

Supplemental Information

Table S1. Effects of different inhibitors on cell viability of DRGN.

Substance	Nimodipine (L-Type VGCC Inhibitor)					A 967079 (TRPA1-Inhibitor)				
	0.1µM	1µM	10µM	100µM	150µM	1nM	10nM	100nM	1µM	10µM
% of VEH	98,8 ± 1,5	97,8 ± 2,5	96,4 ± 2,1	102,3 ± 3,0	93,3 ± 4,2	112 ± 2,5	100,9 ± 3,1	101,2 ± 2,1	100,6 ± 2,3	95,3 ± 4,2
Substance	Efonidipine (L-Type VGCC Inhibitor)					HC 067047 (TRPV4 Inhibitor)				
	0.1µM	1µM	10µM	50µM		1nM	10nM	100nM	1µM	10µM
% of VEH	93,2 ± 2,0	97,8 ± 1,4	90,1* ± 2,9	75,5* ± 3,0		105,7 ± 2,0	95,4 ± 3,0	89,7* ± 3,1	96,1 ± 2,5	91,2 ± 3,2
Substance	Ruthenium Red (unselective including VGCC and TRP Inhibition)					Pyr 3 (TRPC3 Inhibitor)				
	10nM	100nM	1µM	10µM		1nM	10nM	100nM	1µM	10µM
% of VEH	91,9 ± 4,3	98,9 ± 6,6	96,0 ± 4,0	76,5* ± 3,5		100,0 ± 3,1	106,9 ± 2,2	105,2 ± 4,5	106,0 ± 4,9	97,3 ± 3,8
Substance	SNX 482 (R-Type VGCC Inhibitor)					Ononetin (TRPM3 Inhibitor)				
	2nM	20nM	200nM			3nM	30nM	300nM	3µM	30µM
% of VEH	98,3 ± 3,9	102,1 ± 2,5	98,1 ± 4,4			100,0 ± 2,9	100,4 ± 3,4	98,9 ± 3,1	90,5 ± 4,5	92,4 ± 3,8
Substance	Ω-Conotoxin MVIIC (N-,P-,Q-Type VGCC Inhibitor)									
	1nM	10nM	100nM	1µM						
% of VEH	99,7 ± 3,4	95,1 ± 1,9	96,5 ± 2,5	97,6 ± 2,3						

* statistically significant (p<0.05)

