Supplementary material

Figure S1. Expression levels of β_{2a} or $Ca_V1.2$ Ca^{2+}-channel subunits in hearts of transgenic animals. a, Induction of the β_{2a}-subunit by tebufenozide treatment. mRNA copy number of endogenous murine β_2-subunit and overexpressed rat β_{2a}-subunit. tg_{ind} β_{2a} and double-transgenic mice showed approximately 100-fold overexpression of the β_2-subunit compared to wild-type and tg $Ca_V1.2$ mice upon tebufenozide treatment (n=5-15 per genotype, ***p<0.001). **b,** Overexpression of human $Ca_V1.2$-subunit. No differences were observed in mRNA expression levels between tg $Ca_V1.2$ and tg $Ca_V1.2$ x tg_{ind} β_{2a} mice (n=8-9 per genotype).

Figure S2: Gating of single ventricular L-type Ca^{2+}-channels at +20 mV. At this more depolarized test potential the lower basal activity in myocytes from tg $Ca_v1.2$ is confirmed. In accordance with the leftward shift at the whole-cell level (Figure 1), effects of β_{2a} overexpression on single-channel gating are less pronounced at +20 mV compared to +10 mV (cf. Figure 2) (wild-type: n=8, tg_{ind} β_{2a}: n=7, tg $Ca_V1.2$: n=6, tg $Ca_V1.2$ x tg_{ind} β_{2a}: n=8, * p<0.05; ** p<0.01).

Figure S3: Effects of cAMP-stimulation on Ca^{2+} currents in ventricles overexpressing a β_{2a} subunit. Exemplary traces and time courses of ventricular whole-cell Ca^{2+} currents reveal a clear-cut increase of peak current following application of 8-Br-cAMP (1mM) and okadaic acid (1µM) in wild-type (**a, b**) myocytes. This effect was blunted in cardiomyocytes from mice overexpressing the cardiac β_2-subunit (tg_{ind} $\beta_{2a;}$ **d, e**). Current increase was statistically significant in case of wild-type (n=6) but not tg_{ind} β_{2a} myocytes (n=5) (**c, f**).

Tab. S1: Sequences of primers used for quantitative real-time PCR.

Abbreviations: s - sense primer, as - antisense primer, bp - base pairs.

Gene	Gene symbol	Primer [5' → 3']	Product size (bp)
β-actin	*Actb*	s: TCCATCATGAAGTGTGACGT as: GAGCAATGATCTTGATCTTCAT	154
S29	*Rps29*	s: ATGGGTCACCAGCAGCTCTA as: AGCCTATGTCCTTCGCGTACT	155
atrial natriuretic peptide	*Nppa*	s: GCTTCCAGGCCATATTGGAG as: GGGGGCATGACCTCATCTT	126
Connective tissue growth factor	*Ctgf*	s: TGACCCCTGCGACCCACA as: TACACCGACCCACCGAAGACACAG	117
$\alpha_2\delta_1$-subunit	*Cacna2d1*	s: ATGGTCCAGATCCTTGCGA as: CACCACAGTCAGTATAATCCT	102
$\alpha_2\delta_2$-subunit	*Cacna2d2*	s: CAGCTGCGTCATGAAACAGA as: TTGGTCAGTCTCTGCGCAT	114
β_1-subunit	*Cacnb1*	s: TGGACAGCCTTCGTCTGCT as: TGGAACTGGAGTTGTCACCT	75
β_2-subunit (isoform 1)	*Cacnb2*	s: ATGGAAGCACATCGTCAGACACT as: CCTGCCGCTCAGCTTCTCTA	141
β_2-subunit (isoform 2) + rat β_{2a}	*Cacnb2*	s: TGCCACCTCTTCATGCAGTG as: CCTGCCGCTCAGCTTCTCTA	155
β_2-subunit (isoform 3)	*Cacnb2*	s: GAAGGCTGAAGAGTTCGGACAT as: CCTGCCGCTCAGCTTCTCTA	121
β_3-subunit	*Cacnb3*	s: TGGAGTCAACTTTGAGGCCA as: TCCCGATCCACCAGTCATTG	71
murine $Ca_V1.2$-subunit	*Cacna1c*	s: TCCGAACATTACAACCAGCCT as: GCTGTACATCTTCAGGAGCA	105
human $Ca_V1.2$-subunit	*Cacna1c*	s: CACACCAGAAATGACAGACA as: ATTCATGTTGGCGTGATTAT	95

Tab. S2: mRNA expression of endogenous murine Ca^{2+}-channel β- or $Ca_V1.2$- subunits in the heart of wild-type or transgenic mice.

