Histamine has been shown to play a role in arthropod vision; it is the major neurotransmitter of arthropod photoreceptors. Histamine-gated chloride channels have been identified in insect optic lobes. We report the first isolation of cDNA clones encoding histamine-gated chloride channel subunits from the fruit fly *Drosophila melanogaster*. The encoded proteins, HisCl1 and HisCl2, share 60% amino acid identity with each other. The closest structural homologue is the human glycyne α3 receptor, which shares 45 and 43% amino acid identity respectively. Northern hybridization analysis suggested that hisCl1 and hisCl2 mRNAs are predominantly expressed in the insect eye. Oocytes injected with *in vitro* transcribed RNA, encoding either HisCl1 or HisCl2, produced substantial chloride currents in response to histamine but not in response to GABA, glycine, and glutamate. The histamine sensitivity was similar to that observed in insect laminar neurons. Histamine-activated currents were not blocked by picrotoxinin, fipronil, strychnine, or the H2 antagonist cimetidine. Co-injection of both hisCl1 and hisCl2 RNAs resulted in expression of a histamine-gated chloride channel with increased sensitivity to histamine, demonstrating assembly of the subunits. The insecticide ivermectin reversibly activated homomeric HisCl1 channels and, more potently, HisCl1 and HisCl2 heteromeric channels.

Histamine has been recognized for several years as the major neurotransmitter of arthropod photoreceptors (1, 2). In *Drosophila*, immunocytochemistry has shown high levels of histamine in photoreceptors and their synapses (2, 3). Further, histidine decarboxylase activity has been demonstrated in *Drosophila* photoreceptors, suggesting that histamine is synthesized in these cells (2). *Drosophila* mutants that are deficient in the hdc gene coding for histamine decarboxylase have been identified (4), and flies homozygous for the null mutation appear to be blind (5). Although light-dependent release of histamine from photoreceptors has not yet been demonstrated, exposure of the fly postsynaptic neuron to histamine mimics the effects of light (6).

Phototransduction of invertebrates has been most extensively studied in insects, but histamine has been implicated as a neurotransmitter in photoreceptors of several other invertebrate species including barnacles and the horseshoe crab *Limulus* (7, 8), whereas glycine and GABA function as the inhibitory neurotransmitters in vertebrate phototransduction (9). Outside of phototransduction, histamine also appears to be the neurotransmitter in some mechanosensory neurons in *Drosophila* (10) and in lobster stomatogastric, cardiac, and olfactory neurons (11–13). To date, the molecular nature of the histamine receptor in these neurons is unknown. The laminar neurons that are postsynaptic to insect photoreceptors respond to light with a rapid, chloride-mediated hyperpolarization that can be mimicked by application of histamine (6). These laminar neurons were isolated from optic lobes of several insect species, and the histamine receptor was characterized as a ligand-gated chloride channel (14, 15). We report the first cloning of two histamine-gated ion channel subunits. These subunits, HisCl1 and HisCl2, were cloned from *Drosophila* using a genomics approach to identify novel sequences within the *Drosophila* genome that possess homology to ligand-gated ion channel subunits. When expressed in oocytes, the resulting channels are permeable to chloride and activated by histamine but are unaffected by several other neurotransmitters known to interact with ligand-gated ion channels. HisCl1 and HisCl2 subunits can form heteromultimeric channels with increased sensitivity to histamine. Heteromultimeric channels as well as HisCl1 homomultimers are reversibly activated by the insecticide ivermectin.

**EXPERIMENTAL PROCEDURES**

**Materials**—All ivermectin used was in the form of ivermectin phosphate. Ivermectin phosphate and fipronil were from the Merck sample collection. All other compounds were from Sigma.

