THE *DROSOPHILA* COPPER TRANSPORTER CTR1C FUNCTIONS IN MALE FERTILITY

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<u>Supplementary Information</u>

<u>Supplementary Figure and Table Legends</u>

Supplementary Figure 1

Indicated are the proportions of test crosses with offspring numbers of 0, 1-50, 51-100 and <100 for the genotypes whose average offspring numbers are shown in Figure 4C.

Supplementary Figure 2

Clustal W2 protein sequence alignments of the insect Ctr1 genes. **A**: Alignment of human Ctr1 and *Drosophila melanogaster* Ctr1A, Ctr1B and Ctr1C. **B**: Alignment of drosophilid Ctr1A genes. **C**: Alignment of human Ctr1 and insect Ctr1A genes (of the drosophilid Ctr1A genes, only *Drosophila melanogaster* Ctr1A is shown). **D**: Alignment of drosophilid Ctr1B genes. **E**: Alignment of insect Ctr1B genes (of the drosophilid Ctr1B genes, only *Drosophila melanogaster* Ctr1B is shown). **F** and **G**: Alignment of drosophilid Ctr1C genes.

Red vertical lines denote exon-exon junctions. Gray vertical lines in the Ctr1C alignments denote splice sites of coding introns. The three transmembrane domains are indicated in yellow (based on the Uniprot annotation of human Ctr1 (entry: O15431)). Clustal W2 amino acid color code: red: small and hydrophobic (including aromatic, excluding Y) amino acids, blue: the acidic amino acids D and E, magenta: the basic amino acids R and K, green: hydroxyl, amine and basic amino acids, excluding Q. Consensus symbols: " * " amino acids identical in all sequences in the alignment. " : " conserved substitutions. " . " semi-conserved substitutions.

Supplementary Table 1

Gene location and synteny of the drosophilid Ctr1 genes. Indicated are the scaffold or chromosomal locations of the drosophilid Ctr1A, Ctr1B and Ctr1C genes. The arrangement of genes flanking the Ctr1 genes is shown (genes within 50 kb on each side of Ctr1A and Ctr1B, genes within 100 kb on each side of Ctr1C). Homologous genes (as identified by BLAST searches) have matching colors.

Supplementary Data

Fly Genotypes

Figure 1A:
Ctr1A (AttP51D): *y w; UAS-Ctr1A[AttP51D]/actin-GAL4; +*. Ctr1B: *y w; UAS-Ctr1B[AS24e]/actin-GAL4; +*. Ctr1C (AttP51D): *y w; UAS-Ctr1C[AttP51D]/actin-GAL4; +*. Ctr1C (C34): *y w; UAS-Ctr1C[C34]/actin-GAL4; +*.

Figure 1B:
GFP: *y w; UAS-GFP/actin-GAL4; +*. Ctr1C (D19): *y w; UAS-Ctr1C[D19]/actin-GAL4; +*.

Figure 1C:
Ctr1A (AttP51D): *y w; UAS-Ctr1A[AttP51D]/GMR-GAL4; +*. Ctr1B: *y w; UAS-Ctr1B[AS24e]/+; GMR-GAL4/+*. Ctr1C (AttP51D): *y w; UAS-Ctr1C[AttP51D]/GMR-GAL4; +*. Ctr1C (C34): *y w; UAS-Ctr1C[C34]/+; GMR-GAL4/+*.

Figure 1D:
GFP: *y w; UAS-GFP/GMR-GAL4; +*. Ctr1C (D22): *y w; UAS-Ctr1C[D22]/+; GMR-GAL4/+*.

Figure 1E:
w $Ctr1A^{25}$/Y; UAS-Ctr1A[AttP51D]/+; tubulin-GAL4/+ and *w $Ctr1A^{25}$/Y; UAS-Ctr1A[AttP51D]/+; MKRS/+*. *w $Ctr1A^{25}$/Y; UAS-Ctr1C[D19]/+; tubulin-GAL4/+* and *w $Ctr1A^{25}$/Y; UAS-Ctr1C[D19]/+; MKRS/+*. *w $Ctr1A^{25}$/Y; UAS-Ctr1C[D28]/+; tubulin-GAL4/+* and *w $Ctr1A^{25}$/Y; UAS-Ctr1C[D28]/+; MKRS/+*.

Figures 2A and 2B:
y w hs-flp/[y w or Y]; UAS-Ctr1C[AttP51D]/+; actin>CD2>GAL4 UAS-GFP/+ (">" designating FRT sites).

Figures 2C and 2D:
y w hs-flp/[y w or Y]; UAS-Ctr1C-FLAG/+; actin>CD2>GAL4 UAS-GFP/+.

Figures 3B and 3C:
y w; +; $Ctr1C^{6D}$.

Figure 4A:
Control: *y w*. $Ctr1C^{6D}$: *y w; +; $Ctr1C^{6D}$*. $Ctr1B^{3-4}$: *w; +; $Ctr1B^{3-4}$*. $Ctr1B^{3-4}$ $Ctr1C^{6D}$: *y w; +; $Ctr1B^{3-4}$ $Ctr1C^{6D}$*.

Figure 4B:
Control: *y w*. Ctr1B-GFP^{genomic} $Ctr1B^{3-4}$ $Ctr1C^{6D}$: *y w; Ctr1B-GFP^{genomic}[AH3b]/+; $Ctr1B^{3-4}$ $Ctr1C^{6D}$*. Ctr1C^{genomic} $Ctr1B^{3-4}$ $Ctr1C^{6D}$: *y w; Ctr1C^{genomic}[D5]/+; $Ctr1B^{3-4}$ $Ctr1C^{6D}$*. $Ctr1B^{3-4}$ $Ctr1C^{6D}$: *y w; +; $Ctr1B^{3-4}$ $Ctr1C^{6D}$*.

Figure 4C:
Control: *y w; [AttP51D]/[[AttP51D] or CyO, y^+]; $Ctr1B^{3-4}$ $Ctr1C^{6D}$/TM6B*. Ctr1C-GFP^{genomic} $Ctr1B^{3-4}$ $Ctr1C^{6D}$: *y w; Ctr1C-GFP^{genomic}[AttP51D]/[Ctr1C-GFP^{genomic}[AttP51D] or CyO, y^+]; $Ctr1B^{3-4}$ $Ctr1C^{6D}$*. $Ctr1B^{3-4}$ $Ctr1C^{6D}$: *y w; [AttP51D]/CyO, y^+; $Ctr1B^{3-4}$ $Ctr1C^{6D}$*.

Figure 5A:
y w; Ctr1C-GFP^{genomic}[AttP51D].

Figures 5B and 5C:
Control: *y w; [AttP51D]; +*. Ctr1C-GFP^{genomic}: *y w; Ctr1C-GFP^{genomic}[AttP51D]; +*.

Figure 6A:
Control: *y w/Y; [AttP51D]/+; +*. Ctr1C-GFP^{genomic} (AttP2A): *y w Ctr1C-GFP^{genomic}[AttP2A]/Y; +; +*. Ctr1C-GFP^{genomic} (AttP51D): *y w/Y; Ctr1C-GFP^{genomic}[AttP51D]/+; +*. Ctr1C-GFP^{genomic} (AttP86Fb): *y w/Y; +; Ctr1C-GFP^{genomic}[AttP86Fb]/+*. Figure 6B: *y w; UAS-lacZ[AttP51D]/armadillo-GAL4; +. y w; armadillo-GAL4/+; UAS-lacZ[AttP86Fb]/+. y w UAS-lacZ[AttP2A]/y w; armadillo-GAL4/+; +. y w; UAS-lacZ[AttP51D; +. y w; +; UAS-lacZ[AttP86Fb]. y w UAS-lacZ[AttP2A]; +; +. y w.*

Insect Ctr1 protein sequences

Species abbreviations

D_mel	Drosophila melanogaster
D_ana	Drosophila ananassae
D_ere	Drosophila erecta
D_gri	Drosophila grimshawi
D_moj	Drosophila mojavensis
D_per	Drosophila persimilis
D_pse	Drosophila pseudoobscura
D_sec	Drosophila sechellia
D_sim	Drosophila simulans
D_vir	Drosophila virilis
D_wil	Drosophila wilistoni
D_yak	Drosophila yakuba
A_aeg	Aedes aegypti
A_gam	Aedes gambiae
A_mel	Apis mellifera
A_pis	Acyrthosiphon pisum
B_mor	Bombyx mori
C_pip	Culex pipiens
N_vit	Nasonia vitripennis
P_hum	Pediculus humanus corporis
T_cas	Tribolium castaneum

Drosophilids: Ctr1A homologs, protein sequences

>D_mel_Ctr1A
MDHAHHSAPGVDHSMHHDHVGMHHDHSGIPAATASPMDAASMFDLIPDTSDLQASHAGHAAH
GAHNHGGGSGTGMEHMMPMAFHFGYNETILFSWWHIETVAGLIGSMIAIFLLALMYEGLKYYR
EYLFWKTYNLLEYRPVTGPQRNPEAPRIPSPAAAAPSPVQYVGEVVHKQPPSMLSINHLLQTLLH
VLQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH

>D_ana_GF22272_[Ctr1A]
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YYREYLFWKTYNLLEYRPVTGPQRNPEAPRLPSPAAAAPSPVQYVGEVVHKQPPSMLSFNHLLQ
TLLHVLQVTLSFLLMLIFMTYNVWLCLMVVLGAGVGYFLFCWKKSVIVDVTEHCH

