

**Supplemental Table 1 | qPCR primer list.**

Housekeeping gene	Forward primer sequence (5'-3')	Reverse primer sequence (5'-3')
<i>Gapdh</i>	TGGATCTGACGTGCCGC	TGCCTGCTTCACCACCTTC

Negative control gene	Forward primer sequence (5'-3')	Reverse primer sequence (5'-3')
<i>Gfp</i>	GAAGCGGATCACATGGT	CCATGCCGAGAGTGATCC

GPCR-encoding genes	Forward primer sequence (5'-3')	Reverse primer sequence (5'-3')
<i>Adcyap1r1</i>	TATGGACTTCAAGCACCGGC	TCTTGCTCAGGATGGACAGC
<i>Adora2a</i>	GTTAGGTAGGCAGAGGGACAGG	CTGCGATTGCTTCCCTTCTCTG
<i>Adora2b</i>	GGAACCGAGACTTCCGCTAC	GACTGAGAGTAGACTGCGCC
<i>Adrb1</i>	CTACAACGACCCCAAGTGCT	ACGTAGAAGGAGACGACGGA
<i>Adrb2</i>	TACACAGGGGAGCCAAACAC	TCAACGCTAAGGCTAGGCAC
<i>Adrb3</i>	CAGGCTCTGTGTCTCTGGTTA	GAGGAGACAGGGATGAAACCTC
<i>Agtr1a</i>	CTTAGGGTTGGAACCTGCGG	TCATCCAGTCCCTCCCAACT
<i>Bdkrb1</i>	CCGCTACAGGTTGCTGGTAT	TTGACGGAACGCAGAAGGAA

