Shal, Shab, and Shaw: three genes encoding potassium channels in *Drosophila*

Alice Butler¹, Aguan Wei¹ and Lawrence Salkoff^{1, 2*}

¹Department of Anatomy and Neurobiology, ²Department of Genetics, Washington University School of Medicine, Box 8108, 660 South Euclid Avenue, St Louis, MO 63110, USA

Submitted March 16, 1990

GenBank accession nos M32660, M32659, M32661

We have shown that potassium channel diversity results from an extended gene family coding for homologous proteins by isolating and expressing three genes from *Drosophila* (1, 2) that encode proteins homologous to the *Shaker* (3) gene product. These three genes map to the second and third chromosomes (1), whereas *Shaker* maps to the X chromosome. The peptides

encoded by all four genes *Shaker*, *Shal*, *Shab*, and *Shaw* share a conserved organization which includes six hydrophobic domains thought to be membrane-spanning regions (4). Like *Shaker*, each gene expresses a K⁺ current in the *Xenopus* oocyte system. Although the currents share the general feature of voltage-gating they differ greatly in their individual kinetic and voltage-sensitive

Shab11

```

ATGGTCCGGCAATTGCAAGGTGGACAGGCTGCTGGCCAGCAACAGCAACAGCAACAGCGACTCAGCAACAGCAACACTCGAAGCAGCAGCTGCAACAGCAGCAGCAGCAACAGCAGCAA 120
M V G Q L Q G G Q A A G Q Q Q Q Q Q Q A T Q Q Q Q H S K Q Q L Q Q Q Q Q Q Q Q Q (40)
CTGCAACTCAAGCAGCATCAGCAGCAGCAACAGGACATCCTGTATCAGCAACATAACGAGGCAATTGCAATTGCACGGGACTGCAGGCTGCAACACCTGCCGACATCGCGGATAATCAG 240
L Q L K Q H Q Q Q Q Q Q D I L Y Q Q H N E A I A I A R G L Q A A T P A D I G D N Q (80)
CCGTACTACGATACAGCGGTATGTGATTTGGAGCGGGCGATGGGAGCCGGTGGAGCTGGTGCATATGGTGGCATCGGCATCGGATCTCTACCAGCAGCTGGCGGTGCTGCTTATCAC 360
P Y Y D T S G N V D W E R A M G A G G A G A Y G G I G I G S L P A A G G A A Y H (120)
CTTGGGCCAGCTAATCCGCGAGGCTCGTTTCTCGTCACTTGGATTACGGTGATGGCGGCCACTTGTGGCCATCCGCCGCTTCTCTGCTGGAGCTGTGGGATCAGGAGCAGGAGCG 480
L G P A N P A G L V S R H L D Y G D G G H L A G P S A G L P A G A V G S G A G A (160)
GGAAGCCGTCGCGGACATCAGTACGGGATCAGGATCAGGAGCAGGACAGGAACAGGAACCGGACCGGATCTGGATCGGGCAGTGGAGCAGCAGGCAAGGAAGTTCGCTACGCCCT 600
G A G A G A S V T G S G S G A G T G T G T G A G S G S G S G A A G K E V R Y A P (200)
TTCCAGTCGCATCAACACGCACTCGATTCCCAACACCTCCAGCAGATCGTTGGCGCGCTCGGTGGCTGGCGCTGGGTGGTCCAGCAGCAGTTCGATTTCGGCGGTGTACCCACC 720
F P V A S P T H S I P T T S Q Q I V G G V G G V G V G G A S S Q S I S G G V P T (240)
CACAGCCAGAGCAACACCCAGCGCTCTGCAGCGGACACATTCAGATCCATGTCTCCATACCGCCGCCGAGCCGTTTCATGATGCCAGTCGAAGCGGTCAACAGCCGCTGTCC 840
H S Q S N T T G A L Q R T H S R S M S S I P P E P F M I A Q S K A V N S R V S (280)
ATCAACGTGGCGGGGTGAGGACAGAGTCTGTGGAGACGCTGGAGCGGCTGCCACACAGCGGCTCGGGCGGTGGGGGAGTGACCAACCCAGGAGCCATCGTGGAGCTGTGCAC 960
I N V G G V R H E V L W R T L E R L P H T R L G R L G E C T T H E A I V E L C D (320)
GACTACTCGCTGGCGGACCAACAGTACTTCTCGACCGACATCCGAAGAGCTTCAGCTCCATCTGAACTTCTATCGCACCGGCAAGCTGCACATCGTCGACGAGATGTGCGTCTCGG 1080
