

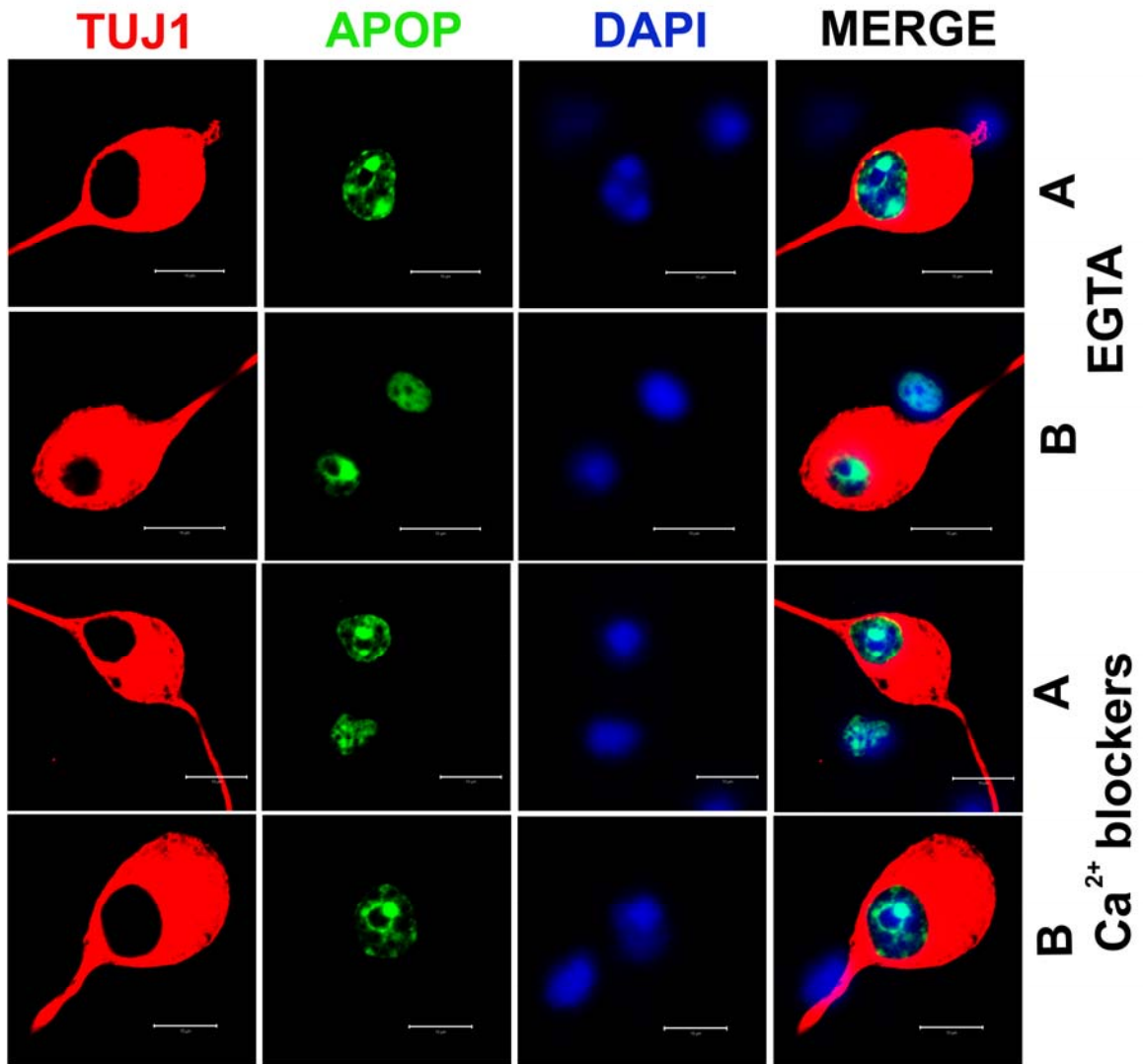
**K<sub>v</sub>7-type Channel Currents in Spiral Ganglia Neurons: Involvement in Sensorineural Hearing Loss**

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Supplementary Figure 1 (S1)

**Effects of linopirdine under reduced extracellular Ca<sup>2+</sup> conditions.** Upper and second panels show apical (A) and basal (B) SGNs in culture with BDNF/NT3 growth factors and reduced bath Ca<sup>2+</sup> (~300 μM). The third and fourth row shows apical (A) and basal SGNs in the presence of 10 μM linopirdine and a cocktail of Ca<sup>2+</sup> channel blockers. TUJ1 = neuronal marker, Apop (apoptosis = TUNEL- positive, DAPI= nuclei stain).