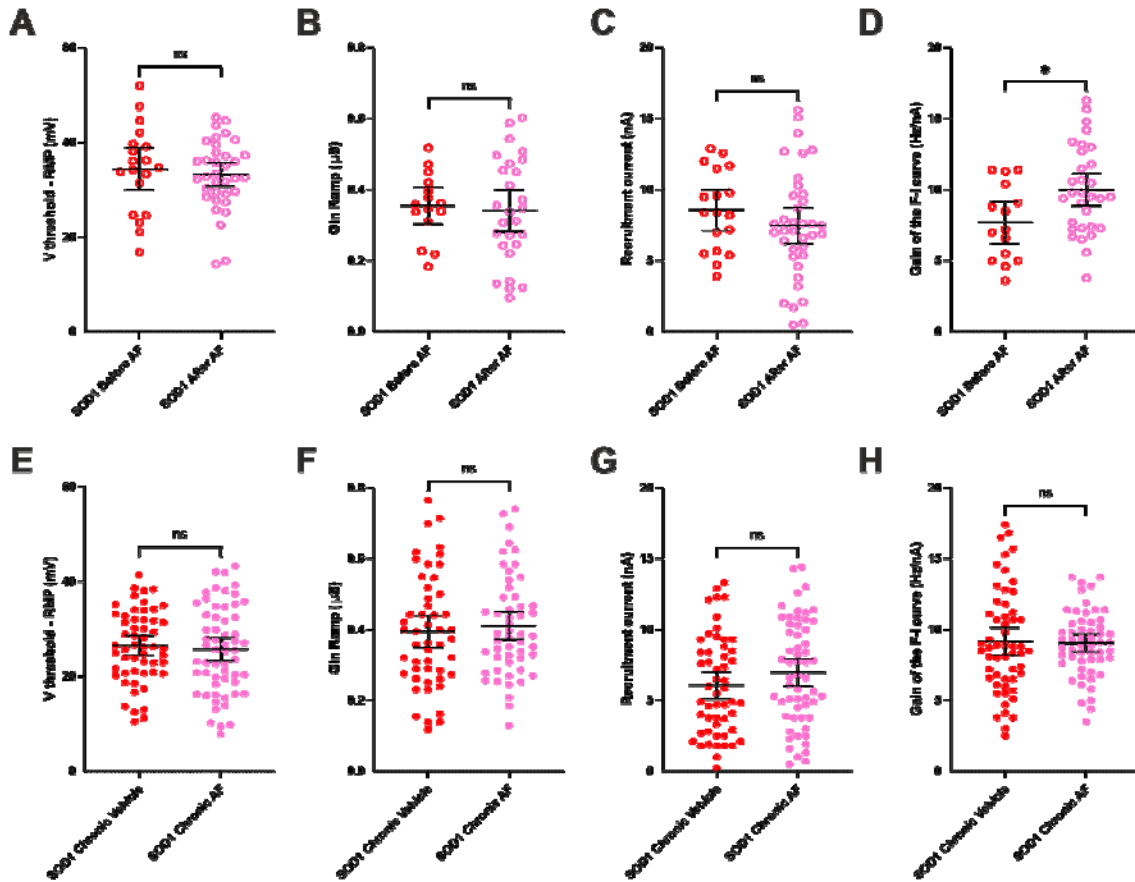
<i>Cckar</i>	ACTGCCAAGTCCACGTTCAA	TCATCTGGGGCGTTCCAAAA
<i>Chrm2</i>	ACTGCCATTGCGGCTTTCTA	TATTCTGCTCTTGCTCGCCC
<i>Chrm4</i>	GCCTCTGGCTAGTTCCGCC	TCGCCATGCTGAACCCAAC
<i>Drd2</i>	GACACCACTCAAGGGCAACT	ATCCATTCTCCGCCTGTTCA
<i>Drd5</i>	CGAACCTACGCCATCTCCTC	GCGCGTGTAGGTCACTATCA
<i>Gabbr2</i>	ACAGGCGATTCCAGTTCACA	CGTAGGCGGTGGTTTTCTGA
<i>Gpr3</i>	ATCTACGCCTTTTCGCAACCA	CGGGACCGGAATGGAATCTT
<i>Gpr65</i>	CATGGGCTACGCAATACCCT	TGTTTTCCGTGGCTTGTTG
<i>Gpr68</i>	ACGATACCAGCCCAAGTGTG	CACCTTAACCAGTCCTCTGGC
<i>Grm4</i>	TACCAGTACCAACGTCGCAA	GCATCCGCTCTATTCTGAGGT
<i>Grm8</i>	TGTGCTCCTAACGGGGATTT	GATGATTGTGTCAGGTGCCG
<i>Hcar1</i>	AGTGTGAAGGAAACCGTGGG	CGCTTTTCTCAGCCATGCAA
<i>Hcar2</i>	GCGGCCATCATTCTTGCTT	GCCTCGCCATTTTTGGTCAT
<i>Hrh3</i>	TTAGAGCATCAACCCGGCAG	CACTCCAGTTCCACCAACGA
<i>Htr7</i>	GTGGTCAAATGGGAAACGGA	CCATTCTGCCTCACGGGGTA
<i>Lpar2</i>	GGCAGATGACTTGACTTCGC	GCCTCCCTGAATGTTTGCTC
<i>Oprd1</i>	TGGATGCTTTTGGGGTTCCT	AAACAAAGGGTCTCGGTGCT
<i>Opr1</i>	TCCTCAGGCACACCAAGATG	GAAGGGCAGTGTGAGCAAGA
<i>P2ry12</i>	AACGCCAGTGCATTTGCTG	TCTCCTTTTATTCTTGCACTGTGAC
<i>Pthr1</i>	AGCGAGTGCCTCAAGTTCAT	TCCCACGGTGTAGATCATGC

<i>S1pr5</i>	AACTCGCTGCTGAATCCCAT	GGAGGAGTCTTGGTTGCAGG
<i>Tacr1</i>	AGGTGTCTGGGGGTTTCTTTA	CCTAGAAGTGACAGGTGACCA

<b>Immediate-early genes</b>	<b>Forward primer sequence (5'-3')</b>	<b>Reverse primer sequence (5'-3')</b>
<i>ΔFosB</i>	AGGCAGAGCTGGAGTCGGAGAT	GCCGAGGACTTGAACCTCACTCG
<i>c-Fos</i>	CCTGCCCTTCTCAACGAC	GCTCCACGTTGCTGATGCT
<i>Egr1</i>	GCCGAGCGAACAACCCTAT	TCCACCATCGCCTTCTCATT
<i>NPas4</i>	GCTATACTCAGAAGGTCCAGAAGG C	TCAGAGAATGAGGGTAGCACAGC

