIHQRNQPPFMEDEGFNIRPGVETSISMKKVSRQQLGGLYSDCTEDGSDIGVENLYNSNYT  
QQACVRSCFQVTLVQRGCGHYFYPLPEGAQYCNKKHKTWGHCCYRLYKEFKANDLGCFTKCRKRCLESEYHQM  
TGYSKWPAKDSGKWIHHILAKQNQYNFTTNSREDVSKLTVYFQELHHKTVGESPSINAATLLSNLGSQWSFWFGSS  
VLSVIEMVELLIDFFVLSTILLFRHYCIQREENQDPEITISTVSYPHYANENSEFNSEESMGNHFDVVADVSAPPAYETL  
DLDLPPSAAQCITGCKCVHCASFISHEVEDLMSDLAGDPEEEDITPHLAGDPEEEDITPHLEGDPEEEDITPHLAGDP  
EEEDITSHLEGDPEVEDITSHLAGDPEVEDITADLAGNHNEEDITPDLVGDPEEDDITLDTLTDGHEEEDIMPDLARDL

### ***P. annectens***

MPNKEENAENGGKKKEGLFEFYDSFQELFEFFCINTTIHGTIRMVCSKHNNMKTAFWTILFIATFGIMYWQFGLLLDQ  
YYSFPVSITMAVNYDKLVFPAVTVCTLNPNRYNAVSTELANLDCYTEQLLSTLYHYTPANSNQSACNNTSNKQDSNN  
KYIPLEFLTYNDTQSGYPFKGTTNGSSFNSEFYRVGFKVCNDTDGVCFYQIYSSGVDALREWYKYQYVNIMGNAP  
LSTYQEDNPQISNFVYACEFNKISCGSGNYTQFNHPQYQGYCYTFNDGDDNNPWISFSPGVESGLSLVLRTEQNDFLP  
YLSNVAGARVMVHDQNPVFMEDSGDIRPGVETSIGIKKEIISRLGGVYGNCTADGSDINVENLYNSDYTQQACI  
RSCFQATIVERCGGYFYPLPAGATYCTNTKHRGWGYCYKLYKAFAADELGCFCRCPKPCIVAEYVKTAGYSKW  
SSSETWIAKVLSQESPYSTSARKVIAKLNIFYELSYKTTGESPSFNVTLLSNMGSQWLSLWFGSSVLSVEMGELVI  
DLIAGVIVLRRRQREKTKATDDTEDNSPSETYVHPRQENSNEHRERAPNRIEVVAEISPPPAYDSLELDTPVACSAD  
CSCTRRMSQTSIKSHTSNSSNTEESTSEGPTAL

### ***N. forsteri***

MTDKEEEAEAGKKKEPMIGFYDSYQELFEFFCNNTTIHGTIRMVCSKHNNMKTVSWTILFITFGVMYWQFGLLLG  
QYYSPVVSITMSVNFDKLIFPAVTVCTLNPNRYNVVSTQLANLDCYTEELLSTLYHYNPLTSGNQSACNSSTAGTRAF  
DESYMKLEFLNDENTAYSQVPGKATNSTSPVNHTEFYRIGFKLCNATGEDCFYQTYSSGVDALREWYKFQYINIMA  
QIPSQSNQEDDSQISNFVYACEFNKISCGVENYTRFRHPVYGNCTYNDGQSATPWASFPVGVGNGLSLVLRTEQ  
NDFLPFLSTVAGARVLVHDQNPVFMEDSGLDIRPGVETSIGMKKEIISRLGGVYGNCTDGSDDVNVLYNSDYNQ  
QACVRSCFQATIVQQCGGYFYPLPSGAEYCSYRNKSWGYCYKLYKAFAADELGCFCRCPKPCQYTDYKMTAG  
YAQWPSSVSESWITSILSQENQYNMTSGRKNIAKLNIFYELNYQTMGESPSFTVVTLLSNMGSQWLSLWFGSSVL  
SVVEMGELVFDLIAVGIVLRRRRREKQASSDGEGETSDSTAGTHRGQENASRSRGRDVACNRFVVVAEISPPPAYD  
TLQLDVPVACAPDCECTQHVSHASVHSQAPCSSQPEQEASEGPTVL