**Identification and Cloning of Novel Ligand-gated Ion Channel Genes**—The *Drosophila* genomic data base was searched for sequences with similarity to *Drosophila* GluC1a (GenBank™ accession number U58776) using a CompuGen Bioel XLP hardware search engine (Petach Tikva, Israel). Two sequences (GenBank™ accession numbers AC007805 and AC007815) potentially encoding novel ligand-gated ion channel subunits were identified from the genomic sequences. Exons from the hisCl1 gene were found on AC007805, whereas hisCl2 exons were found on AC007815. *Drosophila* total RNA was subjected to reverse transcriptase and polymerase chain reactions (RT-PCR) using the following forward primers: for hisCl1, 5′-CTTGCACACAGCCTGCCTG-3′ and 5′-GTTAGCATAGTACTGACAAG-3′ and for hisCl2, 5′-TGTGCACAGCCTGGAAGG-3′ and 5′-ACAGGAATACCGCCTGCTC-3′; and the following reverse primers: for hisCl1, 5′-GTATGTTGATATGTGACAGTACAT-3′ and 5′-ACCTGTGAGTACTCTATAG-3′ and for hisCl2, 5′-TTCCATTGTCGATAGGGCCACTC-3′. The amplified fragments were each ~500 bp in length and were verified by sequencing. 5′ and 3′ cDNA sequences were obtained by the RACE procedure. Poly(A)1 mRNA was purified from *Oregon R* *Drosophila* using the Oligotex mRNA Midi Kit

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(Qiagen), and double-stranded cDNA was generated using the Marathon cDNA amplification kit (CLONTECH). For 3'-RACE, two gene-specific forward primers for hisCl1 were 5'-CATCTCCTTTGCA-CAAAGCTGGCCTG-3' and 5'-CATGATGACGATCTCAGATATTG-3', and for hisCl2 were 5'-CTGCCTTTGCTGACAGCATCATGAG-3' and 5'-TATGACCAAGAATCGGTGCTC-3'. For 5'-RACE, two gene-specific reverse primers were as follows: for hisCl1, 5'-GTCGAACACTCAATTTGCG-3' and 5'-GGCACTCATATCTTGGTGACAT-3'; and for hisCl2, 5'-CCGCTTCTCATTTCGAGTGAGGCCAC-3' and 5'-CAGGGGTCTTTTGCTGTCG-3'.

First round PCR and nested PCR were performed according to the protocol of the cDNA amplification kit with a modified 5'-RACE PCR cycle: 1 cycle at 94 °C for 5 min; 1 cycle at 94 °C for 1 min, 72 °C for 1 min; followed by 25 cycles at 94 °C for 1 min, 68 °C for 1 min, and 72 °C for 2 min. PCR products were cloned into the pCR2.1-TOPO vector (TOPO TA Cloning Kit, Invitrogen). Miniprep DNA was sequenced.

Electrophysiology in Xenopus laevis Oocytes—In vitro transcribed RNAs encoding hisCl1 and hisCl2 were injected into X. laevis oocytes for electrophysiological analysis. Oocytes were prepared as previously described (17) and were studied by two-electrode voltage clamp for 1–4 days following an injection with 50 nl of 100 ng/μl RNA. Co-injections used 50 nl of 100 ng/μl of each RNA species or 200 ng/μl total RNA. In one experiment where the RNA concentration was lowered to 1 ng/μl, no differences were seen in channel properties including histamine sensitivity. Currents were measured using a Dagan CA-1 amplifier interfaced to a Macintosh 7100/80 computer. Data were acquired at 100 Hz using Pulse software (Heka Electronics). During recording, oocytes were continuously superfused with a solution containing 96 mM NaCl, 0.1 mM CaCl2, 1 mM MgCl2, 3.5 mM BaCl2, 5 mM HEPES, pH 7.5. Drugs and solutions were continuously superfused throughout the experiment. All experiments were performed at room temperature under the holding potential of 0 mV. At this holding potential, endogenous currents were 77 ± 20 nA in 14 mock-injected or un.injected oocytes from three frogs. In comparison, histamine-activated currents were typically in the range of 1–2 μA. Between experiments, oocytes were held at −30 mV, close to the oocyte resting potential. Histamine dose-response curves were fit to the Hill equation of the form: I = Imin/L + (Imax−Imin)/L, where n is the Hill coefficient, L is the concentration of drug, and I = Imin is the current activated by saturating drug concentrations.

