A Weakly Inward Rectifying Potassium Channel of the Salmon Brain

GLUTAMATE 179 IN THE SECOND TRANSMEMBRANE DOMAIN IS INSUFFICIENT FOR STRONG RECTIFICATION*

(Received for publication, December 26, 1995, and in revised form, February 23, 1996)

Yoshihiro Kuboš, Tomoyuki Miyashita, and Kaoru Kubokawa

From the Department of Neurophysiology, Tokyo Metropolitan Institute for Neuroscience, Musashidai 2-6, Fuchu, Tokyo 183, Japan and the Department of Molecular Biology, Ocean Research Institute, University of Tokyo, Minamidai 1-15-1, Nakano, Tokyo 164, Japan

A cDNA encoding for a weakly inward rectifying K⁺ channel (sWIRK: salmon weakly inward rectifying K⁺ channel) was isolated from the masu salmon brain by expression cloning. The sWIRK channel exhibited the highest similarity with members of the ROMK1 subfamily, BIR10/Kab2 (70% amino acid identity) and ROMK1 (46%). An ATP binding motif which is characteristic of this subfamily was also conserved. The sWIRK RNA was detected in the brain, but not in the heart, kidney, skeletal muscle, liver, testis, and ovary. In the brain, the expression was observed in the ependymoglial cells on the surface of the ventricles as well as in the small perineuronal glia-like cells in the midbrain and the medulla. When compared with the strong inward rectifier IRK1 channel, the sWIRK channel showed a much weaker inward rectification property, and the activation kinetics upon hyperpolarization was slower and less voltage-dependent. The slope conductance of the single channel inward current was 37 pS (140 mM K⁺,o), and outward current channel events were also observed. The weak rectification of sWIRK is significant in that it has a negatively charged residue (glutamate) in the M2 region which is reported to cause strong inward rectification.

By introducing a point mutation to remove this negative charge (glutamate), the sWIRK E179Q mutant channel lost its inward rectification property completely, and the single channel property (45 pS; 140 mM K⁺,o) was ohmic up to highly depolarized potential, even in the presence of the physiological cytoplasmic blockers such as Mg²⁺ and polyamines.

Weakly inward rectifying K⁺ channels play roles in the maintenance of resting potential and in the regulation of excitability in cells, and the presence has been reported in various cells of vertebrates such as skeletal muscle (1, 2), heart (3), neurons (4, 5), glial cells (6), blood cells (7, 8), and epithelial cells (9). The presence has also been known in egg cells of starfish (10, 11) and tunicates (12), which suggests the functional significance in wide ranged species of the animal kingdom.

In 1993, first cDNA clones of inwardly rectifying K⁺ channels ROMK1 (13) and IRK1 (14) were isolated by expression cloning, and it was uncovered that channels of this family have two transmembrane-type structures in contrast with voltage-gated K⁺ channels which have six transmembrane regions. Since then, cDNA clones which belong to new subfamily, GIRK1/GA1 (15, 16), cKATP/CIR (17, 18), uKATP (19) and members of each subfamily (e.g. ROMK1 splice variants (20, 21), BIR10/Kab2 (22, 23), IRK2,3 (24, 25), GIRK2,3 (26), mBIR (27)) were isolated, suggesting the functional and structural diversity. However, all cloned so far are from mammalian cells and no clones have yet been isolated from non-mammalian species.

We isolated a cDNA clone, sWIRK (salmon weakly inward rectifying K⁺ channel), by expression cloning method using Xenopus oocytes. The isolated cDNA belonged to the ROMK1 family, and was characterized by the weak inward rectification and the slow activation upon hyperpolarization. In this article, we describe the primary structure, distribution, and electrophysiological properties of the sWIRK channel.

Weakly inward rectifying K⁺ channels cloned so far (e.g. ROMK1(13), mBIR (27)) do not have a negatively charged amino acid in the M2 region, which is known to have a predominant role for determining the extent of inward rectification (28-30). In the case of the sWIRK channel, it showed a weak rectification in spite of the presence of a negatively charged amino acid (glutamate) at this site. We introduced a point mutation to remove the negatively charged amino acid (Glu to Gln: glutamate to glutamine), and observed that the E179Q mutant lost the inward rectification property completely up to +100 mV. In addition, in low K⁺o condition, the sWIRK mutant exhibited rather outward rectification.

