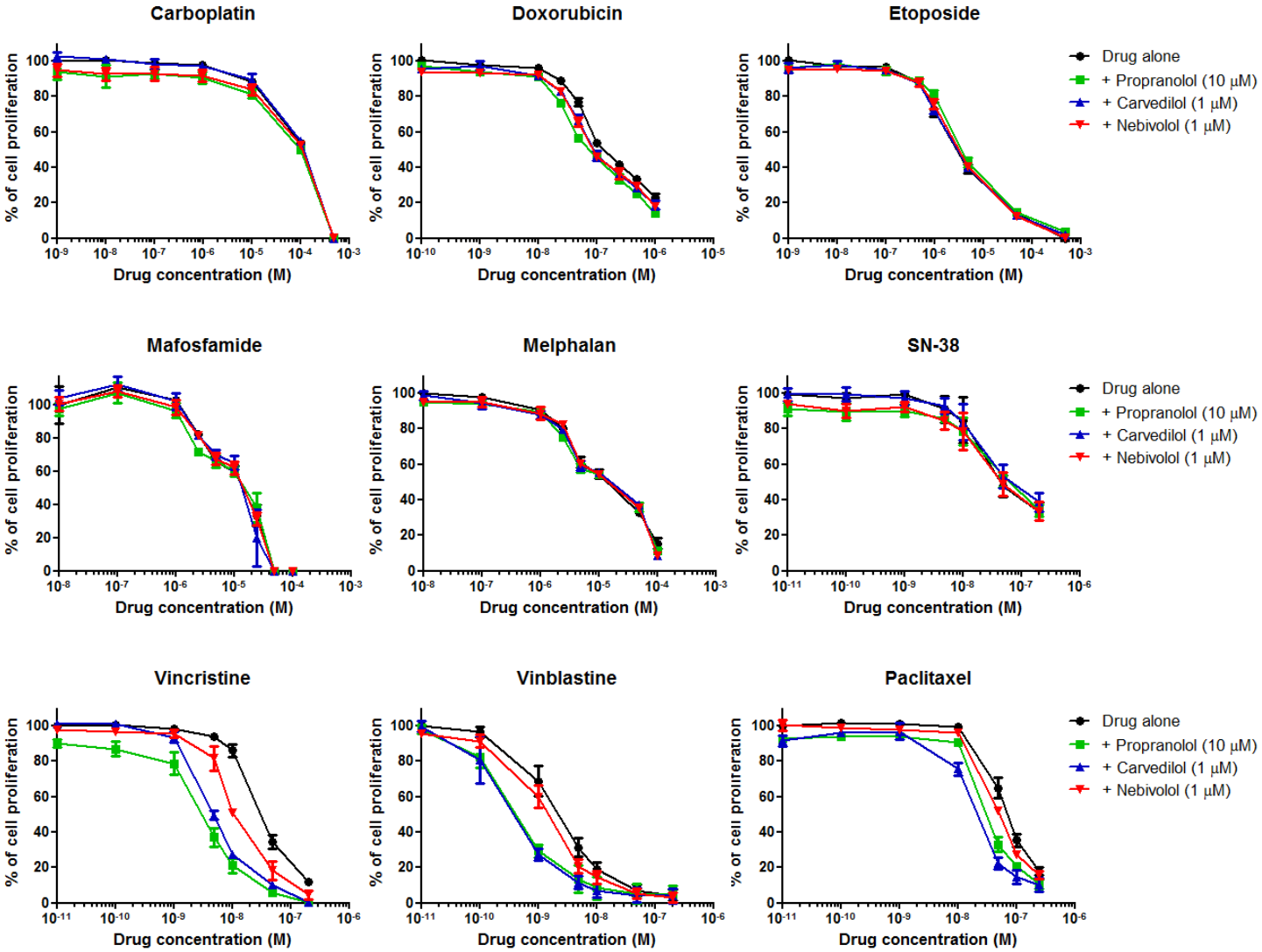

Figure S1. ***In vitro*** **drug combinations**
Growth inhibition assays performed on BE(2)-C neuroblastoma cell line using Alamar Blue after 72 h incubation with a range of concentrations of chemotherapy agents in absence (*black*) or presence of propranolol (*green*), carvedilol (*blue*) and nebivolol (*red*) at non-toxic concentrations. *Points*, % of cell proliferation as compared to untreated control cells, means of at least three individual experiments; *bars*, SEM; log scale for x axis.

