

**Loop A**                    **Loop E**                    **Loop B**                    **Loop F**

GluCl a C.ele (AAA50785.1) \* \* \* \* \* GQDPFVILTVHQHQLNMPDFFPNEKOA YKHTID1KPNVLIR1HHDGTFLVISVRLS1LSCPNLYLQHYPN0WQC5C1DLASKAHT -- TTD1EYLWKEH-SPLQKVLGSLSPLQF-QLRINTSTTCVSRVNGTYIYSC--- -LRIT1OLES  
 GluCl a A.mel (D0667185.1) GLRKLXLYLTLTDAWSVMPDLSFNEKEGHFHN1IMPNVY1RFPNGS1YI1SLCSCPMLKLQYDPRQCS1CLRSMA5GWT-TDNDLFLWKEC- DPVQVVKNL--HLRP-F-TLEKFTD1YCNSKTNGYECS--- -LKVLDFLWKE  
 GluCl d M.dom (AF297500.1) GLRKLXLYLTLTDAWSVMPDLSFNEKEGHFHN1IMPNVY1RFPNGS1YI1SLCSCPMLKLQYDPRQCS1CLRSMA5GWT-TDNDLFLWKEC- DPVQVVKNL--HLRP-F-TLEKFTD1YCNSKTNGYECS--- -LKVLDFLWKE  
 GluCl e M.dom (AB177546.1) GLRKLXLYLTLTDAWSVMPDLSFNEKEGHFHN1IMPNVY1RFPNGS1YI1SLCSCPMLKLQYDPRQCS1CLRSMA5GWT-TDNDLFLWKEC- DPVQVVKNL--HLRP-F-TLEKFTD1YCNSKTNGYECS--- -LKVLDFLWKE  
 GluCl n N.vit (FJ851099.1) GLRKLXLYLTLTDAWSVMPDLSFNEKEGHFHN1IMPNVY1RFPNGS1YI1SLCSCPMLKLQYDPRQCS1CLRSMA5GWT-TDNDLFLWKEC- DPVQVVKNL--HLRP-F-TLEKFTD1YCNSKTNGYECS--- -LKVLDFLWKE  
 GluCl p P.xut (XM013318157.1) GLRKLXLYLTLTDAWSVMPDLSFNEKEGHFHN1IMPNVY1RFPNGS1YI1SLCSCPMLKLQYDPRQCS1CLRSMA5GWT-TDNDLFLWKEC- DPVQVVKNL--HLRP-F-TLEKFTD1YCNSKTNGYECS--- -LKVLDFLWKE  
 HCL A.mel (D0667187.1) SEYRLLLEVWDLKNMWRPDLSFFFNAKS5VPTQTMPIHNYL1YKDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-TDEMPLQNPNDP-TPLVVDVN1-EHLQPL-QLVKNYTA DCTVYSTGNFTC--- -LEVVFVLM  
 HCL A.mel (AY049774.1) QYERYLLEVWDLKNMWRPDLSFFFNAKS5VPTQTMPIHNYL1YKDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-TDEMPLQNPNDP-TPLVVDVN1-EHLQPL-QLVKNYTA DCTVYSTGNFTC--- -LEVVFVLM  
 HCL B.mom (XM001583483.3) TERYLLEVWDLKNMWRPDLSFFFNAKS5VPTQTMPIHNYL1YKDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-TDEMPLQNPNDP-TPLVVDVN1-EHLQPL-QLVKNYTA DCTVYSTGNFTC--- -LEVVFVLM  
 HCL C.purp (LC373509) SXYLMLD1LXNLYLHNM1IRPDCCPFNAKKVTFHEMS1IPNHYL1YHDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-TDEMPLQNPNDP-TPLVVDVN1-EHLQPL-QLVKNYTA DCTVYSTGNFTC--- -LEVVFVLM  
 HCL B.mel (D0667188.1) EYDYL1DUDLHN1M1IRPDCCPFNAKKVTFHEMS1IPNHYL1YHDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-TDEMPLQNPNDP-TPLVVDVN1-EHLQPL-QLVKNYTA DCTVYSTGNFTC--- -LEVVFVLM  
 HCL D.mel (AY049775.1) EYDYL1DUDLHN1M1IRPDCCPFNAKKVTFHEMS1IPNHYL1YHDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-TDEMPLQNPNDP-TPLVVDVN1-EHLQPL-QLVKNYTA DCTVYSTGNFTC--- -LEVVFVLM  
 HCL B.mom (XM001591486.2) EYR1LDLUDLHN1M1IRPDCCPFNAKKVTFHEMS1IPNHYL1YHDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-VNDL1WNPNTD-DPLVVSNE1-EHLQPL-DISNNYTTDCTIEYSTGNFTC--- -LAIVFVNL  
 HCL B.n.vit (FJS51090.1) EYR1LDLUDLHN1M1IRPDCCPFNAKKVTFHEMS1IPNHYL1YHDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-VNDL1WNPNTD-DPLVVSNE1-EHLQPL-DISNNYTTDCTIEYSTGNFTC--- -LAIVFVNL  
 HCL P.xut (LC373509) EYR1LDLUDLHN1M1IRPDCCPFNAKKVTFHEMS1IPNHYL1YHDKT1LYMVKL1LSCSMANLYLQHDTQEKCLQMELES5HT-VNDL1WNPNTD-DPLVVSNE1-EHLQPL-DISNNYTTDCTIEYSTGNFTC--- -LAIVFVNL  
 RDI A.mel (JK485710.1) VETLTSVGSEKF1IN1VWP7FNFNEKQSYHIAATSFN1HHS1GTS1R1LTACSCPNLYQFPMDRQHIEIESFGT--MDR1YKNGEPNSGVWSNEV-SLQP-KVLGRHQAEISLT1TGNSYR--- -LACE1OF  
 RDI D.mel (M69057.2) VETLTSVGSEKF1IN1VWP7FNFNEKQSYHIAATSFN1HHS1GTS1R1LTACSCPNLYQFPMDRQHIEIESFGT--MDR1YKNGEPNSGVWSNEV-SLQP-KVLGRHQAEISLT1TGNSYR--- -LACE1OF  
 RDI M.dom (AB177547.2) VETLTSVGSEKF1IN1VWP7FNFNEKQSYHIAATSFN1HHS1GTS1R1LTACSCPNLYQFPMDRQHIEIESFGT--MDR1YKNGEPNSGVWSNEV-SLQP-KVLGRHQAEISLT1TGNSYR--- -LACE1OF  
 RDI N.vit (FJ851097.1) VETLTSVGSEKF1IN1VWP7FNFNEKQSYHIAATSFN1HHS1GTS1R1LTACSCPNLYQFPMDRQHIEIESFGT--MDR1YKNGEPNSGVWSNEV-SLQP-KVLGRHQAEISLT1TGNSYR--- -LACE1OF  
 RDI P.xut (XM01332602.1) VETLTSVGSEKF1IN1VWP7FNFNEKQSYHIAATSFN1HHS1GTS1R1LTACSCPNLYQFPMDRQHIEIESFGT--MDR1YKNGEPNSGVWSNEV-SLQP-KVLGRHQAEISLT1TGNSYR--- -LACE1OF  
 RDI N.mel (FRE89750.1) GGVELMLW-PDH1RDF1LY1ZLADNGDNFVPLATAK---TLYTGRVEPPR1PAPAYKSCS1EVFFPDEQCTCFMRGFS1YDGFQVDLRHLDELM-C7TVEWVG---SDPLF7TSV2DILEVPAWNEKYYTCDDPEYDITFN1W  
 160...180...200...220...240...250...260...270...280...290...300...