RESULTS

To identify novel invertebrate ligand-gated ion channels, the Drosophila genomic data base was examined for sequences sharing homology with the Drosophila glutamate-gated chloride channel subunit GluClα. Two partial sequences were identified, AC007805 (hisCl1) and AC007815 (hisCl2), which are located on Drosophila melanogaster chromosome 3 at map positions 86F and 92B, respectively. The full-length cDNAs, hisCl1 (1518 nucleotides) and hisCl2 (2073 nucleotides), corresponding to these partial sequences were cloned by PCR and 5'- and 3'-RACE. The hisCl1 and hisCl2 cDNAs contain 199 and 330 nucleotides 5' of the open reading frame with TGA and TAA stop codons at base 1477 and 1785, respectively. The largest open reading frames share 67% nucleotide identity and predict proteins of 426 and 485 amino acids for HisCl1 and HisCl2 respectively, which share 60% amino acid identity (Fig. 1). The amino acid sequences for both genes contain four predicted transmembrane regions (M1–M4) and four cysteine residues homologous to the cysteine residues conserved in all glycine- and glutamate-gated chloride channels. HisCl1 and HisCl2 share the greatest identity with human glycine receptor α subunits and exhibit 45 and 43% amino acid identity with human Gly α3, respectively (Fig. 1). A cDNA clone encoding HisCl1 and containing a four amino acid deletion (Ser155-Ala-Leu-Gln265) within the M3–M4 intracellular loop was identified suggesting the existence of splice variants. No functional difference between the two clones was observed, and data shown were obtained with the larger of the two.

Phylogenetic analysis confirmed that HisCl1 and HisCl2 subunits are most closely related to the human glycine receptor α subunits and show that the protein sequences used in the neighbor-joining plot of Fig. 2. Both the human glycine receptors and the HisCl channels reside in the same subclade, whereas the invertebrate glutamate and vertebrate GABA receptors are found in separate subclades. These results suggest that the glycine receptors and the HisCl channels share a common origin. To date, glycine-gated chloride channels have not been identified in inverte-
brates. Drosophila rdl, a GABA-gated chloride channel subunit, is the most closely related insect homologue to the HisCl proteins. Likewise, human GABA receptors appear to be closely related to the HisCl proteins, although more distantly than the glycine receptors.

Expression of the hisCl genes was assessed by Northern hybridization analysis of RNA of wild-type and eyeless Drosophila strains (Fig. 3). Total RNA was isolated from whole animals and heads of wild-type Oregon R and the vision-deficient mutant Eya, which lacks eyes and lamina and has a smaller medulla. hisCl1 and hisCl2 DNA probes hybridized with transcripts in RNAs isolated from heads of both strains. The size of the detected transcripts was 2.1 kb for hisCl1 and 2.5 kb for hisCl2, in agreement with predictions from the primary sequence. No hybridization was detected in the lanes corresponding to whole Drosophila RNA from either strain, suggesting that hisCl1 and hisCl2 are primarily expressed in the head. Further, the intensity of the bands detected by hisCl1 and hisCl2 in head RNA from Oregon R flies was greater than that seen with Eya flies, indicating that the two genes are most abundantly expressed in Drosophila eyes.

Injection of hisCl1 RNA into Xenopus oocytes resulted in expression of substantial histamine-activated currents not seen in uninjected oocytes (Fig. 4A). At a holding potential of 0 mV, micromolar concentrations of histamine rapidly activated outward currents that deactivated quickly after wash-out of histamine. In the same oocytes, 1 mM glutamate, glycine, aspartate, GABA and acetylcholine failed to elicit a response.