D Y S L A D N E Y F F D R H P K S F S S I L N F Y R T G K L H I V D E M C V L A (360)
TTTGGTGATGACCTGGAGTCTGGGCGCTGACGAACTGTACCTGGAGTCTGCTGCCAGCACAAGTACCACAGCGCAAGGAGAAGCTTCACGAGGAGATGCGTAAGGAGCGGAGTCC 1200
F G D D L E Y W G V D E L Y L E S C C Q H K Y H Q R K E N V H E E M R K E A E S (400)
CTCGCGCCAGCGGACAGGAGGAATTCCGCGAAGTAAATTCCTCGAGTACCAAGTATCTGTGGGAGCTCTCGAAGGCTAACACTAGTTTCGCGCCCGGGTATCGCAGTGATA 1320
L R Q R D E E E F G E G K F S E Y Q K Y L W E L L E K P N T S F A A R V I A V I (440)
TCCATACTATTCATGCTGTCTACCATAGCCCTGACGTGAACACCTACCACAACTACACACATGACAAACGCTACACACAGGATAATCCGAATTGGCAATTGGTGGAGCCGTG 1440
S I L F I V L S T I A L T L N T L P Q L Q H I D N G T P Q D N P Q L A M V E A V (480)
TGATCAGTGTTCACTCTAGAGTACATCTAGGTTTAGCTCTCGCCGACAAAGTGAAGTCTTTAAGGCGGCCCTAACATAATCGATCTATTGGCAATCTCCCATCTTGTGT 1560
C I T W F T L E Y I L R F S S S P D K W K F F K G G L N I I D L L A I L P Y F V (520)
TCGTTATTCTATTGGAACGAATAAGAATGCAACGACGAGTCCAGGATGTGCGTGGGTGGTGGAGGTTTCGCACTATCGCATCTCGCGGCTCTTAAGCTGGCCGCTCACTCA 1680
S L F L L E T N K N A T D Q F Q D V R R V V Q V F R I M R I L R V L K L A R H S (560)
ACGGGCTCGAGTCGTTAGGCTTTACGCTGCGTAACATATAGGAACCTCGGTCTACTAATGCTGTTCTCGGCCATGGCGTTCATATTTCTTCGCTGGCATATTTTCCGGAAG 1800
GATGAAAGGATACAAAATTGTTTCAATACCGGAAGCATTTTGGTGGCGGGTATTACAATGACAACCTTTGGCATACGGGACATCTGTCCACAACCTGCACTGGGAAAGTTATTGGT 1920
D E K D T K F V S I P E A F W W A G I T M T T V G I R D I C P T T A L G K V I G (640)
ACTGTGTGTCATATCGGTTGTTGGTGGTGGCTTTCCTATTCCTATCATCGTTAAACAATTTTGTGAATTTTATAAGAATCAGATGCGCCGCGAAAGGCCCTCAAGCGTCGCGAG 2040
T V C C I C G V L V V A L P I P I I V N N F A E F Y K N Q M R R E K A L K R R E (680)
GCACCTCGATGTCGAAGCGGAGGGCAGCATTTGCTCTTCCATCATATCAATCTGAAAGTGCCTTCGCAAGTCCATGGATCTCATCGATGTGTTGTGCACACAGGAAGCAACA 2160
A L D R A K R E G S I V S F H H I N L K D A F A K S M D L I D V I V D T G K Q T (720)
AATGTCGTGCATCCGAAGGGTAAAGACAAAGCACCCTCAATATAGGCAGGCAGACCTCGATGTGCAAGCGGCCAGGCGCAATCTCTCGCAACCGGACCGCAACCGAAGGC 2280
N V V H P K G K R Q S T P N I G R Q T L D V Q S A P G H N L S Q T D G N S T E G (760)
GAGTCTACCAAGCGGACGAATCCGGCCACCGGACCGGATGCTATAAGAATACGACACCTGAGCAACCTGCGCAACTCCAACCTGCACACCGCAGCGGATCCAGCTTGAGGAG 2400
E S T S G R N P A T T G T G C Y K N Y D H V A N L R N S N L H N R R G S S E Q (800)
GATGCAAGTGGCGCCCTACAGCTTCGACAATCCCAATGCCCGCAGACCTCAATGATGGCATGGAGAGCTATCGGCGGACGACGACGAGCACTGTCGACGCAACAGCAACGAGCAGCAA 2520
D A V P P Y S F D N P N A R Q T S M M A M E S Y R R D E Q A L L Q Q Q Q Q Q Q Q (840)
CAGATGTTGCAGATGCAACAGATTGAGCAGAAGGCCCAACGGAATGGAGGTGCAACCGGAGGAGGTGGCCAAACCTGGCCATGTTGGCGCATCAAGTGGCGGACGAGCGGTG 2640
Q M L Q Q Q I Q Q K A P N G N G G A T G G G V A N N L A M V A A S S A G T A V (880)
GCCACCGCCCAATGCGAGTAATGCCAGCAATACCGCCCGGGTCAGAGGCGCGGAGGAGGCGTGTGAGATGGGGCGGTGTGATGACGACAACCTTCCAGCGCAAGGGAC 2760
A T A T N A S N A S N T A P G S E G A E G G V M E M G A V S M T T T F P R P R D (920)
TGCCCATCCAGATGATGA 2778
C P S R U U (926)