**Transmembrane 1**                    **Transmembrane 2**                    **Transmembrane 3**

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-KAEIPL-          -LQNLHNHDVPTKV-          -FNEEKVR2-          -VFLNRJ-
-STSMDL-          -PSDQVEPDNNSN-          -FAMKPLVRQPEDTMSVDRMHCCELJM-  -QPRKKK-
-QASLDA-          -ASDLDDTDSNAT-          -FAMKPLVRQIPGDPLALEKRLQCEVH-  -MOAFPKR-
-QASIDA-          -ASDLDDTDSNAT-          -FAMKPLVRQIPGDPLALEKRLQCEVH-  -MOAFPKR-
-STSVPD-          -ASEPFPDAAAAN-          -FAMKPLVRQAEDSMSMEKRQEICHT-   -OPFKK-
-GPDSAK-          -SSSPLDAAK-          -FAMKPLVRQAEDSMSMEKRQEICHT-   -OPFKK-
-GPDSAK-          -IEKIFDPLATKNEAML-          -LSGRSQRST-          -TOPPGP-
-GCACPCCGSNSTASKQATMLPLADEKTIK-          -RIVTTTRVVRPPLDADCPWIPROSFRLITPT-  -IAPPPPP-
-KPAPEAPKPKPLTDEK-          -IEKIFDTEMTKN-          -RIPHHTHRVVRPPLDADCPWIPRQESRILITPG-  -IAPPPPP-
-LDKIPIDAISKEN-          -LDKIPIDIAISKEN-          -AMLLSGRSQRSQGAAAGPP-          -PPPPP-
-PKEPAEAAKARL-          -LREAIDEFKTP-          -RNDSERRNSPVRPATVQYDT-          -
-ISDLDDLKHHRE-          -ITDFTPIKRN-          -SIIEFOYDT-          -
-LSDRDLAFCRKHIF-          -LSDRDLAFCRKHIF-          -AIIKQYDT-          -
-LSDRDLAFCRKHIF-          -LSDRDLAFCRKHIF-          -RSSSEDRNSPVRPPTVQYDT-          -
-NPGPPG-          -VPGDHGHDHAPKQ-          -PNVSUDPRASTSSALSQYDT-          -
NPNPMPANVGGPGGVGGPGVGGPGVGGNVVGVMGMGPFEHG-HHHGHGHANHSCHPHAP-          -TVFRKVHDHKPAHSKGTLTENINGRADE-  -EAAPAPQO-
OLGDGPQPPNPNPTNTVDHGHGHGHGHHSCHPHFV-          -KQTQVSNRNPIFGFSNI-QONQVUTRGCSIVGPLF-TEVRKFVHDHKPAHSKGTLTENINGRADE-  -EAAPAPQO-
NPGPFG-          -PKTQVSNRNPIFGFSNI-QONQVUTRGCSIVGPLF-TEVRKFVHDHKPAHSKGTLTENINGRADE-  -EAAPAPQO-
VPGDHGHDHAPKQ-          -TEVRKFVHDHKPAHSKGTLTENINGRADE-          -EAPPGPQ-
VSDPHTLKSIGT-          -MSRCPGPGRSPVHDKPVKSKGTLTENINGRADE-          -EDNPPQ-