**Fig. 1.** Alignment of DmHisCl1, DmHisCl2, and HsGlyα3 protein sequences. The four putative transmembrane domains and the conserved cysteines thought to form two cysteine loops are indicated by the boxes.
insecticide ivermectin activated a current, although with a much slower time-course. The current produced in response to 1 μM ivermectin was ~10% of the histamine-activated current (Fig. 4A); the average value seen in eight oocytes was 13 ± 5%. Compared with glutamate-gated chloride channels, HisCl1 channels were less sensitive to ivermectin, and the response was readily reversible upon wash-out. Under standard recording conditions, histamine-activated currents reversed at ~21 mV, consistent with the equilibrium potential for chloride. Reducing the extracellular chloride concentration from 105 to 14 mM, by substituting gluconate for chloride, produced a 29 mV positive shift in the reversal potential and greatly reduced the outward current during voltage ramps from −120 to +60 mV (Fig. 4B). These results suggest that in hisCl1 RNA-injected oocytes, histamine activates a chloride conductance.

Oocyte injection of hisCl2 RNA also resulted in histamine-activated chloride currents insensitive to glutamate, glycine, GABA, and acetylcholine (Fig. 4C). In contrast to HisCl1-expressing oocytes, 1 μM ivermectin did not activate measurable currents or potentiate histamine-activated currents in oocytes injected with hisCl2 RNA. Neither HisCl1 nor HisCl2 channels were blocked by 10 μM fipronil, picrotoxinin, or strychnine, drugs known to block other ligand-gated chloride channels, or by 10 μM of the H2 antagonist cimetidine (data not shown).

Co-injection of hisCl1 and hisCl2 RNAs produced a spontaneous current in the absence of channel agonists. This spontaneous current was dependent on external chloride concentration and reversed near the predicted reversal potential for a chloride current (data not shown). It was seen in all oocytes co-injected with hisCl1 and hisCl2 RNAs, but not in oocytes injected with equal amounts of either RNA alone or with either RNA combined with RNA-encoding Drosophila GluClα. The spontaneous current is thought to result from the opening of heteromeric channels in the absence of an agonist, although direct proof for this hypothesis awaits the discovery of a HisCl channel blocker. Application of micromolar and submicromolar concentrations of histamine but not glutamate, glycine, GABA, or acetylcholine activated additional current (Fig. 4D). Oocytes expressing both subunits were more sensitive to histamine than oocytes expressing HisCl1 or HisCl2 homomultimers. Representative histamine dose-response curves are shown in Fig. 4E. Fitting the data to the Hill equation yielded an EC50 of 0.78 μM for the hisCl1 and hisCl2 co-injected oocytes as compared with 3.1 and 15.5 for the hisCl1-injected and the hisCl2-injected oocytes, respectively. Average EC50 were 0.87 ± 0.38 μM (mean ± S.D., n = 4) for the coexpression of hisCl1 and hisCl2, 4.2 ± 1.3 μM (n = 3) for hisCl1, and 14.0 ± 2.5 μM (n = 5) for hisCl2. Statistical analysis shows that the EC50 obtained with oocytes coexpressing HisCl1 and HisCl2 was significantly

**Fig. 3. Northern analysis.** A, total RNA from heads of Oregon R flies (lane 1), heads of Eya flies (lane 2), whole Oregon R flies (lane 3) and whole Eya flies (lane 4) was hybridized with a DNA probe specific for hisCl2. B, the blot in panel A was re-hybridized with a DNA probe specific for hisCl1.