EXPERIMENTAL PROCEDURES

Molecular Biology—Poly(A)⁺ RNA was isolated from the male masu salmon (Oncorhynchus masou) brain of the breeding season using a

*This work was supported in part by research grants from the Human Frontier Science Program (to Y. K.) and the Ministry of Education, Science and Culture of Japan (to Y. K. and K. K.). The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

The abbreviations used are: ROMK1, ATP regulated inward rectifying potassium channel of the renal outer medulla; sWIRK, salmon weakly inward rectifying potassium channel; IRK1, inward rectifier potassium channel; GIRK1, G protein coupled muscarinic potassium channel; KGA, G protein-activated potassium channel; cKATP, cardiac ATP-sensitive inward rectifying potassium channel; CIR, cardiac inward rectifying potassium channel; mBIR, mouse pancreas β cell specific inward rectifying potassium channel; β, time constant; Eₜ, equilibrium potential of potassium; pS, picosiemens; Kᵢₑ, extracellular potassium; [K⁺], extracellular potassium concentration; M2, the second transmembrane region of the inward rectifying potassium channel; kb, kilobase pair(s).

1 The abbreviations used are: ROMK1, ATP regulated inward rectifying potassium channel of the renal outer medulla; sWIRK, salmon weakly inward rectifying potassium channel; IRK1, inward rectifier potassium channel; GIRK1, G protein coupled muscarinic potassium channel; KGA, G protein-activated potassium channel; cKATP, cardiac ATP-sensitive inward rectifying potassium channel; CIR, cardiac inward rectifying potassium channel; mBIR, mouse pancreas β cell specific inward rectifying potassium channel; β, time constant; Eₜ, equilibrium potential of potassium; pS, picosiemens; Kᵢₑ, extracellular potassium; [K⁺], extracellular potassium concentration; M2, the second transmembrane region of the inward rectifying potassium channel; kb, kilobase pair(s).
Fast Track RNA isolation kit (Invitrogen), and fractionated as described previously (14). A cDNA library was constructed as follows. The 4.5–5.5-kb enriched RNA fraction was reverse transcribed using SuperScript 2 (Bethesda Research Laboratories) at 42°C by priming with NotI-oligo(dT) primer adaptors. After ligating an EcoRI adapter and digestion with NotI, cDNA was size fractionated on an agarose gel. cDNAs of longer than 4 kb were collected by Gelzyme (Invitrogen) and were ligated to an EcoRI-NotI digested pT7T3D plasmid (Pharmacia). Recombinant plasmids were electroporated into DH12S bacteria (BRL). The initial library was composed of 400,000 independent recombinants. This primary library was further size selected by digesting plasmids with NotI, selecting DNA fragments longer than 7 kb (approximately one-fourth of the total library) on an agarose gel, religating, and transforming bacteria. 24 pools of 8,000 recombinants were screened. RNA was transcribed as described previously (14). Subdivision of a positive pool was repeated until a single clone was obtained.

To determine the nucleotide sequence, the deleted clones were prepared from both ends using exonuclease 3 (Takara) and mung bean nuclease (Takara). The obtained clones were sequenced using the PRISM sequence reaction kit (ABI) and a DNA sequencer (ABI, 373A). For the electrophysiological analysis and the mutagenesis, EcoRI-BamHI 1.7-kb fragment which contains the entire coding region of the original sWIRK cDNA was subcloned into the Bluescript SK(−) vector (Stratagene). Point mutants were made by the Sculptor Kit (Amerham) using oligonucleotide DNA primers and singlestranded template DNA. The mutations were confirmed by sequencing the primer and the surrounding regions. The electrophysiological property of the mutant was confirmed to be identical using two independent mutant clones.

Northem Hybridization—Poly(A)+ RNA was isolated from the male and female masu salmons of the non-breeding season. Concentrations of the RNA sample were determined by absorbance at 260 nm and 2 μg of poly(A)+ RNA was fractionated on 0.7% agarose-formaldehyde gel and transferred to a nylon membrane. The entire 3.5-kb sWIRK cDNA was labeled with 32P by random priming. Hybridizations were performed as described previously (14). Filters were washed with 0.1× SSC, 1.0% SDS at 65°C for 15 min, and exposed to a x-ray film for 1 day.
day. A RNA size marker (BRL) was loaded on the same gel, transferred, and visualized by staining with ethidium bromide.