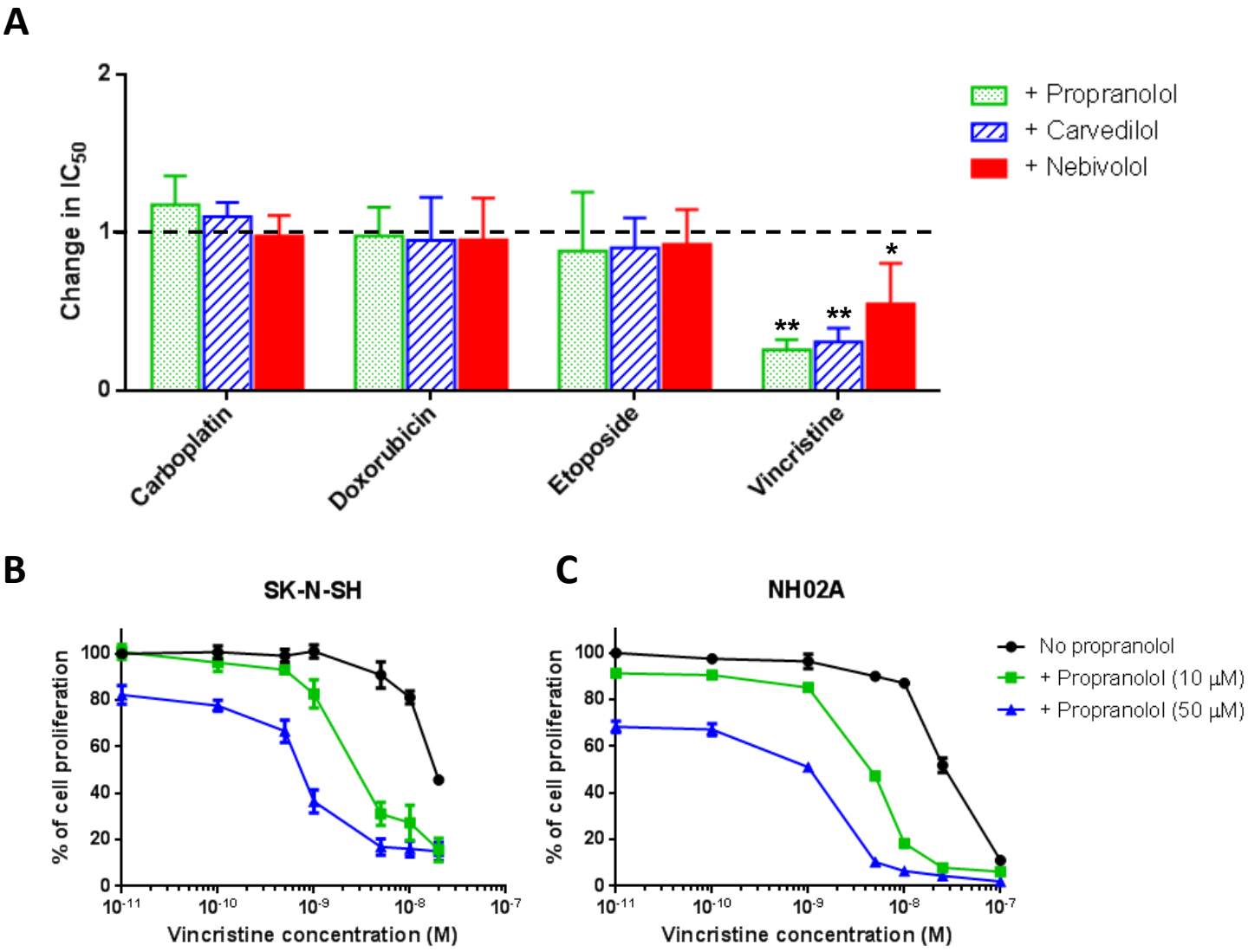

Figure S2. Confirmation of synergy between β-blockers and vincristine in neuroblastoma cells
(**A**) Histogram representation of change in IC_{50} values in SHEP neuroblastoma cells when chemotherapy agents are used in combination with non-toxic concentrations of propranolol (10 µM – green), carvedilol (1 µM – blue) and nebivolol (1 µM – red) as compared to chemotherapy alone. Columns, means of at least four individual experiments; bars, 95% CI. Statistical analysis was performed by comparing the IC_{50} values of chemotherapy alone or in combination with propranolol, carvedilol and nebivolol using Student's t test (*, $p<0.05$; **, $p<0.01$). (**B-C**) Growth inhibition assays performed on SHEP and NH02A cells using Alamar Blue after 72h incubation with vincristine