```

* To whom correspondence should be addressed

Shal2

ATGGCTCTGGTGGCCGCTTGGCTGCCCTTGC	CGCCGGCGGCCCATCGGTTGGTGCCGATGCCAC	CCACCCTGCCACGCCGCCGATGCCAAGGATGCCG	CAAAACGGACGAC	120
M A S V A A W L P F A R A A A I G W V P I A T H L P P P P M K D R R K T D D				(40)
GAGAAGCTCTGATCAACGCTCTCGGGCGGCCGCTCGAGACGTGGCGGAATACTTTGGAGAAGTATCGGACACCCCTTTAGTTTCCAATGAAAGGGAGTTCTTCTACGACGAGGACTGC				240
E K L L I N V S G R R F E T W R N T L E K Y P D T L L G S N E R E F F Y D E D C				(80)
AAGAATACTTCTTCGATCGGACCGGACATCTTCGGGCACATACTGAACACTACCGGACGGGCAADTGCATACCCGAAGCCGAATGCTCACCAGCTACGAGGAGCTGGCC				360
K E Y F F D R D P D I F R H I L N Y Y R T G K L H Y P K H E C L T S Y D E E L A				(120)
TTCTTTGGAATAATGCCGAGTGTCATTGGCGATTGCTGCTACGAGGACTACCGGACCGGAAGCGGGAACCGGAGCGGCTGATGAGCAACAAGCTGTGGGAACCGGGGATCAGAAT				480
F F G I I M P D V I G D C C Y E D Y R D R K R E N A E R L M D D K G S N E N G D Q N				(160)
CTGCAGCAGCTGACCAACATGCCGCAAGAATGTGGCGGCTCTCGAAGATCCGACAGCTCGACGACGGCCGTTGGTTCTACTATGTACCGGTTTCTTCTACGCGCTTCGCTGATG				600
L Q Q L T N M R Q K M W R A F E N P H T S T S A L V F Y Y V T G F F I A V S V M				(200)
GCCAACTGTGGTGGAGCGGTGCCGTGTGGCCACCGGCCGGGACAGCGGGAAGCTTGCCTCGGGCAGCGCTCAAGAATCGTCTTCTTCGCTGGATACCGCTCGCTGATGATCTTT				720
A N V V G A E T V P C G H R P G R A G T L P C G E R Y K I V F F C L L D T A C V M I F				(240)
ACGGCGGAGTACTCACTTCGACTCTTCGCGGCCGCCGATCGCTCAAGATTCGTCGCGCTGGTGAGCATATTTGATGGTGGCCCATTCGGCTACTACATTGGCCCTCGGATCACC				840
T A E Y G G A T T C A C T T C G A C T T C G C G C C C C C G A T C G T C A A G A T C G T C G C G T G G T G A G C A T T A T T G A T G G T G G C C A T T C G C C T A C T A C A T T T G C C C T C G G A T C A C C				(280)
G A C A C G A C G A C G T G A G C G G T G C T T C G T C A C G T C G C G C G T T T C C G T G T C T C C G A T T C A A G T T C T C G C G C C A C T C G C A A G G A C T T C G G A T C C T C G G C T A C A C G C T C A A G T C C T G C				960
D N D D V S G A F V T L R V F R V F R I F K F S R H S Q G L R I L G Y T L K S C				(320)
G C C A G C G A A C T G G G C T T C C T T G T C T T C G C T G G C C A T T G C C A T T A T C A T C T T T G C C A C C G T C A T G T T C A C C G C G A G A A A C G T C A A T G C C A A C T T C A C A T C G A T T C C G G C G G C C				1080
A S E L G F L V F S L A M A I I I F A T V M F Y A E K C N V N G T N F T S I P A A				(360)
T T C T G G T A T A C C A T C G T C A A A T G A C G A C G T G G G A T T G G C G A C A A T A G C T G C C A A A T G T T G G C G C G C T G T C G C T C G C T A G C G G T G T C G T G T C G T C A T C G C C T T A				1200
F W Y T I V T M T T L G Y D M V P E T I A G K I V G G V C S L S G V L V I A L				(400)
C C T G T A C C T G T A T C G T A T G A A A C T T A G T A G A A T C T A T C A C C G A A A C A G C G A G C G G A C A A G C G A A G C G G A A A G C T G C C T G C C G C G C A T C C G A T T G C C A A G C C T C G T C C				1320
P V P V I V I V S N F S R I Y H Q N R A D K R K A Q R K A R L A R I A K A S S				(440)
G G A C G C C C T T T G T T A G A A A A G A G C G C C G A G C C G T G G G C T G C C A G G A T C G A G C T G G A T G A C A A T C G G G A G G A G A C A T C T C G A G C T G C A G C A C C A T C A T				1440
G A A F V S K K A A E A R W A A E Q S E G I E L D N Y R D E D I F E L Q H H H				(480)
TTGCTGCGATGTCTGGAGAAGCAACGATGAG				1473
L L R L C L E K T T M U				(491)