>D_ere_GG19602_[Ctr1A]
MDHTHHSAPDVDHSMHHDHAGMHHDHSGMAAATASPLDPASMLDLIPQTSDLQASHTGHVGH
GAHNHGGGSGTGMEHMMPMAFHFGHNETILFSWWHIETVAGLVGSMIVIFLLALMYEGLKYY
REYLFWKTYNLLEYRPVTGPQRNPEAPRIPSPAAAAPSPVQYVGEVVHKQPPSMLSVNHLLQTL
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>D_gri_GH24714_[Ctr1A]
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WKTYNLLEYRPVTGPQRNPEAPRLPPPSAAAAPSPVQYVGEVVHKQPPTMLSINHLYQTLLQVL
QVTLSFLLMLIFMTYNVWLCMMVVLGSGVGYFLFCWKKSVIVDVTEHCH

>D_moj_GI21812_[Ctr1A]
MDPHAHHNAPAVDHSMHGHDHANMHHDHDHMGLDATTLTPPLATTHGDLPMTMHAGHHHG
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KTYNLLEYRPVTGPQRNPEAPRLPTPAAAAPSPVQYVGEVVHKQPPTMLSINHLYQTLLHVLQV
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>D_per_GL13345_[Ctr1A]
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LIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH

>D_pse_GA17816_[Ctr1A]
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YRPVTGPQRNPEAPRLPSAAAAPSPVQYVGEVVHKQPPSMLSVNHLYQTLLHILQVTLSFLLM
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>D_sec_GM12509_[Ctr1A]
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YREYLFWKTYNLLEYRPVTGPQRNPEAPRIPSPAAAAPSPVQYVGEVVHKQPPSMLSINHLLQTL
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>D_sim_GD16812_[Ctr1A]
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YREYLFWKTYNLLEYRPVTGPQRNPEAPRIPSPAAAAPSPVQYVGEVVHKQPPSMLSINHLLQTL
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>D_vir_GJ16985_[Ctr1A]
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>D_wil_GK25589_[Ctr1A]
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LFWKTYNLLEYRPVTGPQRNPEAPRLPSPAAAAPSPVQYVGEVVHKQPPSMLSLNHLFQTLLHIL
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>D_yak_GE16762_[Ctr1A]
MDHAHHSAPGVDHSMHHDHAGMHHDHSGMAASTASPSDSASMFDLIPDTSDLQASHAGHGAH
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FWKTYNLLEYRPVTGPQRNPEAPRIPSPAAAAPSPVQYVGEVVHKQPPSMLSVNHLLQTLLHVL
QVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH

Non-drosophilid insects: Ctr1A homologs, protein sequences

>A_aeg_AAEL013309_[Ctr1A]
MDHSEHHDYSHQMNHSSDADMMHHGHEGHHGSMEHSLQDHTMDQGASAHAAAGHSGHAG
MVHHMMSMAFHGGYNETILFEQWKIDSLSGLLWSMLLIFIMAALYEGLKYYREHLFWKTYNAL
QYRPVTVTEKSPGNGNVANNNGLAANGSGDEASRVVHMVGEVIHKQPRPTMLSTMHLFQTFLH
ILQVTLSFLLMLIFMTYNTWLCIAVVLGAALGYFLFGWKKSVIVDVTEHCH

>A_gam_AGAP002109_[Ctr1A]
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VDV

>C_pip_CPIJ018594_[Ctr1A]
MDHSEHHDYSQHMLMNHSGAGSGAGMHDHSDHHGSMEHSLQDHTMNSGGVATGHGGHGHG
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LCLAVVLGAALGYFLFGWKKSVIVDVTEHCH

>A_pis_LOC100165693_[Ctr1A]
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LKQPLPTMFSLTHLLQTFLHIVQISISYLLMLIFMTYNVWLCLAVLFGATLGYFLFGWKKSVVVD
VTEHCH

>B_mor_LOC692872_[Ctr1A]
MDEHHEHHNMDMGHAGHEHHGIDHSRHIGHQMPINGLLNSSYNRIVHNTDMNDHNVHTFSGH
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>P_hum_PHUM339810_[Ctr1A]
MDHAGHGVSHGDSHVGPHVGPHGGDTSRMGPPSHGVSSHVDHASHNHIIHETNDSHNGSHCHG
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PGDKVVESSSDGNKIVHLVGEVIHKQPPSMWNLMHGYQTFLQAVQMVLSYFLMLIFMTYNVW
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>A_mel_LOC551217_[Ctr1A]
MSHNHMAHMMNATNGHSAHGIHASHQAIDHLNMHGNMHNSMDHANMDHGSHLTSDTNPCA
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NSLQYRSVTMPQEKNVVAEDNRVVHMVGEVIHKQPPTMLSWMHTFQTCLHIVQIVLSYFLMLIF
MTYNVWLCFAVVLGAAIGYFLFGWKKSVIVDVTEHCH

>N_vit_LOC100122867_[Ctr1A]
MAHHDHMAHMMAMNTSGSPDMTGMDHMDHGHMANTNHHMDHGSMSHDHGSAQGSSDAC
SAMSHAMHGMSMAFHGGYCEKILFETWQISSVAGLIGSVIGIVIMSALYEGLKYYREYLFWKTY
NALQYRSVSMPQEKNVVNDDNRVVHMVGEVIHKQPPTMLSWMHAFQTLLHIIQIILSYFLMLIF
MTYNSWLCAGVVLGAAIGYFLFGWKKSVIVDVTEHCH

>T_cas_LOC660576_[Ctr1A]
MEHHNHDMHEPLDHNMHQGMGHMGHDMGGTTMPKHDMMSHMMSMAFHTGYNETVLFDQ
WKFSTIGGLIGSMIGIFFMAALYEGLKYYREYLFWKTYNALQYRAVTLPEKGVVSEDNQIVHMV
GEVIHKQPPTMLSGMHFYQTLLHMIQMVLSYFLMLIFMTYNVWLCLAVVIGAGVGYFLFGWKK
SVIVDVTEHCH

Drosophilids: Ctr1B homologs, protein sequences

>D_mel_Ctr1B
MDHGSDDSTSTAKSCPMIMVFHAGHCERILWRGWVASTVTEFVLSALAIFLVSFLYEALKFLRQ
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>D_ana_GF18342_[Ctr1B]
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FLYEALKFLRQHLARRDARKESERLAEEQRRKNENPTAGGCCSETPLAEERDPSYWQRLFASTHI
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>D_ere_GG25028_[Ctr1B]
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>D_gri_GH14206_[Ctr1B]
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>D_moj_GI24869_[Ctr1B]
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>D_per_GL23430_[Ctr1B]
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KFLRQHLARRVARKERLAEEQRRKNDNPSGCTGCSDTPLAEAREKSYWQRLLDSTHIIQSLLNLL
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>D_pse_GA20368_[Ctr1B]
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>D_sec_GM23723_[Ctr1B]
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LLQIVISYLLMLIFMTFNYWLCLAVILGLGLGYFFFGWNKKNPDESECCP

>D_sim_GD15144_[Ctr1B]
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>D_vir_GJ24513_[Ctr1B]
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>D_wil_GK13179_[Ctr1B]
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LMRIEARKLAQRLAEDQRRKNNVSDCGGCSDTPLADPREKTYWQQLVEYSHIVQSLLNLLQIIVS
YLLMLIFMTYNYWLCLAVVLGLGVGYFFFGWNKKDAQESECCP

>D_yak_GE25868_[Ctr1B]
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FLRQQLARREARKESERLAAEQRRKNEAPAAGGCCSETPLAEPREQTYWQRLFASTHIVQSLLN
LLQIVISYLLMLIFMTFNYWLCLAVILGLGLGYFFFGWNKKNPDESECCP

Non-drosophilid insects: Ctr1B homologs, protein sequences

>A_aeg_AAEL013263_[Ctr1B]
MDHNHGGPDDMEMLCPMKMSFHGGTCEVILFPSWATTKTGQFVGAWIGFFLMALLYEGLKFY
REILAQKEAEKHCSPGTKRSMRHFMTDKLHILQSLLHLIQVSVSYILMLIVMLFNLWLCLAIVSG
AAVGYYFFGWIRRSKMDPNECCN

>A_gam_AGAP000100_[Ctr1B]
MDHNHGGPDDMEMLCPMQMSFHAGSCEVILFPSWATTEVGAFVGAVIGFFLLAFAYEGLKYGR
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AVVCAADYYVFGWVRNSSVDPTENCN

>C_pip_CPIJ016468_[Ctr1B]
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YREVLAQRERKPCSEPASEKKSISLLHHLTNKLHIVQSLLHLLQVSVSYVLMLIIMLFNLWLCLAI
VTGAALGYYIFGWIRQSTIDANECCN

>A_mel_LOC725845_[Ctr1B]
MHDDELTKSPNSSTMSARYILPMSFHIGENEVILFDEWHPVDWQGLGWSMVGVILIASIYEGIKN
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ALGYWLFSWDKSNGDSDDCCL

>N_vit_LOC100120065_[Ctr1B]
MSFHWGFGETILFEGWKTTDVGGIVGSMVGVILLGMIYEALKNYREYLNVSNAVHNPKEALSR
NEAMFSLIHVVQTLLQGIQIIVGYFLMFIFMTYNTYLCIAVVAGSMLGYFLFAWKNSKCDISECCS

Drosophilids: Ctr1C homologs, protein sequences

>D_mel_Ctr1C
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QYNRPRRYREANYNYNQPTYPPRTNQQSGTQVYAYRPRSPSMPPLQPPGRSSPQAQSSLILTQHT
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GYYIFCAFRTNVQEHCN