### ***X. laevis***

MTKEEKNEKEALIEFFSSYRELFEEFFCSNTTIHGAIKLVCSRNRNMKTAFWLVFLVTFGLMYWQFGLLFGQYFSYPV  
SINLNVNSDKLPFAVTVCTLNOPYRYKAIQNDLQELDKETQRTLYELYKYNSTGVQGWIPNNQRVKRDRAGLPYLLE  
LLPPGSETHRVSRSVIEEELQVKRREWNIQFKLCNETGGDCFYQTYTSGVDAIREWYRFHYINILARVPQEAIDGEO  
LENFIFACRFNEESCTKANYSSFHAIYGNICYTFNQNSDQSNLWSSSMPGIKNGLTLVLRTEQHDYIPLSSVAGA  
RVLVHGHKEPAFMDNNGFNIPPGMETSIGMKKETINRLGGKYSDCSEDGSDVDVKNLQSEYEQVCRSCFQAA  
MVARCGCYAFYPLSPGDQYCDYNKHKSWGHCYKLIIEFTSNKLGCFKCRKPCLVSEYQLTAGYSKWPNRVSQD  
WVLHTLSRQYNLTDNRNGIAKLNIFEELNYKTILESPTINMAMLLSLLGSQWLSLWFGSSVLSVEMLELVIDFVIIGV  
MILLHRYYYKKANEGETTVVPTPAPAFADLEQQVPHIPRGDLSQRQISVVADITPPPAYESDLRSVGTLSRSSSM  
RSNRSYEEENGGRN

***N. parkeri***

MAEEKTKGKEGLIEFYSSYRELFEEFFCNNTTIHGAIKLVCSRNRNMKTAFWLVFLVTFGLMYWQFGLLFGQYFSYP  
VSINLNVNSDRLLFPAVTVCTLNOPYRYHSILGDLQDRDQQLLYSLYQYNVTGVQGRVPTNRRRRQAMEPLPFPL  
QRVPVEGGAHRVRSVSAEDNTDQKPIVNRQDWHIGFKLCNETDGGDCFYQTYSSGVDAVQEWYRFQYINILARVPK  
DGEVTEEQLENFIIACRFNEEHCMQAGNYSHFHPIYGNICYTFNHNHSEGDTWSSSMPGMKNGLTLVHTEQHD  
YIPLSSVAGARVLVHGHHEPAFMDDSGFNIQPGVETSLGMRKETISRLGGDYSDCEDGSDVDVKNLNFSEYEQQ  
VCRSCFQAEMVKRCGCAYAFYPLPEGAELCDYKHKHKSWSGHCYRLSKEFNLDLGCFTKCRKPCLVTDYILNAGYS  
RWPTKVSEWVVFHTLSQTNQTERNMVAKLNIFYQEMNYKTQVESPTINMVTLLSLCGSQWLSLWFGSSVLSVAEM  
GELVIDVVIISVILLQRYRNRKTPSVEDTGDSDPPDPSPGPTERRSSHMPHNIPQCQTQMSVVADITPPPAYETLDSL  
GGSSRSSSIRSHVSQRRNSGWRGE

***P. sinensis***

MHQVVTVKAEKVPMGKRLRRCQEAENQKQVEEVAEKLEKEHEGLIEFHKSYPHELFFQFFCNNTTIHGAIKLVCSKR  
NKMKTAFWVSVLFFLTFGLMYWQFGILYREYFSPVNLNLNLSDKLTFPAVTLCTLNOPYRYSAVRKELDELDRITHQT  
LMDLYNYSMSQVQSNAAQSSQKRSQRSLSHHVQRHPLRRRKRNEPVSLSKGNPVDKSDWKIGFILCNETNEDC  
FHQTYSSGVDAVREWYSFHYINILARMPDTKALDESNEFESFIYACRFNEVTCDKANYTHFHHPYGNICYTFNDRNN  
SLWTSSLPGINNGLSLLVLRTEQNDYIPLSTVTGARVMVHEQNEPAFMDGGFNVRPGIETSISMRKETTMLLGG  
YSDCTEDGSDVPVQNLVSSRYTEQVCIRSCFQIHMVKRCGCAYFYPLPPGAEYCDYTKHIAWGYCYKQVEFKSNI  
LGCFSKCRKPCVTKYQLSAGYSHWPSAVSENWVVFHLSQQNKYNITSKRNGVAKVNIFFEEWKYKTNGESPAFTV  
VTLLSQLGNQWLSLWFGSSVLSVVELAELILDFAITILSFKRFRSRQVPAPSVPPGPAHDNTAFQSEPADPSAPHRFT  
VEAVVTTLPSYNSLEPCRRDGEAVIGLE