**Fig. 4. Expression of HisCl1 and HisCl2 in oocytes.** A, an oocyte expressing HisCl1 exhibited rapidly activating reversible currents of 0.52 and 0.86 μA in response to bath application of 3 and 100 μM histamine, respectively. In the same oocyte, 1 μM ivermectin reversibly activated ~10% (90 nA) of the maximal histamine-activated current. B, an oocyte expressing HisCl2 was subjected to 2 s of voltage ramps from −120 to +60 mV in the presence of 100 μM histamine and either 105 or 144 mM Cl− in the bathing solution. Currents reversed at ~21 mV in 105 mM Cl− and at +8 mV in 14 mM Cl−. C, an oocyte expressing HisCl2 exhibited rapidly activating reversible currents of 0.50, 1.65, and 1.98 μA in response to bath applications of 10, 30, and 100 μM histamine, respectively. D, an oocyte co-injected with hisCl1 and hisCl2 RNA showed a rapidly activating current of 1.2 μA in response to 100 μM histamine. In the same oocyte, 1 μM ivermectin reversibly activated a current of 0.54 μA. E, representative data from oocytes expressing HisCl1 (triangles) or HisCl2 (squares) or co-expressing HisCl1 and HisCl2 (circles) were used to generate histamine dose-response curves. For each oocyte, currents were normalized to the current activated in the same oocyte by saturating concentrations of histamine. Data were fit to the Hill equation yielding for HisCl1: EC50 = 3.1 μM and nH = 2.0, for HisCl2: EC50 = 15.5 μM and nH = 2.4, and for HisCl1 + HisCl2: EC50 = 0.78 μM and nH = 1.3.
different from that obtained with expression of either clone alone \((p < 0.05)\). Therefore, HisCl1 and HisCl2 subunits appear to form a functional heteromultimer with properties distinct from the two homomultimers. Histamine dose-response curves in co-injected oocytes were slightly less steep than those in oocytes injected with either subunit alone, illustrated by a Hill coefficient of 1.3 ± 0.1 \((n = 4)\) for co-injected oocytes compared with 1.6 ± 0.5 \((n = 3)\) and 2.7 ± 1.0 \((n = 5)\) for hisCl1- and hisCl2-injected oocytes respectively. A possible explanation for the reduced steepness is the presence of HisCl1 and/or HisCl2 homomultimers in addition to the heteromultimer. Like HisCl1 homomultimers, the heteromultimer was reversibly activated by micromolar concentrations of ivermectin (Fig. 4D). In oocytes co-injected with hisCl1 and hisCl2 RNAs, 1 μM ivermectin activated 46 ± 13% \((n = 7)\) of the current activated by saturating concentrations of histamine (data not shown), compared with 13 ± 5% \((n = 8, p < 0.001)\) in oocytes expressing HisCl1 alone. The increased sensitivity to ivermectin in the co-injected oocytes is inconsistent with activation of a subpopulation of HisCl1 homomultimers and provides further evidence for the formation of HisCl1/HisCl2 heteromultimers.

**DISCUSSION**

DNAs encoding two histamine-gated chloride channel subunits from the fruit fly *D. melanogaster* have been cloned and expressed in oocytes. The subunits, HisCl1 and HisCl2, belong to the family of ligand-gated chloride channels and are phylogenetically related to vertebrate glycine-gated channel α subunits. Histamine is known as a neurotransmitter in arthropod photoreceptors and histamine-activated chloride conductances, as well as single channels, have been reported in insect laminar neurons. The histamine sensitivity and pharmacology obtained with oocytes expressing HisCl1 and/or HisCl2 were similar to what has been reported for native histamine-activated chloride channels from insect laminar neurons (14, 15). We propose that HisCl1 and HisCl2 are the molecular correlates of the histamine-gated chloride channels known to play a role in arthropod phototransduction.

Northern blot analysis suggested that hisCl1 and hisCl2 are predominantly expressed in the *Drosophila* eye. Earlier observations have shown that histamine synthesis and histidine decarboxylase activity are reduced in extracts of *Eya* heads compared with extracts of wild-type heads (Sarthy, Ref. 2). Interestingly, hisCl2 is located in a region on chromosome 3 known to contain genes that play a role in the visual system. The *ora* transainless or *ort* gene was mapped to an interval including hisCl2, and mutations in the *ort* gene lead to visual behavior-defective phenotypes (18). Electrophorograms obtained from *ort* mutants lack the membrane potential transients typically seen at the onset and offset of a light stimulus (19). Because these transients originate from cells in the lamina (20), it was suggested that the *ort* gene may play a role in photoreceptor signaling (19). Indeed, it has been postulated that the *ort* gene may encode a histamine-gated ion channel. The chromosomal map location of *hisCl2* is consistent with *hisCl2* being the *ort* gene; however, future identification of the molecular nature of the genetic defects in *ort* mutants will confirm whether *hisCl2* is the *ort* gene. The *hisCl1* gene maps to a region on chromosome 3 separate from *ort*, and genes involved in *Drosophila* phototransduction or vision have not been reported in this region.