>D_ana_GF23301_[Ctr1C]
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YEALKFFREWLYAKQNKRLAAGKEMKKSSGRVSYNQPTRLPPTMQQGSSQIYVNRPRSPSMPPL
RSGTTAANSISNPHAGHNRVHNHPGRGQGRGRRILPEAIPPAQVPCHKVWCSRMHLLQTFLHVI
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>D_ere_GG11899_[Ctr1C]
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TMAMFFHTGDAETILFKFWRTESAMALTLSCLLIFVFAVLYEALKFFREWLFAWDRKRLAGGRD
QNNPPRRYREANYNYNQPTYPPRTNPQSGTQIYAYRPRSPPMPPLQPPGHSSPQAQSSLILTPHTH
HHVQESTPPAGRTSKLKVYCSGMHILQTFLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGVG
YYVFCAFRTNVQEHCN

>D_gri_GH14352_[Ctr1C]
MDLGYDNGQLYTALSREPRHHPDHHHHDEHHEPGSTAGSEDGSPVTRNTHAEPRCGHGGHGGS
MIFHFGCTETILFEFWQTKSTDNLLLSCLIVFIMAVFYEALKCYREWLKKCEKQRLDGGANPTRH
FRSAVPIPQRIDAPPPSAQQISVPLTIAAESVLQPPMAVPPIGELALSQRYPWLDLRHWFQTLLHM
LQVTISFMMMLIFMTFNVYLCIAVVAGAGVGYFIFFARRENISDHCN

>D_moj_GI10446_[Ctr1C]
MDLRYDRVPFPTGFTRESRHDHSHEHHEAASSGQAAERQTENPQPEHSCHGSAGHGGSMVFHV
GNRETILFGFWTTSTTTSLVLSCLIVFIIAVGYEALKCYREWLKKCYKKRQEGGSDRGGTTATQL
APAPTLIDAYSSPLSPVVLSGVGAGAGADQSQNQRPPLTTRVPWLAPIHWYQTLLHMLQVTISFL
LMLIFMTFNVWLCIAVVMGAGVGYFIFFARSENVSDHCN

>D_per_GL13975_[Ctr1C]
MSLRHDHYGGIEYFQEAEALPHPQHGPADKMADDHVGRGHDMPMVFHGGYNETILFKFWQCD
TRLALAFSCLSIFILAILYEALKFFRDWLFRKRKRRIQGGYDNYSPSRNRPYNYYDYYRQPHPQM
QRHLQPHLQPRLQPQPQLQPQPQLTGRIQTYVYRPPQVRRPAQTQSPAPTAAPTAAPTSITYFSDG
ESISTLGDLPTSSSSDQAVPRSASNRSATTDAQAIQTSDFQAATASDDKSPKTSLISQAWKKLRLD
ASSASRSGGQGTSTSAAQGVSTANAHTHIRRPGPPGPPGPPGPSRLLAAVESQDTGESFTCDFYLS
PLHIAQTFLHMLQVLISFLLMLVFMSFNVWLCLAVLLGAGMGYFLFFPLCTSVQEHCN

>D_pse_GA13809_[Ctr1C]
MSLRHDHYGGIEYFQEAEALPHPQHGPADKMADDHVGRGHDMPMVFHGGYNETILFKFWQCD
TRLALAFSCLSIFILAILYEALKFFRDWLFRKRKRRIQGGYDNYSPSRNRPYNYYDYYRQPHPQM
QRHLQPHLQPRLQPQPQLQPQPQLTGRIQTYVYRPPQVRRPVQAQSPAPTAAPTSITYFSDGESIS
TLGDLPTSSSSDQAVPRSASNRSATADAQAIQTSDFQAATASDDKSPKTSLISQAWKKLGLDASR
ASRSGGQGTSTSAAQGVSTANAHTHIRRPGPPGPPGPSRLLAAVESQDTGESFTCDFYLSPLHIAQ
TFLHMLQVLISFLLMLVFMSFNVWLCLAVLLGAGMGYFLFFPLSTSVQEHCN

>D_sec_GM12117_[Ctr1C]
MDHHGVDVSEGHVHHHASHGSPAPAPPSSSHEGHHSPEMTHHGSHGEHTKHGHHEGGGHDMS
MAMFFHTGDAETILFKFWRTESAMALTLSCLLIFVVAVLYEALKFFREWLFSWDRRRLAGGRDQ
YNRPRRYREANYNYNQPTYPPRTNQQSGTQIYAYRPRSPSMPPLQPPGRSSPQAQSSLILTQHTH
HHVQENTPPAGKTTKLKVYCSGMHILQTLLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGVG
YYIFCAFRTNVQEHCN

>D_sim_GD16719_[Ctr1C]
MDHHGVDVSEGHVHHHASHGSPAPAPPSSGHEGHHSPEMNHHGNHGEHTKHGHHEGGAHDM
SMAMFFHTGDAETILFKFWRTESAMALTLSCLLIFVVAVLYEALKFFREWLFSWDRKRLAGGRD
QYNRPRRYREANYNYNQPTYPPRTNQQSGTQIYAYRPRSPSMPPLQPPGRSSPQAQSSLILTQHT
HHHVQENTPPAGKTTKLKVYCSGMHILQTFLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGV
GYYIFCAFRTNVQEHCN

>D_vir_GJ10633_[Ctr1C]
MDLRYNVGRVQTAFTRESRHHHQHNHHQGPGSPGSGSAAEAGHAETVETRNAQGCGHGGHGG
SMIFHCSDRETILFKFWTTDSTTSIVLSCLVVFIMAILYEALKCYREWLKKCNKKRLEGGENRPRS
ILTQLSSIPSTPISEAALSMAEQFPPPLPVAAPTAPENSRAGPAAPWLSPMHWYQTLLHMIQVTISF
LLMLIFMTFNVWLCIAVVLGAGVGYYIFFARSENVSDHCN

>D_wil_GK13100_[Ctr1C]
MDIGHEPHTVQPHEHHQDHHEQHHHHHHHDGHAESPSDASEISFKTDHESHYKEHHDEMSGHE
HGHHMSMSFHEGVDETILFKFWHSQTTLVLVLSCVIIFLVAVMYEGLKFYREWLFKKCKRRSEG
GNERYQHYENQQYPPQYPQPTAQTFVFRPRTPATSPRPSKIAPRQSIRTTNPTHVDIPPIFHNASAP
EPSPPDGTPKRKQCSKFKAWFGKFHLFQTFLHMLQVFVSFLLMLVFMTYNVWLCMAVVLGAGF
GYFIFFAYSDKFYDHCN

>D_yak_GE23348_[Ctr1C]
MNHHGVDASEGHVHHHGSHGSAEPAPPTSVHEGHHSHDMSHPGSHGELTKHGHHEGGGHDMS
MAMFFHTGDAETILFKFWRTESAMALTLSCLLIFVFAVLYEALKFFREWLFAWDRKRLAGGRD
QYNPPRRYREANYNYNQPTYPPRINPQSGTQIYAYRPRAPSMPPLQQPLQPPGPGSPQPHSSLILIP
HTHQHIQENTPPAGRTSKLKVYCSGMHILQTFLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAG
VGYYIFCAFRTNVQEHCN

Figure S1

Figure S2

A   Alignment of human Ctr1 and *Drosophila melanogaster* Ctr1A, Ctr1B and Ctr1C

```
hCtrl        MDHSHH-------------MGMSYMDS--------------------NSTMQPSHHHPT   26
D_mel_Ctr1A  MDHAHHSAPGVDHSMHHDHVGMHHDHSGIPAATASPMDAASMFDLIPDTSDLQASHAGHA   60
D_mel_Ctr1B  MDHGSD----------------DSTS---------------------------------   10
D_mel_Ctr1C  MDHHGV---------------DASEGHVHHHASHGSPEPVPPSSGHEGHHSPEMNHHGN   44
             ***

hCtrl        TSASHSHGGGDSS--MMMMEMTFYFGFKNVELLFSGLVINTAGEMAGAFVAVFLLAMFYE   84
D_mel_Ctr1A  AHGAHNHGGGSGTGMEHMMPMAFHFGYN-ETILFSWWHIETVAGLIGSMIAIFLLALMYE  119
D_mel_Ctr1B  ------------TAKSCPMIMVFHAGHC-ERILWRGWVASTVTEFVLSALAIFLVSFLYE   57
D_mel_Ctr1C  HGEHTKHGHHEGGAHDMSMAMFFHTGDS-ETILFKFWRTESAMALTLSCLLIFMVAVLYE  103
                      *  *  *:  *       :*:     .:.    :    :  :  :*:::.:  **

hCtrl        GLKIARESLLRKSQVSIR--------------------------------YNSMP----  107
D_mel_Ctr1A  GLKYYREYLFWKTYNLLE--------------------------------YRPVTGPQR  146
D_mel_Ctr1B  ALKFLRQQLARREARRAS--------------------------------EQLAAEQRR   84
D_mel_Ctr1C  ALKFFREWLFSWDRKRLAGGRDQYNRPRRYREANYNYNQPTYPPRTNQQSGTQVYAYRPR  163
             . **    *:  *                                         .   .

hCtrl        ------VPGPNGTILMETHKT-----------------VGQQ---MLSFPHLLQTVLHI  140
D_mel_Ctr1A  NPEAPRIPSPAAAAPSPVQYVG--------------EVVHKQPPSMLSINHLLQTLLHV  191
D_mel_Ctr1B  KNEAPAAGGCCSEAPLAE--------------PREQTYWQRLFAS-SHIVQSLLNL  125
D_mel_Ctr1C  SPSMPPLQPPGRSSPQAQSSLILTQHTHHHVQENTPPAGRTTKLKVFCSGMHILQTFLHV  223
                                          :   *      *:::*::.*::

hCtrl        IQVVISYFLMLIFMTYNGYLCIAVAAGAGTGYFLFSWKKAVVVDITEHCH  190
D_mel_Ctr1A  LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  241
D_mel_Ctr1B  LQIVISYLLMLIFMTFNYWLCLAVILGLGLGYFFFGWNKKNPD-ESECCP  174
D_mel_Ctr1C  LQVLISFLLMLVFMTFNVWLCVAVLLGAGVGYYIFCAFRTN---VQEHCN  270
             :*: :*::***:**: *  :**: * . *  *   .**::*   :         *  *
```