Supplementary figure 1 (S1)



Supplementary Table S1-8

Table S1

Changes in action potential waveforms at different ages

Apex	2 week old (n = 11)	3-4 month old (n = 12)	17 month old (n = 9)
Rmp (mV)	-63 ± 4	-65 ± 2	-60 ± 3#
Threshold (mV)	-44 ± 3	-39 ± 2**	-35 ± 2**##
AP (duration) (ms)	8 ± 2	6 ± 1**	6 ± 0*
Latency (ms)	5 ± 1	3 ± 0**	4 ± 1*
Max depolarization. slope (mV/ms)	104 ± 38	136 ± 26	118 ± 20
Max repolarization slope (mV/ms)	-54 ± 18	-75 ± 16*	-68 ± 15
Half width (ms)	0.5 ± 0.2	0.5 ± 0.1	0.6 ± 0.1

\*\*p<0.01, \*p<0.05 vs 2 week

##p<0.01,#p<0.05 vs 3-4 month

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

# Functional mechanisms of progressive hearing loss

Table S2

Base	2 week (0.5 months) old (n = 9)	3-4 month old (n = 7)	17 month old (n = 7)
Rmp (mV)	-57 ± 2	-60 ± 4	-54 ± 3*#
Threshold (mV)	-40 ± 2	-38 ± 1	-35 ± 3.0** #
Spike number	43 ± 10	18 ± 5**	34 ± 7*##
AP duration (ms)	6 ± 1	8 ± 2*	8 ± 1**
Latency (ms)	4 ± 1	6 ± 1*	5 ± 1*
Max depolarization slope (mV/ms)	177 ± 40	164 ± 36	129 ± 17*#
Max repolarization slope (mV/ms)	-123 ± 26	-107 ± 26	-90 ± 21*
Half Width (ms)	0.6 ± 0.1	0.7 ± 0.1	0.7 ± 0.2*

\*\*p<0.01, \*p<0.05 *versus* 2 week

##p<0.01, # p<0.05 *versus* 3-4 month

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

## Functional mechanisms of progressive hearing loss

Table S3

The effect of linopirdine on action potentials

2 week (0.5 month) old mice	Base (n = 11)		Apex (n = 12)	
	Linopirdine		Linopirdine	
	Control	(10 $\mu$ M)	Control	(10 $\mu$ M)
Spike number	40 $\pm$ 13	47 $\pm$ 6	1 $\pm$ 0	1 $\pm$ 0
Rmp (mV)	-62 $\pm$ 3	-53 $\pm$ 3*	-63 $\pm$ 4	-57 $\pm$ 3
Threshold(mV)	-39 $\pm$ 3	-38 $\pm$ 3	-43 $\pm$ 3	-43 $\pm$ 2
AP duration (ms)	7 $\pm$ 1	6 $\pm$ 1	9 $\pm$ 2	7 $\pm$ 1
Latency (ms)	5 $\pm$ 1	4 $\pm$ 1*	5 $\pm$ 1	4 $\pm$ 1*
Max depolarization slope				
(mV/ms)	180 $\pm$ 48	156 $\pm$ 55	105 $\pm$ 42	95 $\pm$ 12
Max repolarization slope				
(mV/ms)	-125 $\pm$ 36	-105 $\pm$ 40	-52 $\pm$ 19	-49 $\pm$ 8
Half width (ms)	0.6 $\pm$ 0.1	0.66 $\pm$ 0.2	0.55 $\pm$ 0.1	0.61 $\pm$ 0.1

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

\*p<0.05, \*\*p<0.01 Treatment *versus* control

# Functional mechanisms of progressive hearing loss

Table S4

3-4 month old mice	Base (n = 9)		Apex (n = 8)	
	Linopirdine		Linopirdine (10	
	Control	(10 $\mu$ M)	Control	$\mu$ M)
Spike number	19 $\pm$ 5	40 $\pm$ 7 **	1 $\pm$ 0	1 $\pm$ 0
Rmp (mV)	-57 $\pm$ 4	-51 $\pm$ 3*	-63 $\pm$ 4	-60 $\pm$ 4
Threshold (mV)	-40 $\pm$ 2	-39 $\pm$ 3	-39 $\pm$ 2	-37 $\pm$ 4
AP duration (ms)	8 $\pm$ 2	7 $\pm$ 2	6 $\pm$ 1	6 $\pm$ 1
Latency (ms)	5 $\pm$ 2	5 $\pm$ 1	3 $\pm$ 0	3 $\pm$ 0
Max depolarization slope				
(mV/ms)	182 $\pm$ 46	119 $\pm$ 49	136 $\pm$ 26	79 $\pm$ 26**
Max repolarization slope				
(mV/ms)	-121 $\pm$ 39	-79 $\pm$ 32	-75 $\pm$ 16	-45 $\pm$ 16**
Half width (ms)	0.6 $\pm$ 0.2	0.7 $\pm$ 0.3	0.5 $\pm$ 0.1	0.6 $\pm$ 0.2