Both hisCl1 and hisCl2 mRNAs appear to be abundant in wild-type *Drosophila* eyes. In oocytes HisCl1 and HisCl2 form functional heteromultimeric channels. However, the subunit composition of the native channel in laminar neurons is not known. Histamine dose-response curves in *Drosophila* laminar neurons were characterized by an EC50 of 24 μM (15), and EC95 ranging from 16 to 60 were found for four other insect species (14, 15). In oocytes, the histamine sensitivity of HisCl2 homomultimers most closely matches that seen in native neurons, suggesting that HisCl2 is the major subunit expressed in these neurons. Assuming that the *ort* gene is HisCl2, this predominant expression of HisCl2 would also explain the absence of on- and off-transients in electrophorograms from *ort* flies. However, if HisCl2 homomultimers underlie the chloride conductances in laminar neurons, the role of HisCl1 remains unclear.

The low level expression of hisCl RNAs detected in *Eya* heads parallels the low levels of histamine synthesis found in locust optic lobe and metamorphic ganglion (21). These findings suggest that HisCl1 channels serve a function outside of phototransduction, and a growing body of evidence suggests that histamine is the neurotransmitter in *Drosophila* mechanosensory neurons (5, 10, 22).

In addition to arthropods, histamine functions as a neurotransmitter and neuromodulator in the mammalian brain, and histaminergic neurons play an important role in thermoregulation, cardiovascular control, and arousal (23). Three pharmacologically distinct receptor subtypes (H1–H3) have been described and cloned (24–26). All three subtypes appear to be G-protein coupled receptors and share no significant sequence homology with hisCl1 or hisCl2. Recently, Hatton and Yang (28) inferred the existence of a mammalian ionotropic histamine receptor from electrophysiological and pharmacological studies of an intact synapse in slices of rat hypothalamus. Histaminergic neurons in the tuberomammillary (TM) region of the hypothalamus are well characterized and project to many areas of the brain including the suprachiasmatic nucleus, hippocampus, and brain stem (23). In the suprachiasmatic nucleus, projections from the TM region synapse on vasopressin and oxytocin neurons. Studying the histaminergic input to oxytocin neurons, Yang and Hatton (27) found that TM region stimulation inhibited oxytocin neurons by activating a chloride conductance that was insensitive to bicuculline and strychnine and blocked by picrotoxin and the H2 antagonists famotidine and cimetidine (27, 28). Because the inhibition of oxytocin neurons did not appear to be G-protein mediated, Hatton and Yang concluded that it was caused by activation of histamine-gated chloride channels with pharmacology overlapping that of H2 receptors. In contrast to the chloride conductance described by Yang and Hatton, HisCl1 and/or HisCl2 channels expressed in oocytes were not sensitive to block by picrotoxin and cimetidine. A search of the human genomic data base did not reveal any obvious human homologues of the *Drosophila* hisCl1 and hisCl2 genes. Until the molecular nature of the channels underlying the inhibitory chloride conductance in oxytocin neurons has been determined, the existence of human homologues of HisCl1 and HisCl2 remains uncertain.