alone (*black*) or in combination with propranolol at 10 µM (*green*) or 50 µM (*blue*). *Points*, % of cell proliferation as compared to untreated control cells, means of at least three individual experiments; *bars*, SEM; log scale for x axis.

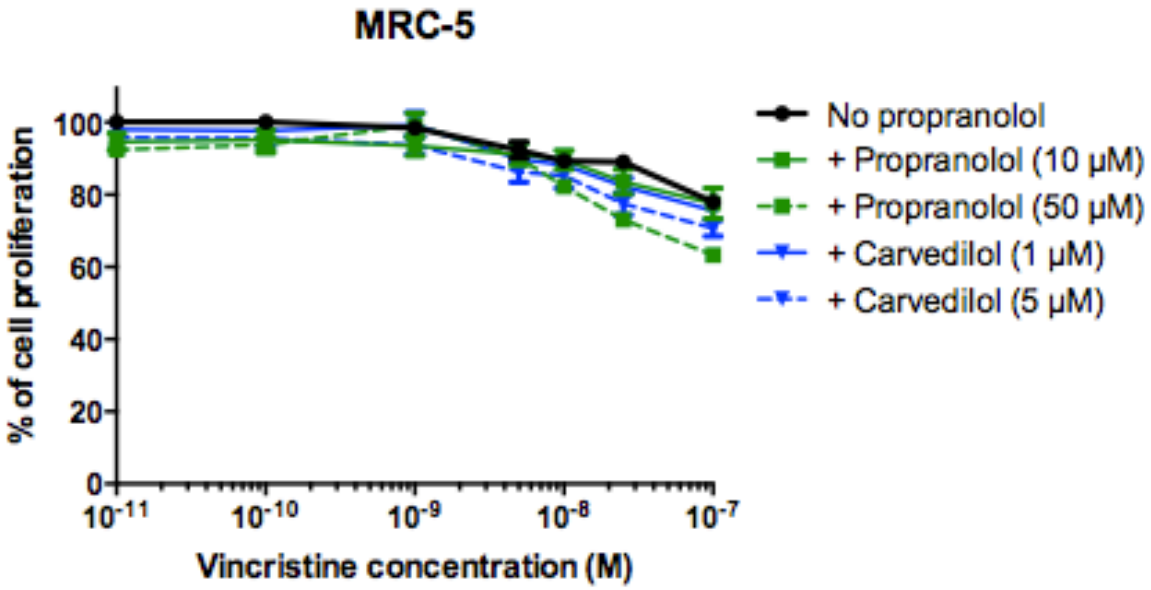

Figure S3. Lack of synergy between β-blockers and vincristine in normal fibroblasts
Growth inhibition assay performed on MRC-5 fibroblasts using Alamar Blue after 72 h incubation with vincristine alone (*black*) or in combination with propranolol (*green*) at 10 µM (*solid line*) or 50 µM (*hashed line*), or with carvedilol (*blue*) at 1 µM (*solid line*) or 5 µM (*hashed line*). *Points*, % of cell proliferation as compared to untreated control cells, means of five individual experiments; *bars*, SEM; log scale for x axis.