In Situ Hybridization—Freshly isolated brains of the male masu salmon of the breeding season were fixed by 4% paraformaldehyde, and 15-μm frozen sections were prepared in a cryostat (Leica). Before hybridization, the sections were pretreated with 10 μg/ml proteinase K at 37°C for 30 min. Digoxigenin-labeled antisense and sense strand probes were prepared from the EcoRI-BamHI 1.7-kb fragment of sWIRK cDNA by T3 and T7 RNA polymerase using a digoxigenin labeling kit (Boehringer Mannheim). The transcribed probes were treated with NaOH to yield an average 600-base pair length. Hybridization was done at 50°C for 16 h in 50% formamide, 10 μl Tris (pH 7.6), 200 μg/ml tRNA, 1 × Denhardt’s solution, 10% dextran sulfate, 600 μg/ml NaCl, 0.25% SDS, 1 ml EDTA (pH 8.0). After hybridization, the sections were washed several times at low and then high stringent conditions (0.2 × SSC, 50% formamide, 55°C, 30 min). After rinsing off the formamide by 0.1 × SSC, the sections were incubated with anti-digoxigenin antibody alkaline phosphatase conjugate (Boehringer Mannheim) and then 4-nitro blue tetrazolium chloride substrate solution.

Two Electrode Voltage Clamp—Oocytes were treated with collagenase (2 mg/ml) for 2 h at room temperature to remove follicle cells and injected with 50 nl of in vitro transcribed cRNA solution. Electrophysiological recordings were carried out 2–3 days later at room temperature (23 ± 2°C) under two electrode-voltage clamp (OC-725BHV, Warner Co.). Data acquisition and analysis were done on a 80486-based computer using Digidata 1200 and pCLAMP program (Axon Instruments). Intracellular glass microelectrodes were filled with 3 M KCl and 3 mM MgCl2, and 5 mM Hepes (pH 7.4). The bath (extracellular) solution contained 140 mM KCl, 3 mM MgCl2, and 5 mM Hepes (pH 7.4). To lower the K+ concentration, KCl was replaced with N-methylglucamine Cl.

Patch Clamp—Single channel recordings were carried out in the cell attached or the inside-out excised patch configuration of the patch clamp (Axopatch-1D, Axon Instruments) at 22–25°C. Data were filtered at 1 kHz by an 8 pole bessel filter, sampled at 5 kHz through the Digidata 1200 (Axon Instruments), and stored in an 80486-based computer using Digidata 1200 and pCLAMP program (Axon Instruments). The resistance of the patch pipettes were in the range of 3–6 megaohm. To avoid interaction between two electrodes, the current passage electrode was wrapped in aluminum foil which was connected to the ground. The bath solution contained 90 mM KCl, 3 mM MgCl2, 5 mM Hepes (pH 7.4). To lower the K+ concentration, KCl was replaced with N-methylglucamine Cl.

Primary Structure—We isolated a cDNA done, sWIRK (salmon weakly inward rectifying K+ channel), by expression cloning method using Xenopus oocytes. The sWIRK cDNA was approximately 3.5 kb (GenBank accession number D83537) and had one open reading frame that encoded 426 amino acids. The sWIRK channel had two transmembrane regions (M1 and M2) together with the pore region (H5) like other inward rectifying K+ channels (Fig. 1A). When compared with other members of inward-rectifying K+ channel family, sWIRK was most similar with the BIR10 (22)/Kir AB-2 (23) (K1 1.2) and the ROMK1 (13) (K1 1.1). The alignment of the sWIRK with the KAB-2 and the ROMK1 is shown in Fig. 1A. The identities of the deduced amino acid sequences with the BIR10/KAB-2 and the ROMK1 were 70 and 46%, respectively, and it was thought to be the third member (Kir 1.2) of the ROMK1 family. The characteristic Walker type A motif of ATP binding site (GX4GKX7I/V), which was found in the COOH-terminal cytoplasmic domain of the ROMK1 (13) and the KAB-2 (23), was also conserved in the sWIRK. The amino acid of the sWIRK channel at the site in M2 which is known to have a key role to determine the extent of rectification (28–30) was negatively charged (glutamate). In Fig. 1B, the extent of the similarity was displayed schematically, which shows that the sWIRK channel belongs to the ROMK1 family.