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**REFERENCES**

1. Stuart, A. E. (1999) *Neuron* **22**, 431–433.
2. Sarthy, P. V. (1991) *J. Neurochem.* **57**, 1757–1768.
3. Pollack, I., and Hofbauer, A. (1991) *Cell Tissue Res.* **266**, 391–398.
4. Burg, M. G., Sarthy, P. V., Koliantz, G., and Pak, W. L. (1993) *EMBO J.* **12**, 911–919.
5. Melzig, J., Buchner, S., Wielch, W., Wolf, R., Burg, M., Pak, W. L., and Buchner, E. (1996) *J. Comp. Physiol. A* **179**, 763–773.
6. Hardie, R. C. (1987) *J. Comp. Physiol. A* **161**, 201–213.
7. Callaway, J. C., and Stuart, A. E. (1996) *Microbes Res Tech* **44**, 94–104.
8. Battelle, B. A., Calman, B. G., Andrews, A. W., Grieco, F. D., Mleziva, M. B., Callaway, J. C., and Stuart, A. E. (1993) *J. Comp. Physiol. A* **175**, 527–542.
9. Wasse, H., Koulén, P., Brandtstätter, J. H., Fletcher, E. L., and Becker, C. M. (1993) *Vision Res.* **33**, 1411–1430.
10. Buchner, E., Buchner, S., Burg, M. G., Hofbauer, A., Pak, W. L., and Pollack, I. (1993) *Cell Tissue Res.* **273**, 119–125.
11. Claiborne, B. J., and Selverston, A. L. (1984) *J. Neurosci.* **4**, 708–721.
Cloning of Two Histamine-gated Chloride Channels

12. Hashemzadeh-Gargari, H., and Freschi, J. E. (1992) J. Neurophysiol. 68, 9–15
13. Bayer, T. A., McClintock, T. S., Grunert, U., and Ache, B. W. (1989) J. Exp. Biol. 143, 133–146
14. Hardie, R. C. (1989) Nature 339, 704–706
15. Skingsley, D. R., Laughlin, S. B., and Hardie, R. C. (1995) J. Comp. Physiol. 176, 611–623
16. Yuan, J., Amend, A., Borkowski, J., DeMarco, R., Bailey, W., Liu, Y., Xie, G., and Blevins, R. (1999) Bioinformatics 15, 862–863
17. Arena, J. P., Liu, K. K., Paress, P. S., and Cully, D. F. (1991) Mol. Pharmacol. 40, 368–374
18. The FlyBase Consortium. (1999) Nucleic Acids Res. 27, 85–88
19. O’Tousa, J. E., Leonard, D. S., and Pak, W. L. (1989) J. Neurogenetics 6, 41–52
20. Coombe, P. E. (1986) J. Comp. Physiol. 159, 655–665
21. Elias, M. S., and Evans, P. D. (1983) J. Neurochem. 41, 562–568
22. Melzig, J., Burg, M., Gruhn, M., Pak, W. L., and Buchner, E. (1998) J. Neurosci. 18, 7160–7166
23. Schwartz, J.-C., Arrang, J.-M., Garbarg, M., Pollard, H., and Ruat, M. (1991) Physiol. Rev. 71, 1–51
24. Gantz, I., Schaffer, M., DeValle, J., Lagadc, C., Campbell, V., Uhler, M., and Yamada, T. (1991) Proc. Natl. Acad. Sci. U. S. A. 88, 429–433
25. Yamashita, M., Fukui, H., Sugama, K., Horio, Y., Ito, S., Mizuguchi, H., and Wada, H. (1991) Proc. Natl. Acad. Sci. U. S. A. 88, 11515–11519
26. Lovenberg, T. W., Roland, B. L., Wilson, S. J., Jiang, X., Pyati, J., Huvar, A., Jackson, M. R., and Erlander, M. G. (1999) Mol. Pharmacol. 55, 1101–1107
27. Yang, Q. Z., and Hatton, G. I. (1994) Neuroscience 61, 955–964
28. Hatton, G. I., and Yang, Q. Z. (2001) J. Neurosci. 21, 2974–2982
Identification of Two Novel *Drosophila melanogaster* Histamine-gated Chloride Channel Subunits Expressed in the Eye

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