***P. bivitattus***

MKAENQSEGKIEQPRLEVQKQNMKVATEMEEKKEESDGLIEFFSSYQELFQFFCNNTTIHGAIKLVCSKKNMKT  
AFWSVLFLLTFGLMYWQFGIYRDYFSPVNLNLNLSDRLTFAVTLCTLNOPYRYSAFRKELEELDQMRTRTLLEVF  
KYNMSLGQNTLTKSSKSTRSLYHHMQRYPLHRRKRDTQATMEDNNPQVGKSDWKVGFCLCENKTD CFHQ  
MYSSGVDAVREWYSFHYINILAKFPDTKALEESNFTSFIYACRFNELTCNKANYTHFHHPYGNICYTFNDSSTLWM  
SSLPGINNGLSLVVRTQQNDFIPLSTVTGARIMVHNQNEPAFMDDEGGFNVRPGIETSISMRKETTQRLGGTYSGCT  
EDGSDVPVKNLSSRYTEQVCIRSCFQNSMVEQCQCGHYFYPLPPGAVYCDYTKHVAWGYCYKQAEFKADHLG  
CFTKCRKPCVTEYQLSAGYSRWPSAVSEAWVVFHMLTLQNKYDVISKRNGIAKVNIFFEWNYKSNGESPAFTVVT  
LLSQLGNQWLSLWFGSSVLSVVELAELILDVLTCLVFRRLCLHQSSDLPTPSNSDNSVFHNVFSAPHRIPQEISAEAGI  
AALPSYNSLEALDLHRVSFRTE

***A. mississippiensis***

MPQEESMRQCKQGAHQKHEEVPEKAEKHEGLIEFHNSYRELFQFFCSNTTIHGAIKLVCSKKNMKTAFWSV  
LFFLTFGLMYWQFGILYREYFSPVSLNLNLSDRLTFAVTLCTLNOPYRYSAVQKELDELDRITHQTLMDMYNNM  
SVTQSDWAAQYTHKRSSRSLFHVYQRHPLRRHHRDNPVAVENPPVDKSDWKIGFLLCNEKSDDCFHQTYSSGV  
DAVREWYSFHYINILARMPSTKDLDESNEFESFIYACRFNDVTCDKANYTHFHHPYGNICYTFNDDNSLWTSSLPGI

NNGLSLVVRTEQNDFIPLLSTVTGARVMVHNQNEPAFMDDGGFNIRPGIETSISMRKEMTLRLGGSYSDDCTEDGK  
DVPVQNLVLSHYTEQVCIRSCFQLNMVKRCGCAYFYPLPSGAEYCDYTKHIAWGYCYKLAQAEFKADILGCFRKR  
KPCCKMTEYHLSAGYSRWPSALSEDWVFMHLSQQNKYNITSKRNGVAKLNIFFEWYKKTNGESPAFTVVTLLSQLG  
NQWLSLWFGSSVLSVAELAEILDFVITCILSFRWLRAWHETASTMSPGGHDNTDFQSEVSGPSTPHRFTVEAVV  
TTLPSYNSLEQCESNRDAEMGLE

***G. gallus***

MGTASRGGSVKAEKMPEGEKTRQCKQETEQQQKEDEREGLIEFYGSYQDVFQFFCSNTTIHGAIKLVCSKKNMK  
TAFWSVLFILTFGLMYWQFGILYREYFSYPVNLNLNSDRLTFPAVTLCTLNIPYRYSAIRKKLELDQITHQTLDDL  
DYNMSLARSQSAQFSHRRTSRLLHHVQRHPLRRQKRDNLVSLPENSPVDKNDWKIGFVLCSENNEDCFHQTY  
SSGVDVAVREWYFHYINILAQMPPDAKDLDESDFENFIYACRFNEATCDKANYTHFHHPLYGNCYTFNDNSSSLWTS  
SLPGINNGLSLVRTEQNDFIPLLSTVTGARVMVHDQNEPAFMDDGGFNVRPGIETSISMRKEMTERLGGYSDDCT  
EDGSDVPVQNLVSSRYTEQVCIRSCFQLNMVKRCSCAYFYPLPDGAEYCDYTKHVAVWGYCYKLLAEFKADVLC  
FHKCRKPCCKMTEYQLSAGYSRWPSAVSEDWVFMHLSQQNKYNITSKRNGVAKVNIFFEWNYKTNGESPAFTVVT  
LLSQLGNQWLSLWFGSSVLSVMEAEILDFVITFILAFRWFRSKQWHSSPAPPNSHDNTAFQDEASGLDAPHRF  
TVEAVVTTLPSYNSLEPCGPKDGETGLE

***O. anatinus***

MKGEKRERRSPGRCRPSGSPPTGSPPPPAAPPPAEGLIEFHRSYRDLFRFFCNNTTIHGAIKLVCSQHNRMK  
VFWAALCLCSFGMMYWQFGLLFGDYFSYPVGLHINLNSDKLVFPAVTVCTLNPFYSAAREELEELDRVTEKTLFDL  
YNTTAALPSRPRRRGLGSPLPHPLQVLRPPASQPRRVRSGARGVRENGPRVGKTDWKIGFKLCDQNGSDCFY  
QTYSSGVDVAVREWYRFHYINILARLPDPLVNEAALSNIACRFNQASCNQANYSQFHHPYGNCTYFNGKNTSTL  
WMSSLPGVNNGLSLTLRTEQKDYIPLLSTVTGARVTVHGQDEPAFMDDGGFNLRPGVETSISMQKETLDRLGGDY  
GDCTKDGSDIPVKILYADTRYTQQVCIHSCFQESMVQKCGCAYLYFPRPPGVEFCDYRKHVSWGYCYKLAQAFSS  
DSLGCFTKCRKPCLVTSYQLSAGYSRWPSVMSQDWFQMLNKQNNYLSRRSGVAKLNIYFKELNYKTISESPSVT  
MVTLLSNLGSQWLSLWFGSSVLSVVELAEILDFVIT **FLLLLRRLHRRYWAPGRGQGSEEVATAPLPTLPDLAQLT  
RPPLDSSPSTAPPPAYATLGPPPPGPCL**