Shaw2

ATGAATCTGATCAACATGGACTCGGAAAAACAGGGTGGTGCTCAATGTGGGTGGCATTAGGCACGAAACCTACAAGGCCACGCTGAAGAAGATTCCGGCTACGCGATTATCGCGATTAAACA	120
M N L I L N M D S E N R V L V T G G I R H E T Y K A T L K K I P A T R L S R L T	(40)
GAGGCGCTGGCCAACTGATTCGATCGCATGAATGAGTACTTCTTTGATCGGCACTCGGGGGCTCTTCGCACAAGTCGCAACTATTACAGAAGCTGGAAGCTGCATATCCCCAGGATGTG	240
E A L A N D P I L N E Y F F D R H P G V F A Q V L N Y Y R T G K L H Y P T D V	(80)
TGCGGTCGCTGTTTGAGGAGGAATGGAGTTCTGGGGGCTAGACTCGAACCAGATGGAGGCGCTGCTGTTGGATGACCTACACACAGCATCGCGACACCCAGGAAACCTTAGCCGTACTC	360
C G P L F E E E L E F W G L D S N Q V E P C T T Q H R D T Q E T L A V L	(120)
GATCGTCTCGATCTGGATACGGAACAAACCGTCCGAAGAGGAATGGCAGCGAAATTCGGCTTCGAGGAGGACTACTACAAAGGCACAATATCCTGGTGGCAGGAAATGAAGCCGCGCAT	480
D R L D L D T E K P S E E E L A R K F G E E E D Y Y K G T I S W W Q E M K P R I	(160)
TGGTCTGTGTCGATGAGCCCTACAGTTCCAATCGAGCCAAAGATTTGGCGTGTTTCGGTGTTCTTCATCTGCATTTTCGATCCTGTGCTGTGCTCTGAAGACCCATCCGATATGCGG	600
W S L F D E P Y S S N A A K T I G I V V S V F F I C I S I S L S F C L K L H P D M R	(200)
GTGCCCATCTGTCCGGAACATACAGTGAAGAACTGCGAATGGAAGTAATGGCTGTTTGTGGACAAAACCGACGCAATCGGCACATAGCCTTCTCTATATCGAATCGGTGTGCATGCC	720
V P I V R N I T V K T A N G S N G W F L D K T Q T N A H I A F F Y I E C V C N A	(240)
TGGTTTACTCTTTGAATATTGGTGGCCTTTATCTCATCGCGAACAGATGGAGTTCATCAAGTCATCTGTAAACATCATAGACATACATAGCAGCGCTTAGTTTATATTCGATCTAGTG	840
W F T F E E L I F T S S P N K W F E F I K S S V N I I D Y I A T L S F Y I D L V	(280)
CTTCACGCGGTTCCGATCGCACCTGGAGAACGCTGACATCCTCGAGTCTCTTCGATCATCCGCATCTGTCGCTGTGTTCAAAGCTGACGCGCCACTGTCCGAGCTGAAGATCTGCTGATCCAG	960
L Q R F A S H L E N A D I L E F F S I R I R M L F K L T R H S S G L K I L I	(320)
ACGTTCCGGGCTCGGCCAAGGAGCTGACCTGCTGGTGTCTTCTCTCGTCTGGGCATCGTGATCTTGCCAGCCTTGCTACTACGCGGAGCGCATCCAGGCCAATCCGCACAACGAC	1080
T F R A S A K E L T L L V F F L V L G I V I F A S L V Y Y A E R I Q P N P H N D	1260