<b>Ion channel-encoding genes</b>	<b>Forward primer sequence (5'-3')</b>	<b>Reverse primer sequence (5'-3')</b>
<i>Cacna1d</i> (isof.1)	GCTCGGTGGCTGTATTTTCAA	CCGTGCTTTCTACCGCACTT
<i>Cacna2d3</i>	GCAGATCGCAGGAAGCTTTG	ACGGGAGATTTCCGCTCATC
<i>Hcn1</i>	CGTGAAGCATGACCGAGAGA	GTAGACTGGCGGAGATTGGG
<i>Hcn2</i>	CATCCACACCAAAGCCATGC	CCCGCCTCCTAAGCTACCTA
<i>Kcna1</i>	TGCTGTGTGTCGCTCAATCT	TCTCCGAAGTGGACACTTGC
<i>Kcna2</i>	TACCCATCTGCAAGGGCAACG	CGACTTGAGGAGGAGAGTGGA
<i>Kcnab1</i>	TCTTGGACTGGTCCCCTACC	AGATTCCCCTACCCAGCAT
<i>Kcnb1</i>	GAGAGGGCGTGGCTAAGAAG	GCCCTCTTGGTCCATTCCA
<i>Kcnj14</i>	GCCGAGGACAGACCTGAACAC	ACTGGGGGTTCTCTGCTCA

<i>Kcnn3</i>	ATCCACCGTCATCCTGCTTG	GTAGGTCATGGCTATCCGCC
<i>Kcnn2</i>	ACAAGGCGTCGCTGTATTCT	CTGTATTTCCCTGGCGTGGT
<i>Kcnq2</i>	GCCATTTTGTACGTGCCCTT	TAGAAGACAGCGTCGTGTGC
<i>Kcnq3</i>	AGTCTTGCTTCCCTGGTGATTC	TCGTCCTGCATTTGGCTGATA
<i>Kcnq5</i>	GCAGCCACCAGACTAAAGGA	CTGCCGCTTCCAATTCCAAA
<i>Kcnt2</i>	CTGTGCACTTAAAAGCAATACAGT	AGCATTTTCCACATCCATGACT
<i>Scn1a</i>	TACAGAAGCAGACCGTAGGC	TGTGATTAGCATCATTTTGGGCT
<i>Scn8a</i>	CCTTCTTACGAGACCCGTGG	ACCCTGAAAGTGCGTAGAGC
<i>Tmem16f</i>	TGGAACCCTGATCTTCGCTG	TTGCTGTAGCTCAACGGTGT
<i>Trpm5</i>	GAATGGGGACTACAGAGGCTG	CGAATGTTTCCTGTGGAGGC



**Supplemental Figure 1 | Replication of electrophysiological findings upon acute and prolonged delivery of adrenergic  $\beta 2/\beta 3$  agonists on a different cohort of presymptomatic SOD1 mice. A-H)** Electrophysiological properties were obtained from slow ramps of current, as in Figure 4 and 7. **A-D)** Effect of the acute treatment on Voltage threshold - resting membrane potential (**A**), ramp input conductance (**B**), recruitment current (**C**), gain of the F-I relationship (**D**), in MNs from SOD1 mice. **E-H)** Effect of the chronic treatment on Voltage threshold - resting membrane potential (**E**), ramp input conductance (**F**), recruitment current (**G**), gain of the F-I relationship (**H**), in MNs from SOD1 mice. In all graphs, each point represents one MN and the mean  $\pm$  95% confidence intervals are shown. N = 7 Acute SOD1 mice and N = 11 Chronic SOD1 mice. \* $p < 0.05$ , ns - non significant.