***O. aries***

MKGDKREELGPGPEPSAPPLTEEEAELEFHRSYRELFEFFCNNTTIHGAIKLVCSQHNRMKTVFWAVLWLCTFG  
MMYWQFGQLFGEYFSYPVSLNINLNSDKLIFPAVSICTLNIPYRYKEIQELEDLDRITEQTLFDLYKYNASHTLVAHAR  
SRRDLREPLPHPLQRLPIPAPPHAARRVRRAGSSVRDNNPQVNRKDWKIGFQLCNQNKSDCFYQTYSSGVDVAVRE  
WYRFHYINILSRRRQDTSPLSEEDVLGKIFTCRFNQDSCNEANYSHFHHPMYGNCTYFNDKNSSNLWISSVPGVN  
NGLSLTLRTEQNDFIPLLSTVTGARVMVHERDEPAFMDDAGFNLRPGVETSISMSKEAVDRLGGDYGDCTKNGSE  
VPVENLYNTKYTQQVCIHSCFQESMIKECGCAYIFYPPEGVEFCDYKHNKHSWGYCYKLAQAFSSDRLGCFTKCRK  
PCSVTIYKLSASYSQWPSVTSQDWFQMLSRQNNYTIKNKRDGVAKLNIFFKELNYKSNSESPSVTMVTLLSNLGSQ  
WLSLWFGSSVLSVVEAEILDFLLVITFLMLLRRFRSRYWSPGRGGRTQEVASTPATSLPSSCPYQASSSSFPDPA  
ISPALSAPPPAYSTLGPHAPPTGLAEASASAHAPGEP

***P. troglodytes***

MSSIKGNKLEEQGPRPLQPTPLMEGNKLEEQDSSPPQSTPGLMKGDKREEQGLGPEPAAPQQPTAEAEALIEFHR  
SYRELFEFFCNNTTIHGAIKLVCSQHNRMKTAFWAVLWLCTFGMMYWQFGLLFGDYFSYPVSLNINLNSDKLVFPA  
VTICTLNIPYRYPEIKEELEELDRITEQTLFDLYKYSFTLVAGSRRLRGLTLPHPPLQRLRVPPPPHGARRARSVASSV  
RDNNPQVDWKDWKIGFQLCNQNKSDCFYQTYSSGVDVAVREWYRFHYINILSRPETLPSLEKDTLGNFIFACRFNQ  
VSCNQANYSHFHHPMYGNCTYFNDKNNSNLWMSSMPGINNGLSLMLRAEQNDFIPLLSTVTGARVMVHGQDE  
PAFMDDGGFNLRPGVETSISMRKETLDRLGGDYGDCTKNGSDVPVENLYPSKYTQQVCIHSCFQESMIKECGCAYI  
FYPRQNVYCDYRKHSSWGYCYKLAQVDFSSDHLGCFTKCRKPCSVTSYQLSAGYSRWPSVTSQEVWFQMLSRQ  
NNYTVNNKRNKRVAKVNIFFKELNYKTNSESPSVTMVTLLSNLGSQWLSLWFGSSVLSVVEAEILDFLLVITFLMLL