RESULTS

Electrophysiological Properties—In Fig. 4, current traces and I-V plots in various [K+]o under voltage clamp are shown. Most characteristically sWIRK allowed significant outward current at potentials above EK. When the external K+ concentration is changed, the reversal potential shifts approximately in accordance with EK, which shows that the outward current is not due to leak current. The sWIRK channel also showed significant decay at hyperpolarized potential as reported on the BIR10 channel (22). Another characteristic feature of the sWIRK channel is the slow activation kinetics upon hyperpolarization. In Fig. 5A, the expanded traces of the activation phase and the fitted single exponential curves are shown. The relationship of the activation time constant (τact) and the voltage is shown in Fig. 5B. When the plot is compared with those of the classical strong inward rectifier IRK1 whose activation has been studied most intensively (31, 32), there were remarkable differences. The plot of the sWIRK channel located at the upper or more hyperpolarized position and the slope is less steep. The shift when K+o was changed was more than the shift of EK. The slope factors (voltage which causes e-fold (2.718-fold) change of τact) were 21 mV (IRK1) and 54 mV (sWIRK). The shifts of the τact – V plot when EK was changed by 38 mV were 41 mV (IRK1) and 63 mV (sWIRK), respectively.

The sWIRK channel property was also studied at the single channel level under cell-attached patch condition (Fig. 6). The slope conductance of the inward current events was estimated to be 37 pS (n = 4). In accordance with the macroscopic current, outward current events were also observed at depolarized potential. When the patch membrane was excised from the oocyte...
in ATP-free bath solution, a quick decrease of channel activities was not clearly observed. Electrophysiological Properties of the E179Q Mutant of sWIRK—The negatively charged residue in the M2 region is reported to be a binding site of cytoplasmic blockers such as Mg$^{2+}$ (33–35) and polyamines (36–38), and is known to determine the extent of rectification. In the case of the sWIRK channel, the wild-type which has a negatively charged amino acid (glutamate) at this site exhibited weak rectification (Fig. 5). In this sense, the sWIRK was thought to exhibit extremely weak rectification when compared with other channels cloned so far. To investigate the changes when the charged site was neutralized, glutamate to glutamine mutation (E179Q) was introduced. The activation phase of the sWIRK current, which is known to be a recovery from polyamine block, was not observed in the mutant. The inward rectification property of the mutant was not only attenuated but was completely lost. Furthermore, when $[K^+]_o$ is lowered, the mutant exhibited suppression of the inward current which resulted in rather outward rectification property (Fig. 7). The slope conductance of the mutant in the outward current range was proportional to the square root of $[K^+]_o$ (data not shown), as empirically known for the inward current range of the classical strong inward rectifier K$^+$ channel (3, 10).

The disappearance of the inward rectification property was also observed at the single channel level (Fig. 8). The outward channel events were observed as well as the inward events. At +80 mV, significant downward noises, which were thought to be due to the remiscent flickering block by cytoplasmic blockers, were observed. However, up to +100 mV, the single channel current-voltage plot was straight (Fig. 8B). The slope conductance was 45 pS ($n = 4$), which is slightly larger than that of the wild-type. This result shows that the channel property is ohmic even in the presence of physiological cytoplasmic blockers such as Mg$^{2+}$ and polyamines.

As another critical determinant, E224G in the cytoplasmic region of IRK1 is reported (39), glycine to glutamate mutant of sWIRK (G231E) was also made. The expression of the mutant was lower than the level of the wild-type, but the G231E mutant did not show clear differences in terms of the rectification property (data not shown).
DISCUSSION

The presence of the inward rectifier $K^+$ channel in other species than mammals has been known electrophysiologically (10–12), but the cDNA clones isolated so far are all from mammals. Here we report the cDNA cloning of the first inward rectifying $K^+$ channel from the masu salmon.

The physiological role of the sWIRK channel in glial cells may include regulation of $K^+$ concentration of extracellular space as discussed before (6, 40–43). Together with $Cl^-$ and $K^+$...
Fig. 9. Schematic drawing to explain the properties of the ROMK1 channel and the sWIRK channel. Although the ROMK1 wild-type shows weak rectification, it acquires strong rectification by introducing negatively charged amino acid residue (Asp) in M2. In contrast, wild-type sWIRK shows weak rectification in spite of the presence of a negatively charged amino acid (glutamate). As shown in Figs. 7 and 8, by removing this negatively charged residue (glutamine), the sWIRK E179Q mutant lost inward rectification property completely and exhibited outward rectification. The activation phase was observed when there is a negatively charged residue in M2 in both cases of the ROMK1 and the sWIRK.