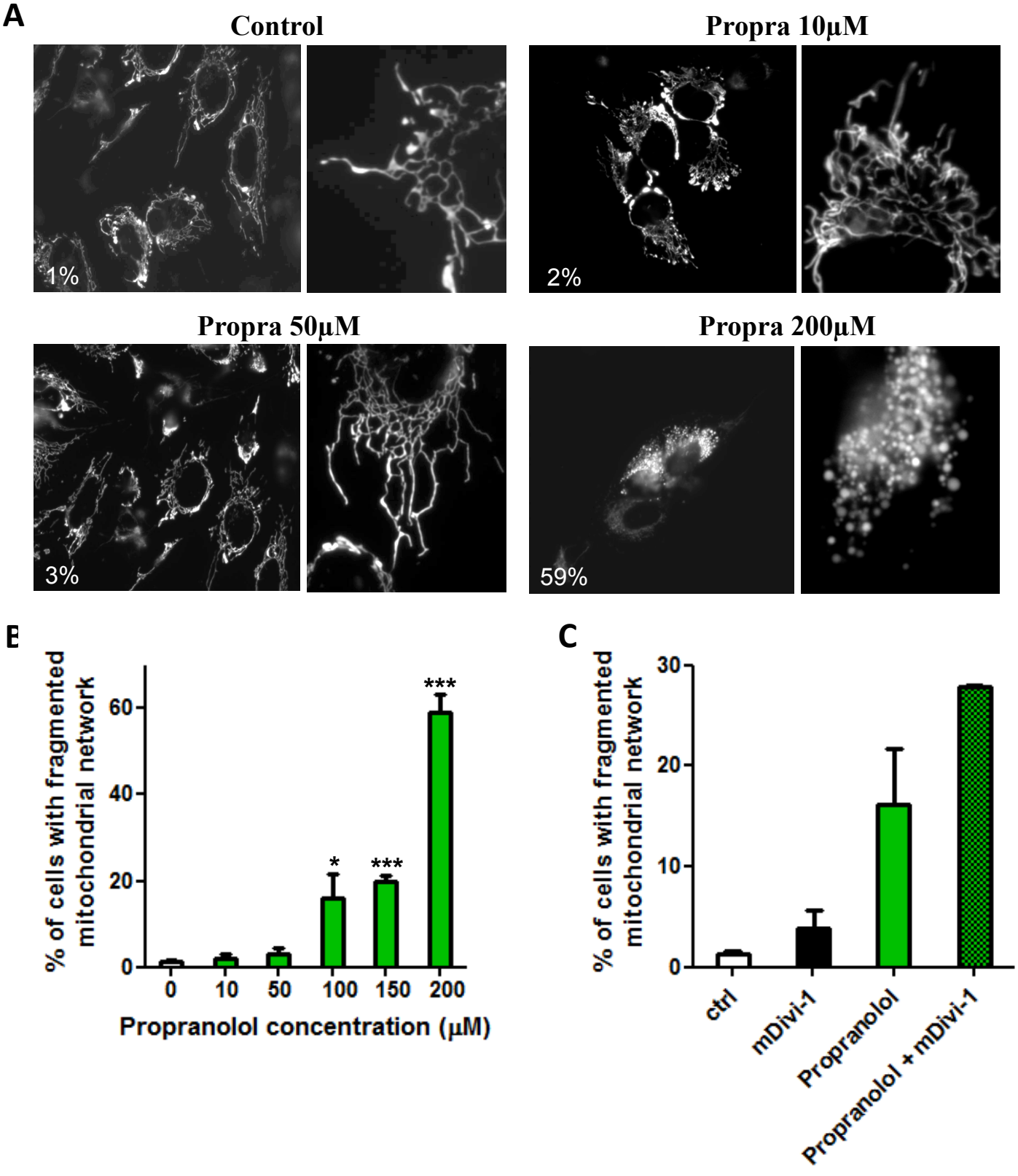

Fig. S4. Anti-mitochondrial effects of propranolol

(**A**) Representative photographs of SK-N-SH cells stably expressing mtDsRed incubated for 6h with propranolol. Photographs were taken with the 40X objective of a Leica DM-IRBE microscope. Amplified views show the mitochondrial network of an individual cell in more details. (**B-C**) Percentage of cells with a fragmented mitochondrial network following 6h incubation with a range of propranolol concentrations (**B**) or with 100 µM propranolol in presence or absence of Drp-1 inhibitor, mDivi-1 (**C**). *Columns*, means of at least three individual experiments; *bars*, SEM. Statistical analysis was performed using Student's t test (*, $p<0.05$; ***, $p<0.001$).