RFRSRYWSPGRGGRGAQEVASTLASSPPSHFCPHPTSLSLSQPGPAPSPALTAPPPAYATLGPRPSPGGSTGAGSSA  
CPLGGP

***H. sapiens***

MEGNKLEEQDSSPPQSTPGLMKGNKREEQGLGPEPAAPQQPTAEELIEFHRSYRELFEFFCNNTTIHGAIKLVCS  
QHNRMKTAFWAVLWLCTFGMMYWQFGLLFGEYFSYPVSLNINLNSDKLVFPAVTICTLNPYRYPEIKEELELDRI  
EQTLFDLYKYSSFTTLVAGSRRRDLRGLPHPLQRLRVPPPHGARRARVASSLRDNNPQVDWKDWKIGFQLCN  
QNKSDCFYQTYSSGVDAREWYRFHYINILSRPETLPSLEEDTLGNFIFACRFNQVSCNQANYSHFHHPMYGNCYT  
FNDKNSNLWMSSMPGINNGLSLMLRAEQNDFIPLLSTVTGARVMVHGQDEPAFMDDGGFNLRPGVETSISR  
KETLDRGGDYGDCTKNGSDVPVENLYPSKYTQQVCIHSCFQESMIKECGCAYIFYPRPQNVEYCDYRKHSSWG  
YYKLQVDFSSDHLGCFKCRKPCSVTSYQLSAGYSRWPSVTSQEWVFMQLSRQNNYTVNKRNGVAKVNIFFKEL  
NYKTNSSEPSVTMVTLLSNLGSQWLSLWFGSSVLSVEMAELVFDLLVIMFLMLLRRFRSRYWSPGRGGRGAQ  
EVA  
STLASSPPSHFCPHMPSLSLSQPGPAPSPALTAPPPAYATLGPRPSPGGSGAGASSTCPLGGP

***C. porcellus***

MKGDELKAQGPLPPQPLQGPLKGDKEQPGLGPEPTAPQQHTEEEALIEFHRSYRELQFFCNNTTIHGAIKLVCS  
KHNRMKTAFWAVLWLCTFGMMYWQFALLFGEYFSYPVSLNINLNSDKLVFPAVTVCTLNPYRYKEIKEQLRELDRI  
TQQTLFDLYNINASTLLAGARSRRSLADTLPYPLQRPVQPEPRRARSDDPSSVRDNNPRVDRRDWRVGFQLCNQ  
NKSDCFYQTYSSGVDGVDREWYRFHYINILAQVADTSPSEEEALGNFIFACRFNQAPCTQENYSHFHHPYGNCTF  
NNKNDSSLWMASMPGINNGLSLTLRTEQNDYIPLLSTVTGARVTVHGQDEPAFMDDGGFNLRPGVETSISRKE  
ALDRGGSYGDCTQDGSVDPVQNLPSKYTQQVCIHSCFQENMIKQCGCAYIFYPKPKGVFCDYTNHSAWGYCY  
YKLQGAFFSSDSLGCFNKCRKPCNVTIYKLSAGYSRWPSAASQDWIFQMLSLQNNYTISNKRNGVAKLNIYFKELNYR  
TNSEPSVTMVTLLSNLGSQWLSLWFGSSVLSVEMAELVFDLLVITLLMLLRRFRSRYWSPGRGARAAREVACTPP  
PSLPSRCAHSAFPTLTAPPPAYATLSACPPLQGLAGASSAACAPREP

***H. glaber***

MKGAELEAGGPSPPQPTQGLAKGDESEQPGLGPEPTAPQQCLEEEALIEFHRSYRELQFFCNNTTIHGAIKLVCSK  
HNRMKTAFWAVLWLCAFGMMYWQFGLLFGEYFSHPVSLINLSDSKLVFPAVTVCTLNPSRYKEIKEQLRELDRI  
EQTLFDLYKNASSTLLAGARGRRDLEETLLHPLQRIPVSPGGRARSAASSLKDNNPQVDRKDWKIGFQLCNQDKS  
DCFYQTYSSGVDAREWYRFHYINILARLADTSPSEEEALGNFIFTCRFNQAPCTQANYSHFHHPYGNCTFNK  
NDSSLWMSSMPGIHNGLSLTLRTEQNDYIPLLSTVTGARVTVHGQDEPAFMDDGGFNLRPGVETSISRKEALHR  
LGGDYGDCTQDGSVDPVQNLPSKYTQQVCIHSCFQESMVENCAYIFYPRPKGVFCDYRNHSAWGYCYKQ  
GAFSSDSLGCFNKCRKPCSVTNYKLSAGYSRWPSVASQDWIFQMLSLQNNYTINNKRNGVAKLNIYFKELNYKNS  
ESPSVTMVTLLSNLGSQWLSLWFGSSVLSVEMAELIFDLLVITLLMLLRRFRSRYWSPGRGAGPAREAACTPARFCPH  
PASPDLAAPPPAYATLSACPPPGWACAPGQP