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.....490.....500.....510.....520.....530.....540.....550.....560.....570.....580.....590.....600

GluClu C. ele (AAA50785.1)	-QMNSSLNLLETKTE-	-WNDSIKRVDLISRA-	**
GluClu A. mel (D0667185.1)	--CCRSWLSKPPT--	--RSKR1DVIISRI-	FPPV
GluClu D. mel (AF297500.1)	--CCKTWSLKPPTRCQ-	--SRSKR1DVIISRI-	TFFPLV
GluClu M. dom (AB177546.1)	--CCKTWSLKPPTRCQ-	--SRSKR1DVIISRI-	TFFPLV
GluClu N. vit (JFB51099.1)	--CCRSWLSKPPT--	--RSKR1DVIAR1-	IFPLV
GluClu P. xut (XMO013318157.1)	--CCRLWMSKPF--	--RSKR1DVIAR1-	TFPLV
HCLA A. mel (D0667187.1)	--PAGKA	--RSKR1DVIISRI-	FPPV
HCLA D. mel (XMO013318157.1)	OPPAPEPKPKPVLPQASRLK	--RAlY1DVSERV-	FPPV
HCLA M. dom (XMO05183483.3)	--PPSPEPKPKPLPQQRERLK	--RAIY1DTSRV-	LFPAL
HCLA N. vit (JFB51089.1)	--PPQOPPLNKTORS	--KVRALN1DRVSRF-	LFPAL
HCLA P. xut (LC373508)		--RAIS1DRSRV-	FPPV
HCLB A. mel (D0667188.1)	--CCCG	--RATA1Y1DKVSRF-	FPPFS
HCLB D. mel (AY049775.1)	--FCHG-	--HATA1Y1DKFCSR-	FPPFS
HCLB M. dom (XMO05191486.2)	--CCGG	--RATA1Y1DKFCSR-	FPPFS
HCLB N. vit (JFB51090.1)	--FCNG	--RATA1Y1DKFCSR-	FPPFS
HCLB P. xut (C373509)	--FCNG	--RETAV1IDDRFSRF-	FPPFS
RDL A. mel (KJ485710.1)	--LIHP--GKDINKLY-	--GMTPSD1DKYSRI-	VFPVC
RDL D. mel (M69057.2)	GGGGGGGPPPECGGDPEAAVPHLLPGKVVKRD1INLLK	--GITPSD1DKYSRI-	VFPVC
RDL M. dom (AB177547.2)	AGGGGGGAPPEGGDAEAVPHLLPGKVVKRD1INLLK	--GITPSD1DKYSRI-	VFPVC
RDL N. vit (JFB51097.1)	--LIHPGKDI1SKLYAQEEEAHSALQTFPKPHTKHTL	--GITPSD1DKYSRI-	VFPVC
RDL P. xut (XMO013323602.1)	--LIHPGKDI1SKLL	--GMTPSD1DKYSRI-	VFPVC

**Fig. S1.** Amino acid sequence alignments of Cys-loop chloride channels and a *Drosophila melanogaster* nicotinic receptor. Amino acids for loops and transmembrane domains are deduced from the alignments to *Caenorhabditis elegans* GluCla (Hibbs and Gouaux, 2011). Asterisks (\*) indicate conserved sites across Cys-loop chloride channels. Sequence gaps are shown by hyphens (-). Accession numbers for each sequence are shown in parentheses. GluCla, glutamate-gated chloride channel alpha; GluCl, glutamate-gated chloride channel; HCLA, histamine-gated chloride channel subunit A; HCLB, histamine-gated chloride channel subunit B; NtR, Nicotinic acetylcholine receptor; RDI, resistant-to-dieldrin and GABA (gamma-aminobutyric acid)-activated chloride-selective receptor. C.ele, *Caenorhabditis elegans*; A.mel, *Apis mellifera*; D.mel, *Drosophila melanogaster*; M.dom, *Musca domestica*; N.vit, *Nasonia vitripennis*; P.xut, *Papilio xuthus*.