Water transporter, the sWIRK channel could function as a regulator of not only K⁺ concentration but also the fluid volume of the extracellular space. As the sWIRK RNA shows intense expression in the ependymal cells on the wall of the ventricles, the function is thought to be significant at the ventricles of the brain.

The sWIRK cDNA was most similar with the BIR10/K₁AB-2 (70%) of the two transmembrane-type K⁺ channels cloned so far. The distribution of the K₁AB-2 in the brain was studied histologically by in situ hybridization using RI-probe, and it was reported to be expressed in glial cells (23). The sWIRK was similar with the K₁AB-2 in that it is predominantly expressed in glial cells. However, the sWIRK was not expressed in the kidney nor in the white matter of the cerebellum where the expression of the K₁AB-2 was observed. The expression of the K₁AB-2 RNA in the ependymoglial cells of the brain ventricle is not reported. Judging from the difference of the distribution and the relatively low identity of the deduced amino acid sequence (70%), the sWIRK channel was thought not to be a salmon equivalent of the BIR10/K₁AB-2 channel, but to be another member of the ROMK1 subfamily.

The most characteristic biophysical feature of the sWIRK channel is its weak rectification property. Although the ROMK1 (13) is reported to show weak rectification, it is due to the absence of negatively charged amino acid in M2, and by introducing a negatively charged residue (asparagine to aspartate) here, it acquires strong rectification (Fig. 9). In contrast, the wild-type sWIRK shows weak rectification property, in spite of the presence of a negative charge (glutamate) here. By mutating it to non-charged amino acid (glutamine), the sWIRK channel was thought not to be the same site. By mutating it to non-charged amino acid (glutamine), it completely lost the inward rectification property and exhibited rather outward rectification in low K⁺ concentration (Fig. 9). The E224G mutation in the COOH-terminal cytoplasmic region of IRK1 is also reported to give effects to the rectification property (39), but this site cannot explain the difference of ROMK1 and sWIRK because this site is Glu in both the ROMK1 and the sWIRK. Thus, it is thought that there is (are) other unknown site(s) which play(s) a key role for the determination of the extent of rectification. The comparison of ROMK1 and sWIRK could be useful for the identification of the site.

The mechanism of the outward rectification of the sWIRK E179Q mutant, in other words, the suppression of the inward current in low [K⁺]ₒ is not clear at present. The Goldman-Hodgkin-Katz current equation predicts a curvature of the current-voltage plot in asymmetric K⁺ condition (44). However, this is not likely in this case, because the I-V curves could not be fitted by the equation, and because the inward rectifier K⁺ channel known to be deviated remarkably from the independence of the permeating ions (45, 46), which is assumed in the equation. Other possible explanations for the suppression of the inward current of the mutant are as follows. (a) As the wild-type sWIRK channel shows decline of current at hyperpolarized potentials, the suppression of the inward current of the E179Q mutant might be also due to a similar, but more intense and instantaneous mechanism. (b) Glu¹⁷⁹ might be a binding site not only for the cytoplasmic blockers, but also for permeating K⁺, and might play a role to facilitate the inward current flow of K⁺. If this is the case, the suppression of the inward current in the mutant is due to the lack of this binding site.

The conductance of the inward current range of the classical strong inward rectifier is empirically known to be proportional to the square root of K⁺₀ (3, 10). The I-V plot of the sWIRK E179Q mutant in various K⁺₀ solution was linear in the outward current range, and the slope conductance was proportional to the square root of [K⁺₀] (data not shown). These facts suggest the possibility that the conductance of the inward rectifier K⁺ channel is regulated by K⁺₀ in all voltage ranges, when the blocking of the outward current by the cytoplasmic blockers were lost completely. By the experiments in which the cytoplasmic blockers were completely removed, Matsuda (47) reported that the single channel conductance of the cardiac inward rectifier K⁺ channel is ohmic in all voltage ranges investigated even under asymmetric K⁺ condition, and that the conductance is determined by the K⁺₀. The ohmic nature of the pore of the inward rectifier K⁺ channel and the dependence of the conductance on K⁺₀ was confirmed by the results of the sWIRK E179Q mutant. The dependence of the conductance on K⁺₀ further suggests the possibility that the inward rectifying K⁺ channel has an aspect of K⁺₀ activated K⁺ channel as postulated before (48–50).