***R. norvegicus***

MMLDHTRAPELNIDLHASNSPKGSMKGNQFKEQDPCPPQPMQGLGKGDKREEQGLGPEPSAPRQPTEEEAL  
IEFHRSYRELQFFCNNTTIHGAIKLVCSKHNRMKTAFWAVLWLCTFGMMYWQFALLFEEYLSYPVSLNINLNSDKL  
VFPVAVTVCTLNPYRYTEIKEELELDRIEQTLFDLYKYNSSYTRQAGARRRSDLLGAFPHPLQRLRTPPPYSGRTA  
RSGSSVRDNNPQVDRKDWKIGFQLCNQNKSDCFYQTYSSGVDAREWYRFHYINILSRSDTSPALEEEALGNFIF  
TCRFNQAPCNQANYSKFHHPMYGNCYTFNDKNSNLWMSSMPGVNGLSLTLRTEQNDYIPLLSTVTGARVMV  
HGQDEPAFMDDGGFNLRPGVETSISRKEALDSLGGNYGDCTENGSDVPVKNLYPSKYTQQVCIHSCFQENMIK  
CGCAYIFYPKPKGVFCDYRKQSSWGYYKLQGAFFSSDSLGCFSKCRKPCSVINYKLSAGYSRWPSVKSQDWIFEM  
LSLQNNYTINNKRNGVAKLNIYFKELNYKTNSSEPSVTMVSLLSNLGSQWLSLWFGSSVLSVEMAELIFDLLVITLLM  
LLRRFRSRYWSPGRGARGAREVASTPASSFSPRCPHPTSPPSLPQQGMPPLALTAPPPAYATLGPSAPPLDSAA  
PDCSACALAL

## $\delta$ -ENaC

### *L. chalumnae*

MAQEEDKEEAVIEFYDSFKDLFQFFCAHTTVHGGIRLICSERNNMMKTAFWIILFFASFGLMYWQFGLLFSQYWGY  
VSVAIRVHSGPKIFPAVTVCTLNRYRYTQVHKYLKELDQMALEVLSTWYGFNASEDITPNDISGDGAGHGKINISDN  
MNITLDQSIPLVLIRKDSLSSSAHSFPLDKKGRVGFRLCNVTGKDCFYQSYSSVMDAIQEWYKFHFINIMSQVSP  
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VAGTRVMIHKQDQPAFMEDEGLNIKPGTETSIGMKQDEVNRLAGNYGQCTFDGTDVKIKLYNTPYSVQACVRSCF  
QYLLIQECGCGYYPPLPPGAQYCNYNKYPSWGHCHYKLYKFFVAGDSGCFQKCPKPCQEFKYKLTGISKWPSQN  
AENWIFHLLSHHNGKLNLTNNRRDVSCLNIFFQKLSYESFDETPSISAVTILSQMGNLWSFWFGSSVLSVIELIELILDVI  
AMSFILTFKWHKLLKQAKKDRCVIATISSAVDNNTFWNQGGSRDLKQYTGNTKQSYWNHTDELVDQDIKSGNSRVE  
AVHNALQNNSSVNFYDVSTIF

MAQEEDKEEAVIEFYDSFKDLFQFFCAHTTVHGGIRLICSERNNMMKTAFWIILFFASFGLMYWQFGLLFSQYWGY  
VSVAIRVHSGPKIFPAVTVCTLNRYRYTQVHKYLKELDQMALEVLSTWYGFNASEDITPNDISGDGAGHGKINISDN  
MNITLDQSIPLVLIRKDSLSSSAHSFPLDKKGRVGFRLCNVTGKDCFYQSYSSVMDAIQEWYKFHFINIMSQVSP  
MTNVSDSSPIGNVIYSCQYNGKSCSGSEYEHFHHHPVYGYCYIFKSNGSDTFWETSKPGIAYGLSLIIGTKQEDFIPLST  
VAGTRVMIHKQDQPAFMEDEGLNIKPGTETSIGMKQDEVNRLAGNYGQCTFDGTDVKIKLYNTPYSVQACVRSCF  
QYLLIQECGCGYYPPLPPGAQYCNYNKYPSWGHCHYKLYKFFVAGDSGCFQKCPKPCQEFKYKLTGISKWPSQN  
AENWIFHLLSHHNGKLNLTNNRRDVSCLNIFFQKLSYESFDETPSISAVTILSQMGNLWSFWFGSSVLSVIELIELILDVI  
AMSFILTFKWHKLLKQAKKDRCVIATISSAVDNNTFWNQGGSRDLKQYTGNTKQSYWNHTDELVDQDIKSGNSRVE  
AVHNALQNNSSVNFYDVSTIF

### *X. laevis*

MESTEKEKKEGLIEFYDSFEDMLTFFCDNTTIHGTVRLNCSRKNMKKTFWLVLYFVSFAMMYWQFGQLTDQYW  
AYPTSTIIGLQSKGKIFPAVTICNLNRYRFDQVNMVYINQLDQLANETLYSLYEYRAPESGQQVVDLQDLLNLTGQV  
NGGFYLDSEIVLLKLQENSGPALPGEKFKVGFKLCNSSRDCCYKVFWSGVNALHEWYKFHYINIMSNIPLAVLNI  
ANNFSKDFILTFHFNEVPCDEREYIHFHHPIYGNCFINNHGKENSWSYSPRPGKQYGLSMVVKADLHDNMPLLSQA  
AGARIMIHNPNQPLVEHEGFDIQPGTETSISVKQEEVIRLGGKYSQCTSDGSDLSIKILYNTSYTMQAACLNCFQYK  
MIEMCGCGYYPPLPPGMEYCNYNKYPGWGHCFYQLEYKMLDHTLICFTQCPKQCKQTQYHLAAGTAKWPSVPS  
KAIQLLSLQERYNSTSERSDVSINVYEEELSYRSVEETPTMSVNVLLSSMGLWSWVFGSSVLSVAEIAELVLDTAA  
MVTIVYQWKKQRANRNDGMNGSNAASNVCSPYIDSKTFSTPQTGLSEKELESKTNDPKFNGEINTFS