Figure S2

B   Alignment of drosophilid Ctr1A genes

```
D_mel_Ctr1A              MD-HAHHSAPG---VDHS-MHHDHVGMHHDHSGIPAATASPMDAASMFD-   44
D_sec_GM12509_[Ctr1A]    MD-HAHHSAPG---VDHS-MHHDHAGMHHDHSGIAAATASPMDAASMFD-   44
D_sim_GD16812_[Ctr1A]    MD-HAHHSAPG---VDHS-MHHDHAGMHHDHSGLAAATASPMDAGSMFD-   44
D_yak_GE16762_[Ctr1A]    MD-HAHHSAPG---VDHS-MHHDHAGMHHDHSGMAASTASPSDSASMFD-   44
D_ere_GG19602_[Ctr1A]    MD-HTHHSAPD---VDHS-MHHDHAGMHHDHSGMAAATASPLDPASMLD-   44
D_ana_GF22272_[Ctr1A]    MD-HAHHNTGG---VDHSMMHHDHPGMHHDHMSAAVATATTEDPAAILAP   46
D_wil_GK25589_[Ctr1A]    MD-HHNHGAPAVETIDHS-MHHGHAGMHHDHSGLGSGTVT--DPTVLAS-   45
D_per_GL13345_[Ctr1A]    MD-HAHHTAPN---VDHS-LHHDHAGMHHDHSGMDSSISP----------   35
D_pse_GA17816_[Ctr1A]    MD-HAHHTAPN---VDHS-LHHDHAGMHHDHSGMDSSISP----------   35
D_moj_GI21812_[Ctr1A]    MDPHAHHNAP---AVDHSMHGHDHANMHHDHDHMG-LDATTLTPP-----   41
D_vir_GJ16985_[Ctr1A]    MDAHAHHSAPNVELIDHSMHGHDHANMHHDHEHMG-LDATTLSPP-----   44
D_gri_GH24714_[Ctr1A]    MDAHAHHSAPS-IGVDHSMHGHDHAGMHHDHAHMAPMDTTTLSPP-----   44
                         **  *  :* :          :::***   *_* _*****

D_mel_Ctr1A              LIPDTSD-LQASHAGHAAHGAHN-HGGGSGTGMEHMMPMAFHFGYNETIL   92
D_sec_GM12509_[Ctr1A]    LIPDTSD-LQASHAGHAAHGAHN-HGGGSGTGMEHMMPMAFHFGYNETIL   92
D_sim_GD16812_[Ctr1A]    LIPDTSD-LQASHAGHAAHGAHN-HGGGSGTGMEHMMPMAFHFGYNETIL   92
D_yak_GE16762_[Ctr1A]    LIPDTSD-LQASHAG---HGAHN-HGGGSGTGMKHMMPMAFHFGYDETIL   89
D_ere_GG19602_[Ctr1A]    LIPQTSD-LQASHTGHVGHGAHN-HGGGSGTGMEHMMPMAFHFGHNETIL   92
D_ana_GF22272_[Ctr1A]    LFTGTSDVLQAAADVHAGHHAGH-HGG-SGTGMEHMMPMAFHFGYNETIL   94
D_wil_GK25589_[Ctr1A]    DISATTP-----MSMGMQHGAGHYHGGGTGTGMEHMMSMAFHFGYNETIL   90
D_per_GL13345_[Ctr1A]    -TTTTTD--STTHDMHAVHHHSG-GGGGTGTGMEHMMSMAFHFGYNETIL   81
D_pse_GA17816_[Ctr1A]    -TTTTTD--STTHDMHAVHHHSG-GGGGTGTGMEHMMSMAFHFGYNETIL   81
D_moj_GI21812_[Ctr1A]    -LATTHG--DLPMTMHAGHHHGGGG---TGTGMEHMMSMAFHFGYDETIL   85
D_vir_GJ16985_[Ctr1A]    -LATPHG--DLAMGMHAGHHHGGGGGGGTGTGMEHMMSMAFHFGYNETIL   91
D_gri_GH24714_[Ctr1A]    -LETSHG--DMGMGGHSSHHHGSGG---TGHGMEHMMSMAFHFGYDETIL   88
                         .                *         :*_**:***_*******::_****

D_mel_Ctr1A              FSWWHIETVAGLIGSMIAIFLLALMYEGLKYYREYLFWKTYNLLEYRPVT  142
D_sec_GM12509_[Ctr1A]    FSWWHIETVAGLVGSMIAIFLLALMYEGLKYYREYLFWKTYNLLEYRPVT  142
D_sim_GD16812_[Ctr1A]    FSWWHIETVAGLVGSMIAIFLLALMYEGLKYYREYLFWKTYNLLEYRPVT  142
D_yak_GE16762_[Ctr1A]    FSWWHIETVAGLVGSMIAIFLLALMYEGLKYYREYLFWKTYNLLEYRPVT  139
D_ere_GG19602_[Ctr1A]    FSWWHIETVAGLVGSMIVIFLLALMYEGLKYYREYLFWKTYNLLEYRPVT  142
D_ana_GF22272_[Ctr1A]    FSWWHIETVAGLVGSMIAIFVLALLYEGLKYYREYLFWKTYNLLEYRPVT  144
D_wil_GK25589_[Ctr1A]    FSWWHIDTVAGLIGSMIAIFLLALLYEGLKYYREYLFWKTYNLLEYRPVT  140
D_per_GL13345_[Ctr1A]    FSWWHIDTVSGLIGSMIAIFLLALLYEGLKYYREYLFWKTYNLLEYRPVT  131
D_pse_GA17816_[Ctr1A]    FSWWHIDTVSGLIGSMIAIFLLALLYEGLKYYREYLFWKTYNLLEYRPVT  131
D_moj_GI21812_[Ctr1A]    FSWWHIDTVAGLIGSMIAIFLLALLYEGLKYYREYLFWKTYNLLEYRPVT  135
D_vir_GJ16985_[Ctr1A]    FSWWHIETVAGLIGSMIAIFLLALLYEGLKYYREYLFWKTYNLLEYRPVT  141
D_gri_GH24714_[Ctr1A]    FSWWHIETVAGLIGSMIAIFLLALLYEGLKYYREYLFWKTYNLLEYRPVT  138
                         ***** :*:**:**:****-**:***:*************************

D_mel_Ctr1A              GPQRNPEAPRIPSPAA-AAPSPVQYVGEVVHKQPPSMLSINHLLQTLLHV  191
D_sec_GM12509_[Ctr1A]    GPQRNPEAPRIPSPAA-AAPSPVQYVGEVVHKQPPSMLSINHLLQTLLHV  191
D_sim_GD16812_[Ctr1A]    GPQRNPEAPRIPSPAA-AAPSPVQYVGEVVHKQPPSMLSINHLLQTLLHV  191
D_yak_GE16762_[Ctr1A]    GPQRNPEAPRIPSPAA-AAPSPVQYVGEVVHKQPPSMLSVNHLLQTLLHV  188
D_ere_GG19602_[Ctr1A]    GPQRNPEAPRIPSPAA-AAPSPVQYVGEVVHKQPPSMLSVNHLLQTLLHV  191
D_ana_GF22272_[Ctr1A]    GPQRNPEAPRLPSPAA-AAPSPVQYVGEVVHKQPPSMLSFNHLLQTLLHV  193
D_wil_GK25589_[Ctr1A]    GPQRNPEAPRLPSPAA-AAPSPVQYVGEVVHKQPPSMLSLNHLFQTLLHI  189
D_per_GL13345_[Ctr1A]    GPQRNPEAPRLPSAAA-AAPSPVQYVGEVVHKQPPSMLSVNHLYQTLLHI  180
D_pse_GA17816_[Ctr1A]    GPQRNPEAPRLPSAAA-AAPSPVQYVGEVVHKQPPSMLSVNHLYQTLLHI  180
D_moj_GI21812_[Ctr1A]    GPQRNPEAPRLPTPAA-AAPSPVQYVGEVVHKQPPTMLSINHLYQTLLHV  184
D_vir_GJ16985_[Ctr1A]    GPQRNPEAPRLPTPAAHAAPSPVQYVGEVVHKQPPTMLSINHLYQTLLHV  191
D_gri_GH24714_[Ctr1A]    GPQRNPEAPRLPPPSAAAAPSPVQYVGEVVHKQPPTMLSINHLYQTLLQV  188
                         **********:*_._:*_*****************:***_**_*****::

D_mel_Ctr1A              LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  241
D_sec_GM12509_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  241
D_sim_GD16812_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  241
D_yak_GE16762_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  238
D_ere_GG19602_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  241
D_ana_GF22272_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAGVGYFLFCWKKSVIVDVTEHCH  243
D_wil_GK25589_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAAIGYFLFCWKKSVIVDVTEHCH  239
D_per_GL13345_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  230
D_pse_GA17816_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCLMVVLGAAVGYFLFCWKKSVIVDVTEHCH  230
D_moj_GI21812_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCMMVVLGAGVGYFLFCWKKSVIVDVTEHCH  234
D_vir_GJ16985_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCMMVVLGAGVGYFLFCWKKSVIVDVTEHCH  241
D_gri_GH24714_[Ctr1A]    LQVTLSFLLMLIFMTYNVWLCMMVVLGSGVGYFLFCWKKSVIVDVTEHCH  238
                         *****************____*:****:.:***********_*********
```
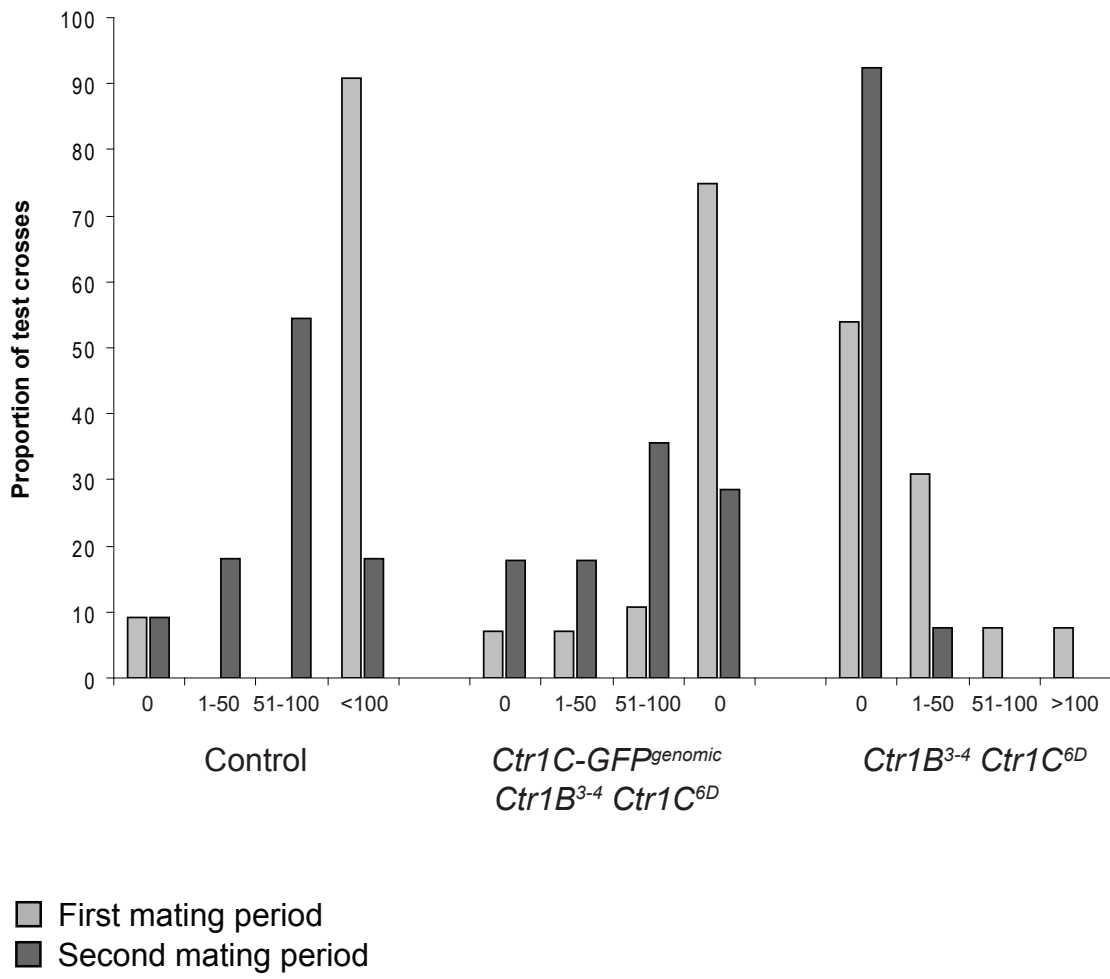
Figure S2