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

\*p<0.05, \*\*p<0.01 Treatment *versus* control

Functional mechanisms of progressive hearing loss

Table S5

17 month old mice	Base (n = 5)		Apex (n = 6)	
	Linopirdine		Linopirdine (10	
	Control	(10 $\mu$ M)	Control	$\mu$ M)
Spike number	22 $\pm$ 7	38 $\pm$ 7 **	1 $\pm$ 0	1 $\pm$ 0
Rmp (mV)	-54 $\pm$ 4	-44 $\pm$ 4*	-60 $\pm$ 4	-60 $\pm$ 4
Threshold (mV)	-37 $\pm$ 4	-35 $\pm$ 5	-36 $\pm$ 2	-34 $\pm$ 4
AP duration (ms)	7 $\pm$ 0	6 $\pm$ 2	6 $\pm$ 1	6 $\pm$ 1
Latency (ms)	5 $\pm$ 1	4 $\pm$ 2	4 $\pm$ 0	3 $\pm$ 0
Max depolarization slope				
(mV/ms)	134 $\pm$ 13	177 $\pm$ 46	139 $\pm$ 26	82 $\pm$ 26*
Max repolarization slope				
(mV/ms)	-99 $\pm$ 8	-129 $\pm$ 40	-89 $\pm$ 16	-65 $\pm$ 16*
Half width (ms)	0.6 $\pm$ 0	0.6 $\pm$ 0	0.5 $\pm$ 0.1	0.6 $\pm$ 0.2

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

\*p<0.05, \*\*p<0.01 Treatment *versus* control

# Functional mechanisms of progressive hearing loss

Table S6

The effect of retigabine on action potentials

2 week (0.5 month) old mice				
	Base (n = 4)		Apex (n = 5)	
	Retigabine (10		Retigabine	
	Control	$\mu\text{M}$ )	Control	(10 $\mu\text{M}$ )
Spike number	29 $\pm$ 12	2 $\pm$ 1	1 $\pm$ 0	0**
Rmp (mV)	-58 $\pm$ 2	-64 $\pm$ 1*	-66 $\pm$ 4	-75 $\pm$ 5*
Threshold (mV)	-40 $\pm$ 2	-40 $\pm$ 1	-39 $\pm$ 3	-
AP duration (ms)	7 $\pm$ 1	6 $\pm$ 3	6 $\pm$ 2	-
Latency (ms)	4 $\pm$ 0	-	4 $\pm$ 1	-
Max depolarization slope (mV/ms)	166 $\pm$ 33	-	131 $\pm$ 109	-
Max repolarization slope (mV/ms)	-104 $\pm$ 41	-	-85 $\pm$ 42	-
Half width (ms)	0.7 $\pm$ 0.2	-	0.6 $\pm$ 0.2	-

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

\*p<0.05, \*\*p<0.01 Treatment *versus* control



## Functional mechanisms of progressive hearing loss

Table S7  
3-4 month old mice

	Base (n = 7)		Apex (n = 8)	
	Control	Retigabine (10 $\mu$ M)	Control	Retigabine (10 $\mu$ M)
Spike number	20 $\pm$ 6	0.4 $\pm$ 0.5**	1 $\pm$ 0	0**
Rmp (mV)	-59 $\pm$ 3	-66 $\pm$ 3 *	-62 $\pm$ 2	-66 $\pm$ 3
Threshold (mV)	-37 $\pm$ 3	-	-42 $\pm$ 3	-
AP duration (ms)	8 $\pm$ 2	-	8 $\pm$ 1	-
Latency (ms)	5 $\pm$ 2	-	6 $\pm$ 2	-
Max depolarization.				
Slope (mV/ms)	152 $\pm$ 37	-	125 $\pm$ 31	-
Max repolarization slope				
(mV/ms)	-94 $\pm$ 27	-	-71 $\pm$ 39	-
Half Width (ms)	0.7 $\pm$ 0.2	-	0.8 $\pm$ 0.5	-

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

\*p<0.05, \*\*p<0.01 Treatment *versus* control

Functional mechanisms of progressive hearing loss

Table S8

17 month old mice

	Base (n = 5)		Apex (n = 6)	
	Retigabine (10		Retigabine (10	
	Control	$\mu\text{M}$ )	Control	$\mu\text{M}$ )
Spike number	$22 \pm 6$	$1 \pm 1^{**}$	$1 \pm 0$	$0^{**}$
Rmp (mV)	$-59 \pm 3$	$-69 \pm 2^*$	$-61 \pm 2$	$-67 \pm 2^*$
Threshold (mV)	$-37 \pm 3$	-	$-42 \pm 3$	-
AP duration (ms)	$6 \pm 2$	-	$7 \pm 1$	-
Latency (ms)	$3 \pm 1$	-	$5 \pm 2$	-
Max depolarization.				
Slope (mV/ms)	$89 \pm 37$	-	$125 \pm 31$	-
Max repolarization slope				
(mV/ms)	$-93 \pm 17$	-	$-71 \pm 39$	-
Half Width (ms)	$0.4 \pm 0.2$	-	$0.5 \pm 0.2$	-

Rmp = Resting membrane potential; Max = Maximum, AP = action potential

\* $p < 0.05$ , \*\* $p < 0.01$  Treatment *versus* control