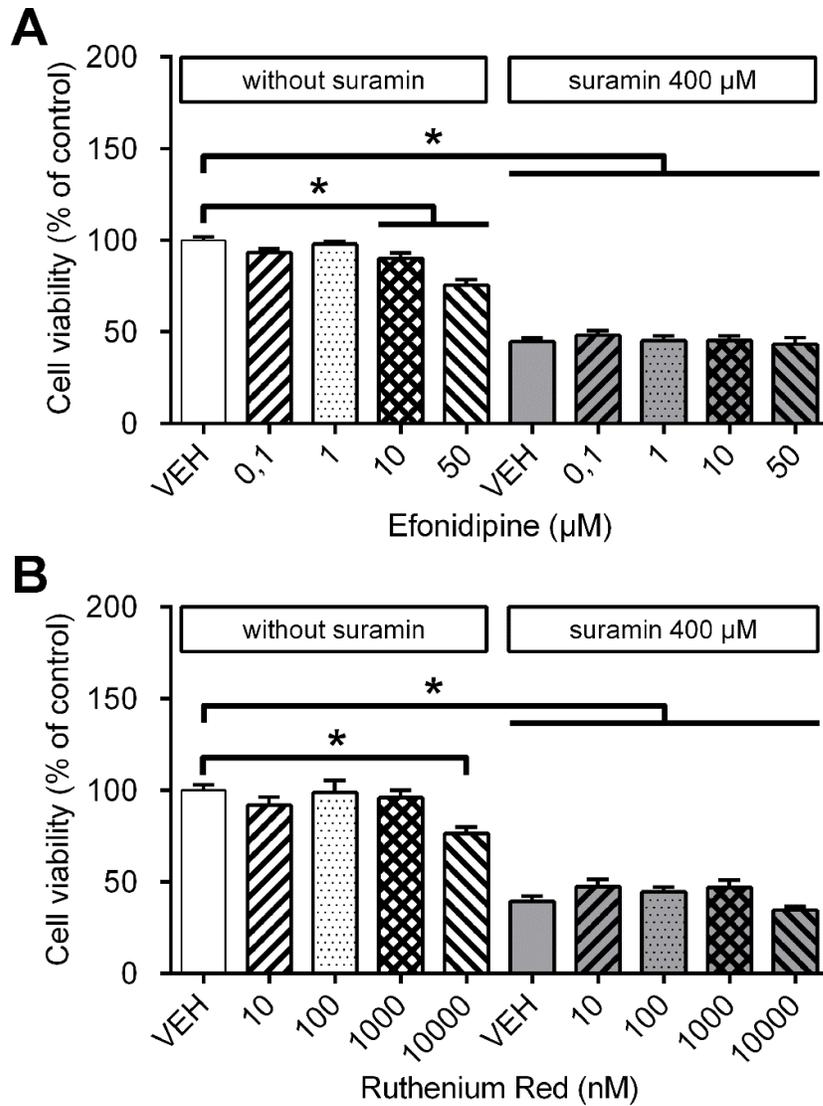


Figure S1. Effects of VGCC inhibitors on cell viability of DRGN.

(a) Cell viability of DRGN was markedly reduced after exposure to suramin and could not be restored by co-incubation with increasing concentrations of the L-type VGCC inhibitor Efonidipine. However, Efonidipine in concentrations ≥ 10 μM itself reduced cell viability. (b) Similar effects were found for the unselective VGCC and TRP inhibitor Ruthenium Red, which was also toxic in higher concentrations and had no influence on cell viability when co-incubated with suramin.

Table S2. Effects of calpain and caspase inhibitors on cell viability of DRGN

Substance	MDL 28170 (Calpain Inhibitor)					Ac DEVD CHO (Caspase-Inhibitor)	
	1nM	10nM	100nM	1µM	10µM	1µM	10µM
VEH (H₂O)+							
% of VEH	99,6 ±5,0	104,3 ±3,2	95,3 ±4,0	93,3 ±4,5	89,7 ±3,1	95,5 ±5,7	91,8 ±5,7
SUR 400 µM+							
Δ% of SUR/VEH	-7,1 ±2,4	+2,0 ±3,6	-2,9 ±3,1	+5,3 ±4,0	+3,8 ±3,3	+6,0 ±3,2	+3,8 ±2,0

* statistically significant (p<0.05)

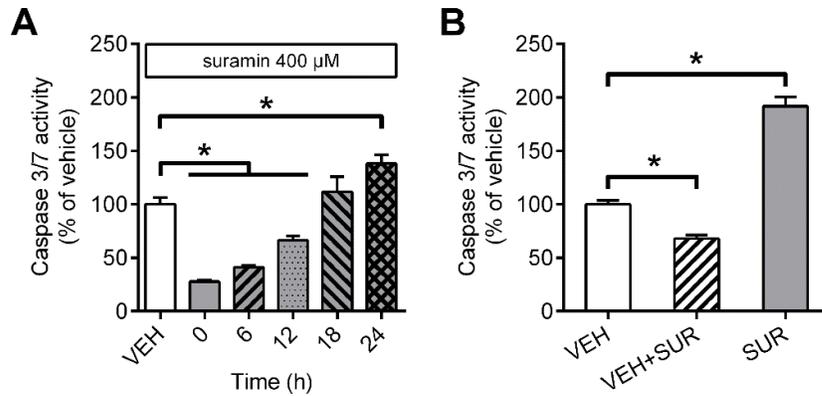


Figure S2: Caspase-3/7 activity of DRGN after suramin treatment.

(a) Caspase 3/7 activity was measured with a luminescent caspase assay. After incubation of DRGN cultures with suramin for 0, 6 and 12 h a significantly reduced luminescent signal was detected. However, the signal was significantly increased after suramin incubation for 24 h. (b) When DRGN were incubated with vehicle for 24 h and suramin was thereafter added to the culture immediately before luminescence signal detection (VEH+SUR), a decrease of caspase activity was observed, suggesting that suramin quenches the luminescence signal. Again, an increase in caspase-3/7 activity was observed when DRGN were treated with suramin for 24 h.