C Alignment of human Ctr1 and insect Ctr1A genes

```
A_mel_LOC551217_[Ctr1A]      -----MSH-----NHMAHMMNATNGHSAHGIHAS-HQAIDHLNMHGNMHN  39
N_vit_LOC100122867_[Ctr1A]   ----MAHH-----DHMAHMMAMNTSGSPD--MTG-MDHMDHGHMA-NTNH  37
T_cas_LOC660576_[Ctr1A]      ----MEHH-----NHDMH------------------EPLDH-----NMHQ  18
A_aeg_AAEL013309_[Ctr1A]     -MDHSEHH-----DYSHQMNHSSDADMMHHGHEGHHGSMEHS---LQDHT  41
A_gam_AGAP002109_[Ctr1A]     -MDHSEHH-----DYSQHANMSSGG--AHAGHTG-HGTVDHS---AHDHT  38
P_hum_PHUM339810_[Ctr1A]     --MDHAGH-----GVSHGDSHVGPHVGPHGGDTSRMGPPSHG-----VSS  38
A_pis_LOC100165693_[Ctr1A]   -----MSH-----DHHNHN----------HQAIEN---------HQ  17
D_mel_Ctr1A                  --MDHAHHSAPGV DHSMHHDHVGMHHDHSGIPAATASPMDAASMFDLIPD  48
B_mor_LOC692872_[Ctr1A]      MDEHHEHH-----NMDMGHAGHEHHGIDHSRHIGHQMPIN GLLN--SSYN  43
hCtr1                        --MDHSHHMG-------------------MSYMDS-------N  15
                                  *                                    .
```

```
A_mel_LOC551217_[Ctr1A]      SMDHANM--DHG-SHLTSDTNPCANMGMHGMST MWFHGGYC-EHVLFESW  85
N_vit_LOC100122867_[Ctr1A]   HMDHGSMSHDHGSAQGSSDACSAMSHAMHGMS- MAFHGGYC-EKILFETW  85
T_cas_LOC660576_[Ctr1A]      GMGHMGH--DMG-----GTTMPKHDMMSHMMS-MA FHTGYN-ETVLFDQW  59
A_aeg_AAEL013309_[Ctr1A]     -MDQGAS--AHAAAG---HSGHAG-MVHHMMS-MA FHGGYN-ETILFEQW  82
A_gam_AGAP002109_[Ctr1A]     MMDHGAHDHHHGAAGGMGAASPAG-MVHHMMS-MS FHGGYD-ETILFEQW  85
P_hum_PHUM339810_[Ctr1A]     HVDHASH---NHIIHET NDSHNGS--HCHGMS- MEFHFGYT-ETILFSTW  81
A_pis_LOC100165693_[Ctr1A]   HPTESSD---SCCSGSEAPASSGQHMMHHMMS- MSFHFGTN-ETVLFDWW  62
D_mel_Ctr1A                  TSDLQASHAGHAAHGAHNHGGGSGTGMEHMMP-MA FHFGYN-ETILFSWW  96
B_mor_LOC692872_[Ctr1A]      RIVHNTDMNDHNVHTFSGHGDHSS--HNMGMS-MT FHGGYI-ETILFSWW  89
hCtr1                        STMQPSH---HHPTTSASHSHGGGDSSMMMM P-MTF YFGFKNVELLFSGL  61
                                  *.  *   * *:  *        :**.
```

```
A_mel_LOC551217_[Ctr1A]      KITSISGLIGSMVGIMIMAALYEGLKYYREYLFWKMYNSLQYRSVTMPQE  135
N_vit_LOC100122867_[Ctr1A]   QISSVAGLIGSVIGIVIMSALYEGLKYYREYLFWKTYNALQYRSVSMPQE  135
T_cas_LOC660576_[Ctr1A]      KFSTIGGLIGSMIGIFFMAALYEGLKYYREYLFWKTYNALQYRAVTLP-E  108
A_aeg_AAEL013309_[Ctr1A]     KIDSLSGLLWSMLLIFIMAALYEGLKYYREHLFWKTYNALQYRPVTVTEK  132
A_gam_AGAP002109_[Ctr1A]     KIDSLSGLLWSMLLIFVMAALYEGLKYYREHLFWRTYNALQYRPVTVTEK  135
P_hum_PHUM339810_[Ctr1A]     KIDSVGGLIGSMFGIVLLAALYEGLKYYREYLFWKTYNSLQYKSVRFPGD  131
A_pis_LOC100165693_[Ctr1A]   TFSTTSGLVYSMIGIFLMATLYEGLKYF REYLFWKSYNAIQYRSVQIPLE  112
D_mel_Ctr1A                  HIETVAGLIGSMIAIFLLALMYEGLKYYREYLFWKTYNLLEYRPVTGPQR  146
B_mor_LOC692872_[Ctr1A]      NVTEVGEFVGSFFAIFIIALLYEG LKYYRKHLLWKTYAGLQYCAVAPPDK  139
hCtr1                        VINTAG EMAGAFVAVFLLAMFYEGLKIARESLLRKSQVSIRYNSMPVPGP  111
                             .   . :  :.. :..:: : ***** *: *: :    :.* .:   .
```

```
A_mel_LOC551217_[Ctr1A]      KNVVA-----------------------------EDNRVVH MVGEV  152
N_vit_LOC100122867_[Ctr1A]   KNVVN-----------------------------DDNRVVH MVGEV  152
T_cas_LOC660576_[Ctr1A]      KGVVS-----------------------------EDNQIVH MVGEV  125
A_aeg_AAEL013309_[Ctr1A]     SPGN-----GNVANNNGLAANGSGD----------EASRVVH MVGEV  164
A_gam_AGAP002109_[Ctr1A]     SNGNGVTVAGGTATDDRAGGAGVGDGLNGASGTGTSAEEGARIVH MVGEV  185
P_hum_PHUM339810_[Ctr1A]     KVVES-----------------------------SSDGNKIVH LVGEV  150
A_pis_LOC100165693_[Ctr1A]   KGPND-----------------------------PVSQ MVGKV  126
D_mel_Ctr1A                  NPEAPR----------------------IPSPAAAAPSPVQ YVGEV  170
B_mor_LOC692872_[Ctr1A]      GVANIC-----------------------AADEPPIVQ PIPHM  159
hCtr1                        NGTIL-----------------------------ME  118
```

```
A_mel_LOC551217_[Ctr1A]      IHKQE -PTMLSWMHTFQTCLHIVQIVLSYFLMLIFMTYNVWLCFAVVLGA  201
N_vit_LOC100122867_[Ctr1A]   IHKQE -PTMLSWMHAFQTLLHIIQIILSYFLMLIFMTYNSWLCAGVVLGA  201
T_cas_LOC660576_[Ctr1A]      IHKQE -PTMLSGMHFYQTLLHMIQMVLSYFLMLIFMTYNVWLCLAVVIGA  174
A_aeg_AAEL013309_[Ctr1A]     IHKQ ERPTMLSTMHLFQTFLHILQVTLSFLLMLIFMTYNTWLCIAVVLGA  214
A_gam_AGAP002109_[Ctr1A]     IHKQE -PTMLSMMHLFQTLLHILQVTLSFLLMLIFMTYNTWLCLAVVLGA  234
P_hum_PHUM339810_[Ctr1A]     IHKQE -PSMWNLMHGYQTFLQAVQMVLSYFLMLIFMTYNVWLCTAVVLGA  199
A_pis_LOC100165693_[Ctr1A]   LLKQE IPTMFSLTHLLQTFLHIVQISISYLLMLIFMTYNVWLCLAVLFGA  176
D_mel_Ctr1A                  VHKQE IPSMLSINHLLQTLLHVLQVTLSFLLMLIFMTYNVWLCLMVVLGA  219
B_mor_LOC692872_[Ctr1A]      LERNV-PTMMSTAHAWQTILHGVQVLVSYMSMLVFMTYNTWLCAAVVLGS  208
hCtr1                        THKTVG QQMLSFPHLLQTVLHIIQVVISYFLMLIFMTYNGYLCIAVAAGA  168
                             :     *.     * ** *: :*: :*:: **:**** :** * *:
```

```
A_mel_LOC551217_[Ctr1A]      AIGYFLFGWKKSVIVDVTEHCH  223
N_vit_LOC100122867_[Ctr1A]   AIGYFLFGWKKSVIVDVTEHCH  223
T_cas_LOC660576_[Ctr1A]      GVGYFLFGWKKSVIVDVTEHCH  196
A_aeg_AAEL013309_[Ctr1A]     ALGYFLFGWKKSVIVDVTEHCH  236
A_gam_AGAP002109_[Ctr1A]     ALGYFLFGWKKSVIVDV-----  251
P_hum_PHUM339810_[Ctr1A]     TIGYFLFGWKKSVVVDVTEHCH  221
A_pis_LOC100165693_[Ctr1A]   TLGYFLFGWKKSVVVDVTEHCH  198
D_mel_Ctr1A                  AVGYFLFCWKKSVIVDVTEHCH  241
B_mor_LOC692872_[Ctr1A]      ATGYFLFGWRESVVVDFTEHCH  230
hCtr1                        GTGYFLFSWKKAVVVDITEHCH  190
                             ***** *:::*:*:**.
```