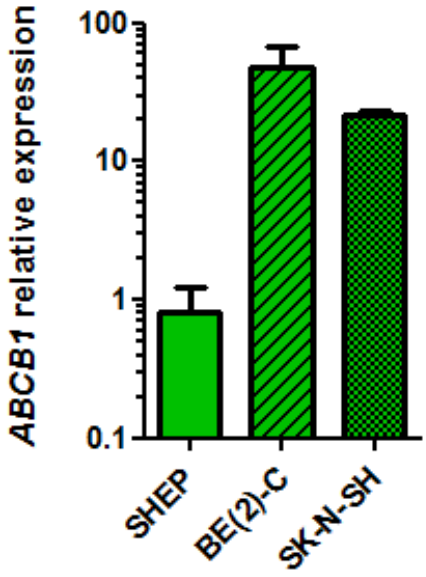

Figure S5. *ABCB1* gene expression in neuroblastoma cell lines
Quantitative real-time PCR data showing the relative gene expression of *ABCB1* in SHEP, BE(2)-C and SK-N-SH neuroblastoma cell lines. *GAPDH* was used as housekeeping gene for data normalization. *Columns*, means of at least three individual experiments; *bars*, 95% CI; log scale for y axis.

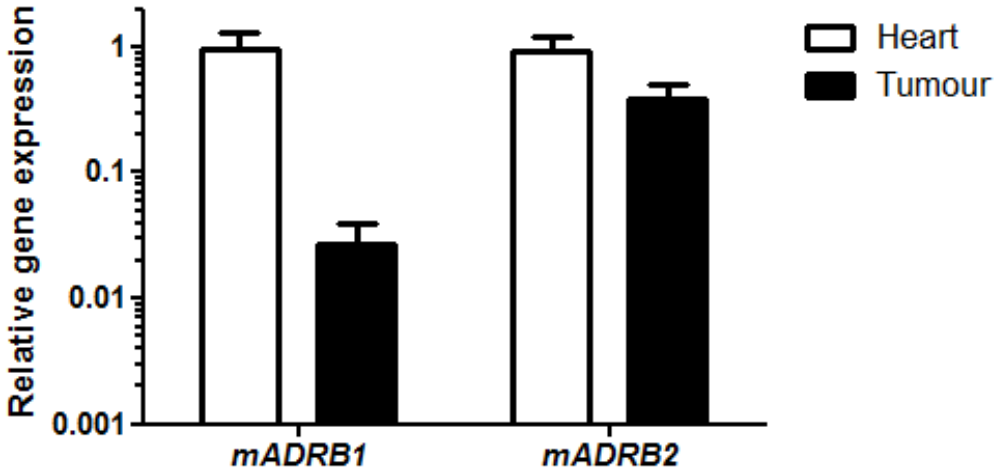

Figure S6. *ADRB1* and *ADRB2* gene expression in mouse tumour tissue
Quantitative real-time PCR data showing the relative gene expression of *mADRB1* and *mADRB2* in tumour tissue at start of treatment as compared to heart tissue. *GAPDH* was used as housekeeping gene for data normalization. *Columns*, means of four individual experiments; *bars*, 95% CI; log scale for y axis.