### *N. parkeri*

MDSA EKENTEEGLFMFYDSFTELEFFCDNTTIHGTVRLNCSRKNMKKTFWVFLYLFAFSTMYFQFGDTFTQYWS  
YPTNLAIHLQTKKSNFPAVTICNMNRYRFDQVNEYLNQLDQLAQETLQTYGYNASLSVNDVVDLQDITDNATSQ  
LDEKFLDSSIKLIKLEDDPNQMSKGNRSKLGFKLCDSTGGDCYRSFWSGVDALHEWYQFHFINIMHKIPSVLQIA  
DQEYVDKFIKCDFNGHSCNRNYTHFHHPTYGTCTINGNENSSALWAAVKPEKKGISLIVKVDQHDNMPILSTTA  
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MIEQCGCGYYPPLPSGSEYCNYNKHPGWGHCFRLEKLLDHQHTCFKCKPIQCTETMYLSAGFARWPSTVSKS  
LFLTQLSSDYGNSTVNRTEFSKINVYFQELNLQSFDETPAISHDLLSTMGNQWSFYFGSSVLSVVEIAELVFDVVA  
MVIIIYAKRKKKQVTNNNEGPYVIRMEGLSGLDGKTLPNSSLNDQDLPSYRSCDTKSEEI

### *P. sinensis*

MEQEWVNEERGDEGLIEFYSSFRDMFEFFCKNTTIHGTVRLVCSNKNMKKTFWTLLLASFGMLYWQFALLFSQY  
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PANQNSSSFQLNHHISLVMLKEPDTGFKRKDSKVGFKLCNATGGNCFYKAYSSGVDTVKEWYRFHYMNIMSQLPV

IINVSAQGEIEENLVYSCRYDGEPCRDSDYIHFHHPVYGSCYTFNKDGTDLFWKATKPGLSYGLSLILKAEHNDRLPLL  
STVAGVQVMIHNNHQTFFLEHEGFDIRPGIVTNGIRQDEVHRLGGNYGKCTTDGEDVDVKLLYNSSYTLQACLVS  
CFQQLMVENCSCGYFLHPLPAGAQCSCARHPAWGHCFYQLYNRLANHHLSCFSNCPKPCWESWYKLSAGTAK  
WPSTKSQDWILPILSRQKGYNSTFNRRDLAKVNIFYQQLSYKSVDESPVYTVNLLSNMGSQWLSLWFGSSVLSVVE  
MFELLDIMVLSLILCYRRLKAKKTLTMSLPPTISSVNLLENYRSTQEDLADDPNCAQANQNGGAIKHKNGDLPYH  
SICNKMQTPELTPPVVLRVRHIRDHCVTIDPSS

***P. bivittatus***

MGENLPKETEAEETKEEDAALIEFYSSFKDLFEFFCLNTTIHGTIRLVCSRNKMKTAFWALLFLASFAMILYWQFALIFN  
QYWAYPVIMSMSVHSEPKMFPAITLCSLNPYRISPISQDIAELDNLARETLYSLYGFHHPKSILEDVGANLEDFSDENP  
GKINGSKFQLDRSIALVKLHGKVGFRCLNTTGGNCYNKVYISGVDVAVQEWYRFHYMNIMSQIPSIKMSQGDHIR  
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KHNQTPFLEHEGFDIRPGIESTIGIKEDEVSRLLGGNYGACTNNGEDVNIKLIYNSTYTLQACLHSCFQHQMIECNGCG  
YYFYPLPSGAEYCNYNKHPTWGHICYLLYKLMDHHLTCFSECPKCKETRYKLSAGYAKWPSTKSENWIHRALQA  
DNRYTTTTNNRNDIAKVNIFYEQLDYYSWDESPEYDNLVMSNMGSQWLSLWFGSSVLSVVEVEMFEFLVDVILSLIFF  
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VLHGFKHQGDQVYRDPKS