Figure S2

D Alignment of drosophilid Ctr1B genes

```
D_sec_GM23723_[Ctr1B]    -----MDHDHDHGSDDSSSTAKSCPMIMVFHAGHCERILWRGWVASTVTE  45
D_sim_GD15144_[Ctr1B]    -----MDHDHDHGSDDSTSTAKSCPMIMVFHAGHCERILWRGWVASTVTE  45
D_mel_Ctr1B              ---------MDHGSDDSTSTAKSCPMIMVFHAGHCERILWRGWVASTVTE  41
D_ere_GG25028_[Ctr1B]    -----MDHNHDHGSDDSTSTAKSCPMIMVFHAGHCERILWRGWVASTVTE  45
D_yak_GE25868_[Ctr1B]    -----MDHDHDHGTDDSTSTAKSCPMIMVFHAGHCERILWRGWVASTVTE  45
D_ana_GF18342_[Ctr1B]    MDLMAMDHDHDHGTSDDDDTTKSCPMIMVFHGGHCERILWRGWVAYTVTE  50
D_per_GL23430_[Ctr1B]    -----MDMDHNHGSDDSTSTAKSCPMIMVFHAGHCERILWRGWVAATVTE  45
D_pse_GA20368_[Ctr1B]    -----MDMDHNHGSDDSNSTAKSCPMIMVFHAGHCERILWRGWVASTVTE  45
D_wil_GK13179_[Ctr1B]    -------MDHNHGSDTSTTSCHS--MSMSFHAGYTEIILWNGWTTKTVAE  41
D_gri_GH14206_[Ctr1B]    -------MDHGSG----GTTAKSCPMIMVFHGGHCERILWRGWVASTVVE  39
D_moj_GI24869_[Ctr1B]    --MDLMSMAHDDGHT--GAAAHTCPMIMVFHGGHCERILWRSWVAYTVTE  46
D_vir_GJ24513_[Ctr1B]    --MDLMTMDHDDHGSESVTAAKSCPMIMVFHGGHCERILWRGWVAATVTE  48
                              .      : ::   * * **.*:  * ***..* .: **.*

D_sec_GM23723_[Ctr1B]    FVLSALAIFLVSFLYEALKFLRQQLARREARRESEQLAAEQRRKNEAPAA  95
D_sim_GD15144_[Ctr1B]    FVLSALAIFLVSFLYEALKFLRQQLARREARRESEQLAAEQRRKNEAPAA  95
D_mel_Ctr1B              FVLSALAIFLVSFLYEALKFLRQQLARREARRASEQLAAEQRRKNEAPAA  91
D_ere_GG25028_[Ctr1B]    FVLSALAIFLVSFLYEALKFLRQQLARREARKESEQLASEQRRKNEVPAA  95
D_yak_GE25868_[Ctr1B]    FVLSALAIFLVSFLYEALKFLRQQLARREAKESERLAAEQRRKNEAPAA   95
D_ana_GF18342_[Ctr1B]    FVLSALAIFVVSFLYEALKFLRQHLARRDARKESERLAEEQRRKNENPTA  100
D_per_GL23430_[Ctr1B]    FVLSALFWFLVSFLYEALKFLRQHLARRVARK--ERLAEEQRRKNDNPSG  93
D_pse_GA20368_[Ctr1B]    FVLSAIFWFLVSFLYEALKFLRQHLARRVARK--ERLAEEQRRKNDNPSG  93
D_wil_GK13179_[Ctr1B]    FVLSAIAIFVVSFLYEALKFLRQNLMRIEARKLAQRLAEDQRRKN-NVSD  90
D_gri_GH14206_[Ctr1B]    FTFSAIAFFVLAFIYELLKFLRNYLLQREARKVAEQTAAEIRRKREINDC  89
D_moj_GI24869_[Ctr1B]    FAFSCIAFFAMSFLYELLKFLRVQLVRREARKEAEQLAEEQRRK-ALGDC  95
D_vir_GJ24513_[Ctr1B]    FAFSCIAFFVLSFLYELLKFLREHLIRREARREAE-LAAELRQKNSVNDC  97
                         *.:*.:  * ::*:**  ** *****   * :  **:  :   * : *:*

D_sec_GM23723_[Ctr1B]    GGCCSETPLAEPREQTYWQRLLASSHIVQSLLNLLQIVISYLLMLIFMTF  145
D_sim_GD15144_[Ctr1B]    GGCCSETPLAEPREQTYWQRLLASSHIVQSLLNLLQIVISYLLMLIFMTF  145
D_mel_Ctr1B              GGCCSEAPLAEPREQTYWQRLFASSHIVQSLLNLLQIVISYLLMLIFMTF  141
D_ere_GG25028_[Ctr1B]    GGCCSETPLAEPKEQTYWQRLFASSHMVQSLLNLLQIVISYLLMLIFMTF  145
D_yak_GE25868_[Ctr1B]    GGCCSETPLAEPREQTYWQRLFASTHIVQSLLNLLQIVISYLLMLIFMTF  145
D_ana_GF18342_[Ctr1B]    GGCCSETPLAEERDPSYWQRLFASTHIIQALLNLVQIVISYLLMLIFMTF  150
D_per_GL23430_[Ctr1B]    CTGCSDTPLAEAREKSYWQRLLDSTHIIQSLLNLLQIVVSYLLMLIFMTF  143
D_pse_GA20368_[Ctr1B]    CTGCSDTPLAETEKTYWQRLLDSTHIIQSLLNLLQIVVSYLLMLIFMTF   143
D_wil_GK13179_[Ctr1B]    CGGCSDTPLADPREKTYWQQLVEYSHIVQSLLNLLQIIVSYLLMLIFMTY  140
D_gri_GH14206_[Ctr1B]    AG-CSETPLAEIREETYWQRIFNSAHIIQSLLYLVQVIISYLLMLVFMNF  138
D_moj_GI24869_[Ctr1B]    NG-CSETQLAEIKDKTYWQRIFNMPHIIQTLLTFIQLIISYLLMLVFMNF  144
D_vir_GJ24513_[Ctr1B]    GGGCSETPLAEIREKTYWQRILNTPHIIQSLLNLVQIIISYLLMLVFMNF  147
                           **:: **: :: :***::.  .* ::*:** ::*:::******:* .:

D_sec_GM23723_[Ctr1B]    NYWLCLAVILGLGLGYFFFGWNKKNPDESECCP  178
D_sim_GD15144_[Ctr1B]    NYWLCLAVILGLGLGYFFFGWNKKNPDESECCP  178
D_mel_Ctr1B              NYWLCLAVILGLGLGYFFFGWNKKNPDESECCP  174
D_ere_GG25028_[Ctr1B]    NYWLCLAVILGLGLGYFFFGWNKKNPDESECCP  178
D_yak_GE25868_[Ctr1B]    NYWLCLAVILGLGLGYFFFGWNKKNPDESECCP  178
D_ana_GF18342_[Ctr1B]    NYWLCLAVILGLGLGYFFFGWNKKSPDESECCP  183
D_per_GL23430_[Ctr1B]    NYWLCLAVVLGLGFGYFFFGWNKKTPDESECCP  176
D_pse_GA20368_[Ctr1B]    NYWLCLAVVLGLGFGYFFFGWNKKTPDESECCP  176
D_wil_GK13179_[Ctr1B]    NYWLCLAVVLGLGVGYFFFGWNKKDAQESECCP  173
D_gri_GH14206_[Ctr1B]    NYWLCLAVVLGLAAGYFFFGCFKKDAQDSDCCP  171
D_moj_GI24869_[Ctr1B]    NYWLCLSVILGLSFGYFFFGYVQKDPKDSDCCP  177
D_vir_GJ24513_[Ctr1B]    NYWLCLSVVLGLGVGYFFFGWIKKDPQESECCP  180
                         *****:*:***. ******  :*  .:.:*:***
```