TTCAACAGCATACGCTGGGCGCTGTGGTGGGCGCTGGTCACAATGACACCGCTGGCTACGGGCACATGGCCCCCAAACTACATATGGCATGTTCTGTGGTGGCTCTCGGCCCTCGGCC	1320
F N S I P L G L W A L V L T M T T V G Y G D M A P K T Y I G M F V G A L C A L A	(400)
GGGCTACTAACCATCGCATCGCAGTGGCCGTCCGTCATCGTCAGCAACATTCGCCATGTACTACTCGCACAGCGAGGCCAGGCCCAAACTGCCAAAGAACGGGAGACGAGTGCTTCCGCTCGAG	1440
G V L T I A L P V P V I V S N F A M Y Y S H T Q A R A K L P K K K R R V L P V E	(440)
CAGCGCGCCACGCCAGCAATGCGACGTCGAGTGGCCCTGGTGGTGTCAGTGGTTGCGGCACCCCGGGCTGGTCCCCACTTCGGTCCGATGGATCCGGCGGAACGTGACCACTGCGATGAAC	1560
Q A P P Q P R L P G A P G G V S G C T P P G S G P H S G P M G S G G T G P R R M N	(480)
AATAAAGCAAAAGGACCTGGTCAGCCCCAAGTCAGATAGGCCCTTCAGTTTCGACTAA	1497
N K T K D L V T S P K S D M A F S F D U	(499)

properties. The differences observed among the currents expressed by the different gene products are greater than the differences produced by alternative splicing of the *Shaker* gene (3). Homologs of *Shaker*, *Shal*, *Shab*, and *Shaw* are all present in mammals; each *Drosophila* potassium channel gene may be representative of a multigene subfamily in mammals (2). In the sequences shown below⁺, proposed membrane-spanning domains are underlined.

ACKNOWLEDGEMENTS

This work was supported by NIH grant 1 RO1 NS24785-01, a research grant from the Muscular Dystrophy Association of America, and a research grant from Monsanto-Searle.

REFERENCES

1. Butler, A., Wei, A., Baker, K. and Salkoff, L. (1989) *Science* **243**, 943–947.
2. Wei, A., Covarrubias, M., Butler, A., Baker, K., Pak, M. and Salkoff, L. (1990) *Science* in press.
3. Timpe, L.C., Schwarz, T.L., Tempel, B.L., Papazian, D.M., Jan, Y.N. and Jan, L.Y. (1988) *Nature* **331**, 143–145.
4. Noda, M. *et al.* (1986) *Nature* **320**, 188–192.

FOOTNOTE

⁺The *Shab11* sequence has corrections from Butler *et al.* (1) resulting in a change in the deduced amino acid