Acknowledgments—We are grateful to Professor H. Nagasawa (University of Tokyo) for support and encouragement, Dr. N. Yamamoto and Professor H. Ito (Nihon Medical College) for advice on histological analysis, S. Suzuki (Kumagaya Branch of Saitama Prefectural Fisheries Experiment Station) for providing us with masu salmons, Dr. H. Okado (Tokyo Metropolitan Institute for Neuroscience) and Professor K. Takahashi (Meiji College of Pharmacy) for discussion and advice.
REFERENCES

1. Katz, B. (1949) Arch. Sci. Physiol. 2, 285–299
2. Standen, N. B., and Stanfield, P. R. (1978) J. Physiol. 280, 169–191
3. Sakmann, B., and Trube, G. (1984) J. Physiol. 347, 641–657
4. Mayer, M. L., and Westbrook, G. L. (1983) J. Physiol. 340, 19–45
5. Mihara, S., North, R. A., and Surprenant, A. (1987) J. Physiol. 390, 335–355
6. Barres, B. A., Chun, L. L. Y., and Corey, D. P. (1990) Annu. Rev. Neurosci. 13, 441–474
7. McKinney, L. C., and Gallin, E. K. (1988) J. Membr. Biol. 103, 41–53
8. Lewis, D. L., Ikeda, S. R., Aryee, D., and Joo, R. H. (1991) FEBS Lett. 290, 17–21
9. Silver, M. R., and DeCoursey, T. E. (1990) J. Gen. Physiol. 96, 109–133
10. Hagiwara, S., and Takahashi, K. (1974) J. Membr. Biol. 18, 61–80
11. Hagiwara, S., Miyazaki, S., and Rothenthal, N. P. (1976) J. Physiol. 261, 621–638
12. Okamoto, H., Takahashi, K., and Yoshii, M. (1976) J. Physiol. 254, 607–638
13. Ho, K., Nichols, C. G., Lederer, W. J., Lytton, J., Vassilev, P. M., Kanazirska, M. V., and Hebert, S. C. (1993) Nature 362, 31–38
14. Kubo, Y., Baldwin, T. J., and Jan, L. Y. (1993) Nature 362, 127–133
15. Kubo, Y., Reuveny, E., Siesler, P. A., Jan, L. Y., and Jan, L. Y. (1993) Nature 364, 802–806
16. Dascal, N., Schreibmayer, W., Lim, N. F., Wang, W., Chavkin, C., D’Mangno, L., Labarca, C., Kieffer, B. L., Gavriaux-Ruff, C., Trolingler, D., Lester, H., and Davidson, N. (1993) Proc. Natl. Acad. Sci. U.S.A. 90, 10235–10239
17. Ashford, M. L. J., Bond, C. T., Blair, T. A., and Adelman, J. P. (1994) Nature 370, 456–459
18. Krapivinsky, G., Wickman, G. K., Velimirovic, B., Krapivsky, L., and Clapham, D. E. (1995) Nature 374, 135–141
19. Inagaki, N., Tsuura, Y., Namba, N., Matsuda, H., Goni, T., Horie, M., Seino, Y., Mizuta, M., and Seino, S. (1995) J. Biol. Chem. 270, 5691–5694
20. Shuck, M. E., Bock, J. H., Benjamin, C. W., Tsai, T. D., Lee, K. S., Slightom, J. L., and Bienkowski, M. J. (1994) J. Biol. Chem. 269, 24261–24270
21. Yano, H., Philipson, L. H., Kugler, J. L., Koyama, Y., Davis, E. M., LeBeau, M. M., Nelson, D. J., Bell, G. I., and Takeda, J. (1994) Mol. Pharmacol. 45, 854–860
22. Bond, C. T., Pesia, M., Xia, X-M., Lagrutta, A., Ravanaugh, M. P., and Adelman, J. P. (1994) Receptors and Channels 2, 183–191
23. Takumi, T., Ishii, T., Horio, Y., Morishige, K., Takahashi, N., Yamada, M., and Kurachi, Y. (1995) J. Biol. Chem. 270, 16339–16346