Figure S2

E   Alignment of insect Ctr1B genes

```
A_aeg_AAEL013263_[Ctr1B]     MDHN--HGGPDDMEMLCP--MKMSFHGGTCEVILFPSWATTKTGQFVGAW  46
C_pip_CPIJ016468_[Ctr1B]     MDHNHNHGGPDDMEMLCP--MQMSFHGGTCEIILFPSWATTEVGQFIGAW  48
A_gam_AGAP000100_[Ctr1B]     MDHN--HGGPDDMEMLCP--MQMSFHAGSCEVILFPSWATTEVGAFVGAV  46
D_mel_Ctr1B                  MDHG--SDDSTSTAKSCP--MIMVFHAGHCERILWRGWVASTVTEFVLSA  46
A_mel_LOC725845_[Ctr1B]      MHDDELTKSPNSSTMSARYILEMSFHIGENEVILFDEWHPVDWQGLGWSM  50
N_vit_LOC100120065_[Ctr1B]   ---------------------MSFHWGFGETILFEGWKTTDVGGIVGSM  28
                                                      *  **  *   * **:   *
```

```
A_aeg_AAEL013263_[Ctr1B]     IGFFLMALLYEGLKFYREILAQKEAEKHCSPGTKR---------------  81
C_pip_CPIJ016468_[Ctr1B]     IGFFLMAVLYEGLKFYREVLAQRERKPCSEPASEKKSI------------  86
A_gam_AGAP000100_[Ctr1B]     IGFFLLAFAYEGLKYGRELLHFSDASKRGGEVNDKRTLRN----------  86
D_mel_Ctr1B                  LAIFLVSFLYEALKFLRQQLARREARRASEQLAAEQRRKNEAPAAGGCCS  96
A_mel_LOC725845_[Ctr1B]      VGVILIASIYEGIKNYRDHLYINTTRLWKNKEINNR--------------  86
N_vit_LOC100120065_[Ctr1B]   VGVILLGMIYEALKNYREYLNVSN-AVHNPKEALSR--------------  63
                             :..:*:.    **.:*   *:  *
```

```
A_aeg_AAEL013263_[Ctr1B]     ----------SMRHFMTDKLHILQSLLHLIQVSVSYILMLIVMLFNLWLC  121
C_pip_CPIJ016468_[Ctr1B]     ----------SLLHHLTNKLHIVQSLLHLLQVSVSYVLMLIIMLFNLWLC  126
A_gam_AGAP000100_[Ctr1B]     ----------HLRQALLNRVHIIQTLLHLLQVSVSYLLMLIVMTYNCWLF  126
D_mel_Ctr1B                  EAPLAEPREQTYWQRLFASSHIVQSLLNLLQIVISYLLMLIFMTFNYWLC  146
A_mel_LOC725845_[Ctr1B]      ------------GTLLFSKIHFLQTIIHVVQLVIGYCLMLIFMTYNIWLC  124
N_vit_LOC100120065_[Ctr1B]   ------------NEAMFSLIHVVQTLLQGIQIIVGYFLMFIFMTYNTYLC  101
                                       :    *.:*:::: :*: :.* **:*.*  *  :* :*
```

```
A_aeg_AAEL013263_[Ctr1B]     LAIVSGAAVGYYFFGWIRRSKMDPNECCN  150
C_pip_CPIJ016468_[Ctr1B]     LAIVTGAALGYYIFGWIRQSTIDANECCN  155
A_gam_AGAP000100_[Ctr1B]     LAVVC--AADYYVFGWVRNSSVDPTENCN  153
D_mel_Ctr1B                  LAVILGLGLGYFFFGWNKKN-PDESECCP  174
A_mel_LOC725845_[Ctr1B]      IAVAFGTALGYWLFSW-DKSNGDSDDCCL  152
N_vit_LOC100120065_[Ctr1B]   IAVVAGSMLGYFLFAW-KNSKCDISECCS  129
                             :*:       .*:.*.*   ..  *   : *
```

Figure S2

F Alignment of drosophilid Ctr1C genes

```
D_sec_GM12117_[Ctr1C]   ------MDHHG--VDVSEGH------VHHHASHGSPAPAPPSSSHEGHH---------SP  37
D_sim_GD16719_[Ctr1C]   ------MDHHG--VDVSEGH------VHHHASHGSPAPAPPSSGHEGHH--------SP   37
D_mel_Ctr1C             ------MDHHG--VDASEGH------VHHHASHGSPEPVPPSSGHEGHH---------SP  37
D_ere_GG11899_[Ctr1C]   ------MNHHG--VDASEGH------VHHHGAHVPPEPAPPSSAHEGHH---------SP  37
D_yak_GE23348_[Ctr1C]   ------MNHHG--VDASEGH------VHHHGSHGSAEPAPPTSVHEGHH---------SH  37
D_ana_GF23301_[Ctr1C]   MVNRGATYHHGHAVTTSEVHSIANKLGHGHNSHNTMDHDMHSDSNHHHHPMPEPEDSMSH  60
D_per_GL13975_[Ctr1C]   ------------------------MSLRHDHYGGIEYFQEAEALPHPQ----------   24
D_pse_GA13809_[Ctr1C]   ------------------------MSLRHDHYGGIEYFQEAEALPHPQ----------   24
D_moj_GI10446_[Ctr1C]   ------MDLRYDRVPFPTGFTRESRHDHSHEHHEAASS---GQAAERQT----------  40
D_vir_GJ10633_[Ctr1C]   ------MDLRYNVGRVQTAFTRESRHHHQHNHHQGPGSPGSGSAAEAGH----------  43
D_gri_GH14352_[Ctr1C]   ------MDLGYDNGQLYTALSREPRHHPDHHHHHDEHHEPGSTAGSEDGS---------  43
D_wil_GK13100_[Ctr1C]   ------MDIGHEPHTVQPHEHHQDHHEQHHHHHHHDGHAESPSDASEIS----------  43
                              *                                    :

D_sec_GM12117_[Ctr1C]   EMTHHGSHGEHTKHGHHEGGG-HDMSMAMFFHTGDAETILFKFWRTESAMALTLSCLLIF  96
D_sim_GD16719_[Ctr1C]   EMNHHGNHGEHTKHGHHEGGA-HDMSMAMFFHTGDAETILFKFWRTESAMALTLSCLLIF  96
D_mel_Ctr1C             EMNHHGNHGEHTKHGHHEGGA-HDMSMAMFFHTGDSETILFKFWRTESAMALTLSCLLIF  96
D_ere_GG11899_[Ctr1C]   EMAHHGHHGEHTKHGHHDGEG-HHMTMAMFFHTGDAETILFKFWRTESAMALTLSCLLIF  96
D_yak_GE23348_[Ctr1C]   DMSHPGSHGELTKHGHHEGGG-HDMSMAMFFHTGDAETILFKFWRTESAMALTLSCLLIF  96
D_ana_GF23301_[Ctr1C]   ENSAGGHHSHHGDHGTGDGGGHHDMSMSMFFHTGYTETILVKFWRTESTLAIVLSCLAIF 120
D_per_GL13975_[Ctr1C]   -------HGPADKMADDHVGRGHDMP--MVFHGGYNETILFKFWQCDTRLALAFSCLSIF  75
D_pse_GA13809_[Ctr1C]   -------HGPADKMADDHVGRGHDMP--MVFHGGYNETILFKFWQCDTRLALAFSCLSIF  75
D_moj_GI10446_[Ctr1C]   ENP------QPEHSCHGS--AGHGGS--MVFHVGNRETILFGFWTTSTTTSLVLSCLIVF  90
D_vir_GJ10633_[Ctr1C]   AET------VETRNAQGCGHGGHGGS--MIFHCSDRETILFKFWTTDSTTSIVLSCLVVF  95
D_gri_GH14352_[Ctr1C]   PVT------RNTHAEPRCGHGGHGGS--MIFHFGCTETILFEFWQTKSTDNLLLSCLIVF  95
D_wil_GK13100_[Ctr1C]   FKTDHESHYKEHHDEMSGHEHGHHHMS--MSFHEGVDETILFKFWHSQTTLVLVLSCVIIF 101
                               *    .   *  **  .   ****.  **    .:    :  :**: :*

D_sec_GM12117_[Ctr1C]   VVAVLYEALKFFREWLFSWDRRRLAGGRDQYNRPRRYREANYNYN-----------QPTY 145
D_sim_GD16719_[Ctr1C]   VVAVLYEALKFFREWLFSWDRKRLAGGRDQYNRPRRYREANYNYN-----------QPTY 145
D_mel_Ctr1C             MVAVLYEALKFFREWLFSWDRKRLAGGRDQYNRPRRYREANYNYN-----------QPTY 145
D_ere_GG11899_[Ctr1C]   VFAVLYEALKFFREWLFAWDRKRLAGGRDQNNPPRRYREANYNYN-----------QPTY 145
D_yak_GE23348_[Ctr1C]   VFAVLYEALKFFREWLFAWDRKRLAGGRDQYNPPRRYREANYNYN-----------QPTY 145
D_ana_GF23301_[Ctr1C]   MVAVFYEALKFFREWLYAKQNKRLAAGKEMKKSSGR-----VSYN-----------QPTR 164
D_per_GL13975_[Ctr1C]   ILAILYEALKFFRDWLFRKRKRRIQGGYDNYSPSRNRPYNYYDYYRQPHPQMQRHLQPHL 135
D_pse_GA13809_[Ctr1C]   ILAILYEALKFFRDWLFRKRKRRIQGGYDNYSPSRNRPYNYYDYYRQPHPQMQRHLQPHL 135
D_moj_GI10446_[Ctr1C]   IIAVGYEALKCYREWLKKCYKKRQEGGSD------------------------------ 119
D_vir_GJ10633_[Ctr1C]   IMAILYEALKCYREWLKKCNKKRLEGGEN------------------------------ 124
D_gri_GH14352_[Ctr1C]   IMAVFYEALKCYREWLKKCEKQRLDGGANPTRHF------------------------- 129
D_wil_GK13100_[Ctr1C]   LVAVMYEGLKFYREWLFKKCKRRSEGGNERYQHYENQQYPPQYPQPT---------AQTF 152
                        :.*:  **.** :*:*.**      .:*    .* :

D_sec_GM12117_[Ctr1C]   PPRTNQQ----------SGTQIYAYRP---RSPSMP----PLQPP--------------- 173
D_sim_GD16719_[Ctr1C]   PPRTNQQ----------SGTQIYAYRP---RSPSMP----PLQPP--------------- 173
D_mel_Ctr1C             PPRTNQQ----------SGTQVYAYRP---RSPSMP----PLQPP--------------- 173
D_ere_GG11899_[Ctr1C]   PPRTNPQ----------SGTQIYAYRP---RSPPMP----PLQPP--------------- 173
D_yak_GE23348_[Ctr1C]   PPRINPQ----------SGTQIYAYRP---RAPSMPPLQQPLQPP--------------- 177
D_ana_GF23301_[Ctr1C]   LPPTMQQ----------GSSQIYVNRP---RSPSMP----PLRSG--------------- 192
D_per_GL13975_[Ctr1C]   QPRLQPQPQLQPQPQLTGRIQTYVYRPPQVRRPAQTQSPAPTAAPTAAPTSITYFSDGES 195
D_pse_GA13809_[Ctr1C]   QPRLQPQPQLQPQPQLTGRIQTYVYRPPQVRRPVQAQSPAPTAAP----TSITYFSDGES 191
D_moj_GI10446_[Ctr1C]   --RGGTT-----------ATQLAPAP-----TLIDA-----YSSP-------------- 141
D_vir_GJ10633_[Ctr1C]   --RPRSI-----------LTQLSSIPS----TPISE-----AALS-------------- 147
D_gri_GH14352_[Ctr1C]   --RSAVP-----------IPQRIDAPP----PSAQQ-----ISVP-------------- 152
D_wil_GK13100_[Ctr1C]   VFRPRTP-----------ATSPRPSKI----APRQS-----IRTTN------------- 178
                                    .
```