***A. mississippiensis***

MKYPPERMDQDLTREEEKEEGELIEFYDSYRDMFEFFCKNTTIHGTIRLVCSNKMKTAFWTLFLASFGLMYWQ  
FALLFSQYWTYPVVTTMSMHSEPKMFPAITLCSLNPYRFATVSDNLAELDFLAVETIASLYGSSATANMFHGEEKIHK  
VKDLARKESDNFGPADFQLNRNIPLVRYVIDPVSKKNISMVGFRLCNATGENCFDKTYSSGVDAILEWYKFHYMNI  
MSQLPVIINITAHEDQIEDLVYSCQYDGEPCRNSDYDHFHHPVYGSCYTFNKDGTNPFWATKPGVAYGLSLILKAE  
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LQACVHSCFQNMIMQRCGCGYYPPLPPDAEYCNYNKHPAWGHCFYQLYNRLADHHLSCFSKCPKPCRESWYKVS  
AGTAKWSPNSDWRQALSQQKGYNSTSNRKDIKVNIFYQQLNYQSVNESPLLTNLLSNMGSQWLSLWFGSS  
VLSVVEMLEFLDITVFLIFGYKLSRSKTKLMAQSPVISSVSLTENYRSVPEGPGTSSSAQTFPNAGTIVASKNGD  
LPLHSISNKIHTPELYPEVVLNGFRYIKDHCVDVEP

***G. gallus***

MEQEAAREEEERKEGLIEFYDSFKDMFEFFCKNTTIHGTIRLVCSNKMKTAFWTLFLASFGLMYWQFALMFSQY  
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GNHNGSSFKLSQKFSLLRTTEFNRTGKRQSLVGFRLCNATGGNCFYKTYSSGMDAILEWYRFHYMNIMSQQPVII  
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TVAGVKVMIHNNHQTFFLEHEGFDIRPGIATTIGIQQDKVNRLGGNYGKCTTDGSDVKVLLYNSYTLQACLHSCF  
QHIMVQKCGCGYYPPLPPGAEYCNYNKPAPWGHCFYQLYSLRNHHLNCFDQCPKPCRESLYKVSAGTAKWPS  
RKSQDWIRQALRHQNGYNSTSNRKDIKVTIYKQLNYQSVNESPLLSNLLSSMGSQWLSLWFGSSVLSVVEMLE  
LLIDTLVLSLLFCYQFRSKTLNVARTPSIPSVSLTLESYRVVQEAGNGTAPAHGHTSGVPMAVANSSDHPHAQLSSK  
AIPEHCPDVVLNGFRYMKDSSLGGEINH

***O. anatinus***

MEPGLGDTPRQRTEEEENDEGLIELFDSFRDLFHFFCNNTTIHGMVRLVCSNHRKLTAFWSLLFLATVGMPLYWQ  
FGLLFDQYWRYPVIMTMSVHSEPKMFPAITLCSLNPYRISPISQDIAELDNLARETLYSLYGFHHPKSILEDVGANLEDFSDENP  
EIQVPLASGLRNFLNRDIRLEKLRSRVSHGDSRVGFKLCSNSSSDCFYREHSSAVDAIQDWYRFHLVNIMALLPPG  
ATEEESHVHSKNFIYSCHYNGEPCQETNYETFHHPMYGSCYTFNSHGTDSFWKANRSGVPYGISLILKAEQNKHLP  
LLSTEAGIKVMIHGKNQTPFLEHEGFDIRPGIETTIGIREDEVHRLGGNYGRCTEDGTDVDVQLLYNSSYTMQACLHS  
CFQQLLIEKCHCGCYFYPLPRGAEYCDYNQHPGWGHCFYSLYKNLETHRLSCFSRCPKPCWQSLHKLKLSAGTAKWPS  
TESEDWILAAIGQKKKQSLSQRSKVAKNIFYQQLNYRVLGERPVYSVNEELLSTMGTHWSLWFGSSVLSVVEMLELL





***H. glaber***

MRMELLAGEGPSLEAGTVAQAASTGSEAMETAPARPPTLSPEQSPRERLVELHTSFRELLTFFCTNTTIHGTIRLVCS  
SPNRLKKVSWGLLLGTLGVLYWQLGLLLEQYWRYPVLMASVHSESKIFPSVTVCDMNPQRPRALRHRLEALDAF  
AQESIYSLYKFNSEGRDSPFSNVPGPPEPLFQLDCGIRLQQLRDLGSQHKVGFRLCNSTGGDCFYRTYSSGVKAAQE  
WYHFHYMDILGLVPTAGGDSHQSRFVLSCHYDSEDCQAQHFRTWHHPTYGSCYTFEGVFAAQRPGVTHKISLVLR  
TQTQVVLPLLSTEPDIKVMIHGHNHTPFLEPRGFSIRPGLLETTIGIREDEVRRLGSPYGRCTDGPEGVDVRLLYNSSYT  
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TTSRWPSAKSADWIFAVLEEQTQSPSLSPGRRWAPPSPGRSRTPRSHMAKVNIIFYQELNYRMVDEAPVYSVPQLLS  
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LVEELG