24. Koyama, H., Morishige, K., Takahashi, N., Tanelli, J. S., Fass, D. N., and Kurachi, Y. (1994) FEBS Lett. 341, 303–307
25. Morishige, K., Takahashi, N., J. A., Yamada, M., Koyama, H., Tanelli, J. S., and Kurachi, Y. (1994) FEBS Lett. 346, 251–256
26. Lesage, F., Duprat, F., Fink, M., Guillemare, E., Coppola, T., Lazdunski, M., and Hugnot, J. P. (1994) FEBS Lett. 353, 37–42
27. Inagaki, N., Goni, T., Clement, J. P., Namba, N., Inazawa, J., Gonzalez, G., Aguilar, B. L., Seino, S., and Bryan, J. (1995) Science 270, 1166–1170
28. Standen, P. R., Davies, N. W., Shelton, P. A., Sutcliffe, M. J., Khan, I. A., Brammar, W. J., and Conley, C. E. (1994) J. Physiol. 478, 1–6
29. Lu, Z., and MacKinnon, R. (1994) Nature 371, 243–246
30. Wible, B. A., Taglialatela, M., Ficker, E., and Brown, A. M. (1994) Nature 371, 246–249
31. Stanfield, P. R., Davies, N. W., Shelton, P. A., Khan, I. A., Brammar, W. J., Standen, N. B., and Conley, C. E. (1994) J. Physiol. 475, 1–7
32. Ishihara, K., and Hiraoka, M. (1994) J. Membr. Biol. 142, 55–64
33. Matsuda, H., Saiguva, A., and Irisawa, H. (1987) Nature 325, 156–159
34. Vandenberg, C. A. (1987) Proc. Natl. Acad. Sci. U.S.A. 84, 2560–2564
35. Matsuda, H. (1988) J. Physiol. 397, 237–258
36. Lopatin, A. N., Makchina, E. N., and Nichols, C. G. (1994) Nature 372, 366–369
37. Ficker, E., Taglialatela, M., Wible, B. A., Henley, C. M., and Brown, A. M. (1994) Science 266, 1068–1072
38. Fakler, B., Brandle, U., Glowatzki, E., Zerena, H. P., and Rupeepsberg, J. P. (1995) Cell 80, 149–154
39. Yang, J., Jan, Y. N., and Jan, L. Y. (1995) Neuron 14, 1047–1054
40. Barres, B. A., Chun, L. L. Y., and Corey, D. P. (1988) Glia 1, 10–30
41. Barres, B. A. (1991) Curr. Opin. Neurobiol. 1, 354–359
42. Sontheimer, H. (1994) Glia 11, 156–172
43. Newman, E. A., Brandebach, D. A., and Odette, L. L. (1984) Science 225, 1174–1175
44. Hillie, B. (1992) Ionic Channels of Excitable Membranes, 2nd Ed., Sunderland, MA
45. Hagiwara, S., Miyazaki, S., Krasne, S., and Cani, S. (1977) J. Physiol. 280, 268–281
46. Hillie, B., and Schwarz, W. (1978) J. Gen. Physiol. 72, 409–442
47. Matsuda, H. (1991) J. Physiol. 435, 83–99
48. Cohen, I. S., DiFrancesco, D., Murline, N. K., and Pennefather, P. (1989) Biophys. J. 55, 197–202
49. Kubo, Y. (1994) Neurosci. Res. 21, 109–117
50. Kubo, Y. (1996) Receptors and Channels, in press
51. Higgins, D. G., and Sharp, P. M. (1988) Gene (Amst.) 73, 237–244
A Weakly Inward Rectifying Potassium Channel of the Salmon Brain: GLUTAMATE 179 IN THE SECOND TRANSMEMBRANE DOMAIN IS INSUFFICIENT FOR STRONG RECTIFICATION
Yoshihiro Kubo, Tomoyuki Miyashita and Kaoru Kubokawa

J. Biol. Chem. 1996, 271:15729-15735.
doi: 10.1074/jbc.271.26.15729

Access the most updated version of this article at http://www.jbc.org/content/271/26/15729

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 49 references, 13 of which can be accessed free at http://www.jbc.org/content/271/26/15729.full.html#ref-list-1