Figure S2

G Alignment of drosophilid Ctr1C genes (continued)

```
D_sec_GM12117_[Ctr1C]   ------------------------------------------------------------
D_sim_GD16719_[Ctr1C]   ------------------------------------------------------------
D_mel_Ctr1C             ------------------------------------------------------------
D_ere_GG11899_[Ctr1C]   ------------------------------------------------------------
D_yak_GE23348_[Ctr1C]   ------------------------------------------------------------
D_ana_GF23301_[Ctr1C]   ------------------------------------------------------------
D_per_GL13975_[Ctr1C]   ISTLGDLPTSSSSDQAVPRSASNRSATTDAQAIQTSDFQAATASDDKSPKTSLISQAWKK 255
D_pse_GA13809_[Ctr1C]   ISTLGDLPTSSSSDQAVPRSASNRSATADAQAIQTSDFQAATASDDKSPKTSLISQAWKK 251
D_moj_GI10446_[Ctr1C]   ------------------------------------------------------------
D_vir_GJ10633_[Ctr1C]   ------------------------------------------------------------
D_gri_GH14352_[Ctr1C]   ------------------------------------------------------------
D_wil_GK13100_[Ctr1C]   ------------------------------------------------------------


D_sec_GM12117_[Ctr1C]   --------------GRSSPQAQSSLILTQHTHHH----------------VQENTPPAG 202
D_sim_GD16719_[Ctr1C]   --------------GRSSPQAQSSLILTQHTHHH----------------VQENTPPAG 202
D_mel_Ctr1C             --------------GRSSPQAQSSLILTQHTHHH----------------VQENTPPAG 202
D_ere_GG11899_[Ctr1C]   --------------GHSSPQAQSSLILTPHTHHH----------------VQESTPPAG 202
D_yak_GE23348_[Ctr1C]   --------------GPGSPQPHSSLILIPHTHQH----------------IQENTPPAG 206
D_ana_GF23301_[Ctr1C]   --------------TTAANSISNPHAGHNRVHNHPGRGQG------RGRRILPEAIPPA- 231
D_per_GL13975_[Ctr1C]   LRLDASSASRSGGQGTSTSAAQGVSTANAHTHIRRPGPPGPPGPPGPSRLLAAVESQDTG 315
D_pse_GA13809_[Ctr1C]   LGLDASRASRSGGQGTSTSAAQGVSTANAHTHIRRPGPPGPPGP---SRLLAAVESQDTG 308
D_moj_GI10446_[Ctr1C]   -----------------LSPVVLSGVGAGAG--------------------ADQSQNQRP 164
D_vir_GJ10633_[Ctr1C]   ----------------MAEQFPPPLPVAAP--------------------TAP-ENSR- 168
D_gri_GH14352_[Ctr1C]   ----------------LTIAAESVLQPPMA--------------------VPPIGELA- 174
D_wil_GK13100_[Ctr1C]   -----------PTHVDIPPIFHNASAPEPS--------------------PPDGTPKRK 206


D_sec_GM12117_[Ctr1C]   KTTKLKVYCSGMHILQTLLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGVGYYIFCAFR 262
D_sim_GD16719_[Ctr1C]   KTTKLKVYCSGMHILQTFLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGVGYYIFCAFR 262
D_mel_Ctr1C             RTTKLKVFCSGMHILQTFLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGVGYYIFCAFR 262
D_ere_GG11899_[Ctr1C]   RTSKLKVYCSGMHILQTFLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGVGYYVFCAFR 262
D_yak_GE23348_[Ctr1C]   RTSKLKVYCSGMHILQTFLHVLQVLISFLLMLVFMTFNVWLCVAVLLGAGVGYYIFCAFR 266
D_ana_GF23301_[Ctr1C]   QVPCHKVWCSRMHLLQTFLHVIQVFISFLLMLVFMTFNVWLCVAVLLGAGVGYYMFCAFS 291
D_per_GL13975_[Ctr1C]   ESFTCDFYLSPLHIAQTFLHMLQVLISFLLMLVFMSFNVWLCLAVLLGAGMGYFLFFPLC 375
D_pse_GA13809_[Ctr1C]   ESFTCDFYLSPLHIAQTFLHMLQVLISFLLMLVFMSFNVWLCLAVLLGAGMGYFLFFPLS 368
D_moj_GI10446_[Ctr1C]   PLTTRVPWLAPIHWYQTLLHMLQVTISFLLMLIFMTFNVWLCIAVVMGAGVGYFIFFARS 224
D_vir_GJ10633_[Ctr1C]   -AGPAAPWLSPMHWYQTLLHMIQVTISFLLMLIFMTFNVWLCIAVVLGAGVGYYIFFARS 227
D_gri_GH14352_[Ctr1C]   -LSQRYPWLDLRHWFQTLLHMLQVTISFMMMLIFMTFNVYLCIAVVAGAGVGYFIFFARR 233
D_wil_GK13100_[Ctr1C]   QCSKFKAWFGKFHLFQTFLHMLQVFVSFLLMLVFMTYNVWLCMAVVLGAGFGYFIFFAYS 266
                          :           *    **:**::**  :**:**:**:*::    **:**:**:   ***  .**::*   .


D_sec_GM12117_[Ctr1C]   TNVQEHCN 270
D_sim_GD16719_[Ctr1C]   TNVQEHCN 270
D_mel_Ctr1C             TNVQEHCN 270
D_ere_GG11899_[Ctr1C]   TNVQEHCN 270
D_yak_GE23348_[Ctr1C]   TNVQEHCN 274
D_ana_GF23301_[Ctr1C]   TRIHEHCN 299
D_per_GL13975_[Ctr1C]   TSVQEHCN 383
D_pse_GA13809_[Ctr1C]   TSVQEHCN 376
D_moj_GI10446_[Ctr1C]   ENVSDHCN 232
D_vir_GJ10633_[Ctr1C]   ENVSDHCN 235
D_gri_GH14352_[Ctr1C]   ENISDHCN 241
D_wil_GK13100_[Ctr1C]   DKFYDHCN 274
                          .  :***
```