gene	gene symbol	wild-type	tg_{ind} β_{2a}	p-value	tg $Ca_V1.2$	tg_{ind} β_{2a} x tg $Ca_V1.2$	p-value
β_1-subunit	*Cacnb1*	100 ± 17	82 ± 12	p = 0.56	100 ± 13	95 ± 5	p = 0.71
β_2-subunit (isoform 1)	*Cacnb2*	100 ± 13	116 ± 21	p = 0.51	100 ± 13	109 ± 6	p = 0.52
β_2-subunit (isoform 3)	*Cacnb2*	100 ± 13	112 ± 22	p = 0.85	100 ± 10	106 ± 19	p = 1.00
β_3-subunit	*Cacnb3*	100 ± 19	85 ± 16	p = 0.56	100 ± 23	84 ± 9	p = 0.51
$Ca_V1.2$-subunit	*Cacna1c*	100 ± 14	96 ± 17	p = 0.86	100 ± 12	100 ± 10	p = 1.00

Figure S1

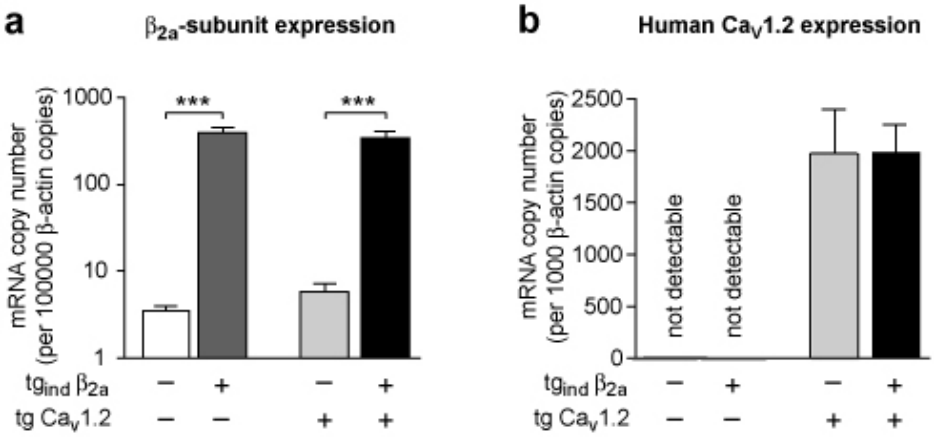

a
β2a-subunit expression
mRNA copy number (per 100000 β-actin copies)
1000
100
10
1
***
***
tgind β2a − + − +
tg Cav1.2 − − + +
b
Human CaV1.2 expression
mRNA copy number (per 1000 β-actin copies)
2500
2000
1500
1000
500
0
not detectable
not detectable
tgind β2a − + − +
tg Cav1.2 − − + +

Figure S2

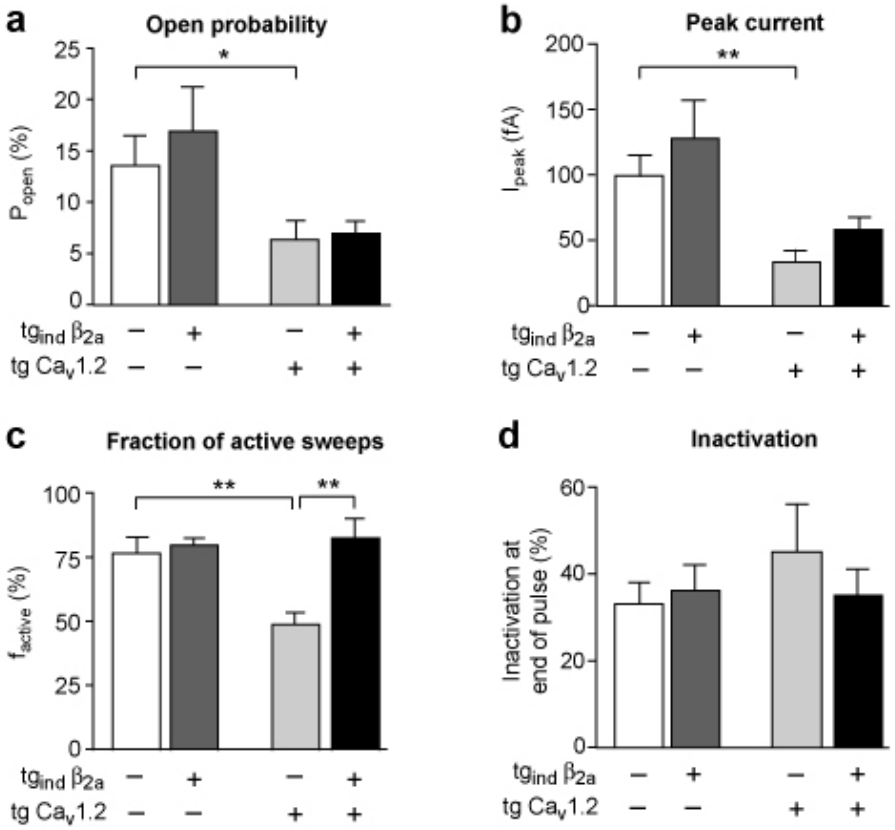
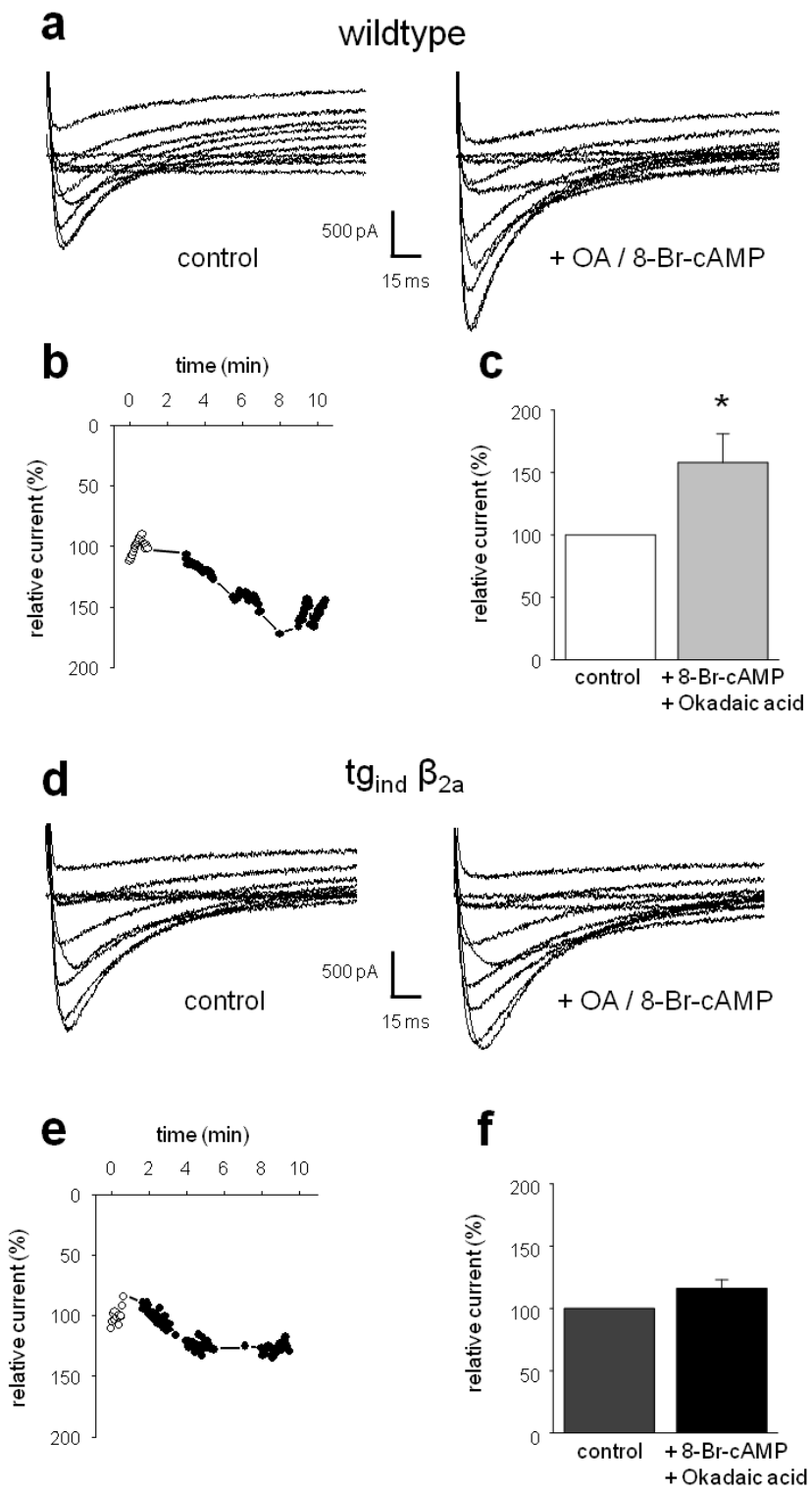

a
Open probability
*
P_{open} (%)
25
20
15
10
5
0
tg_{ind} β_{2a} – + – +
tg $Ca_v1.2$ – – + +
b
Peak current
**
I_{peak} (fA)
200
150
100
50
0
tg_{ind} β_{2a} – + – +
tg $Ca_v1.2$ – – + +
c
Fraction of active sweeps
** **
f_{active} (%)
100
75
50
25
0
tg_{ind} β_{2a} – + – +
tg $Ca_v1.2$ – – + +
d
Inactivation
Inactivation at end of pulse (%)
60
40
20
0
tg_{ind} β_{2a} – + – +
tg $Ca_v1.2$ – – + +

Figure S3


a
wildtype
500 pA
15 ms
control
+ OA / 8-Br-cAMP
b
time (min)
0 2 4 6 8 10
0
50
100
150
200
relative current (%)
c
*
200
150
100
50
0
relative current (%)
control
+ 8-Br-cAMP
+ Okadaic acid
d
tg$_{ind}$ β$_{2a}$
500 pA
15 ms
control
+ OA / 8-Br-cAMP
e
time (min)
0 2 4 6 8 10
0
50
100
150
200
relative current (%)
f
200
150
100
50
0
relative current (%)
control
+ 8-Br-cAMP
+ Okadaic acid