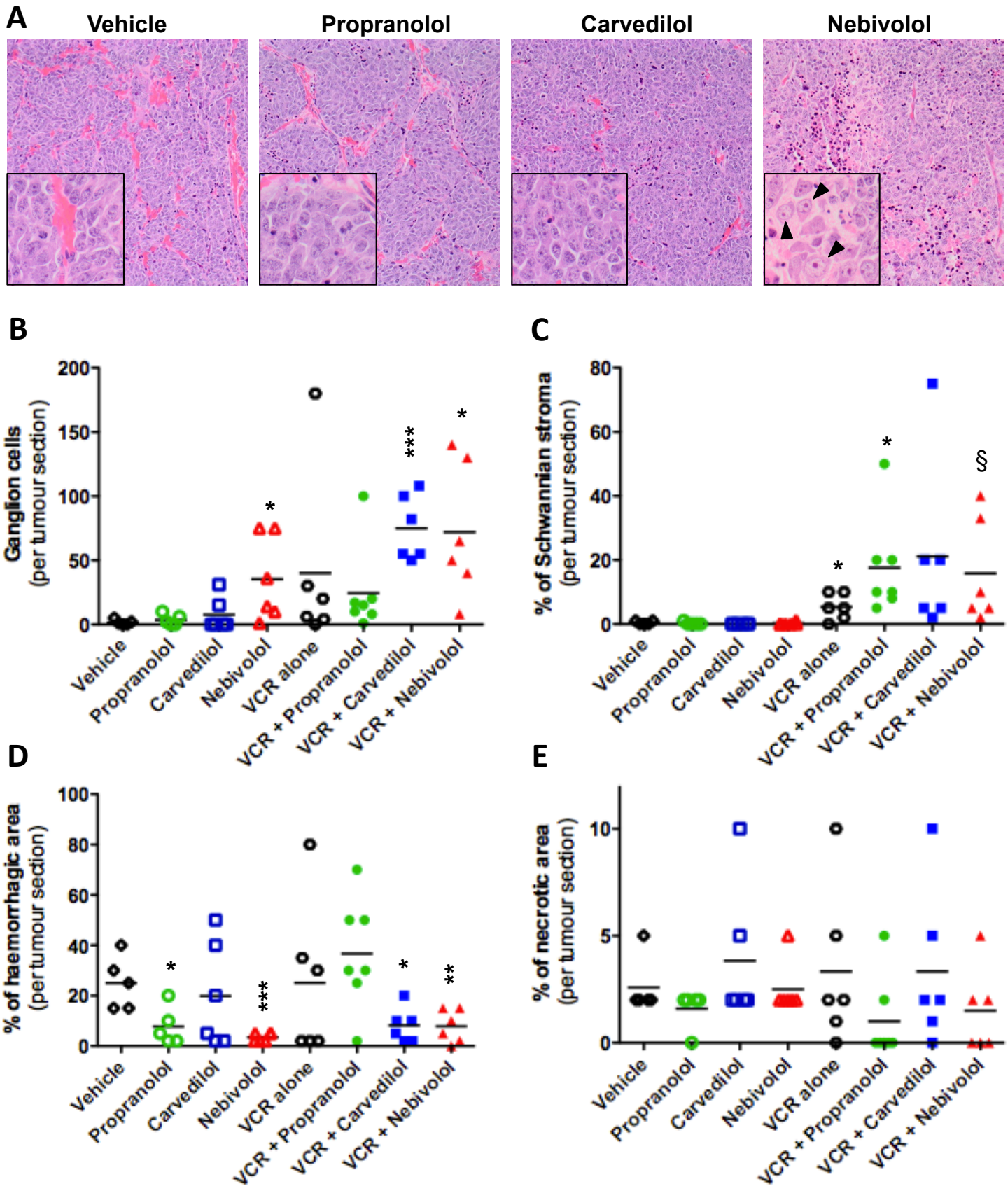

Figure S7. Histological analysis of tumour tissue

(**A**) Representative photographs of H&E tumour sections at day 4 of treatment with vehicle only (*left*) or β-blockers. Arrowheads point to ganglion cells. (**B-E**) Scatter plot representations of the number of ganglion cells per tumour section (**B**), the percentage of area covered by Schwannian stroma (**C**), the percentage of haemorrhagic area (**D**) and the percentage of necrotic area (**E**) at day 4 of treatment. Statistical analysis was performed using Student's t test (§, $p=0.06$; *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$).

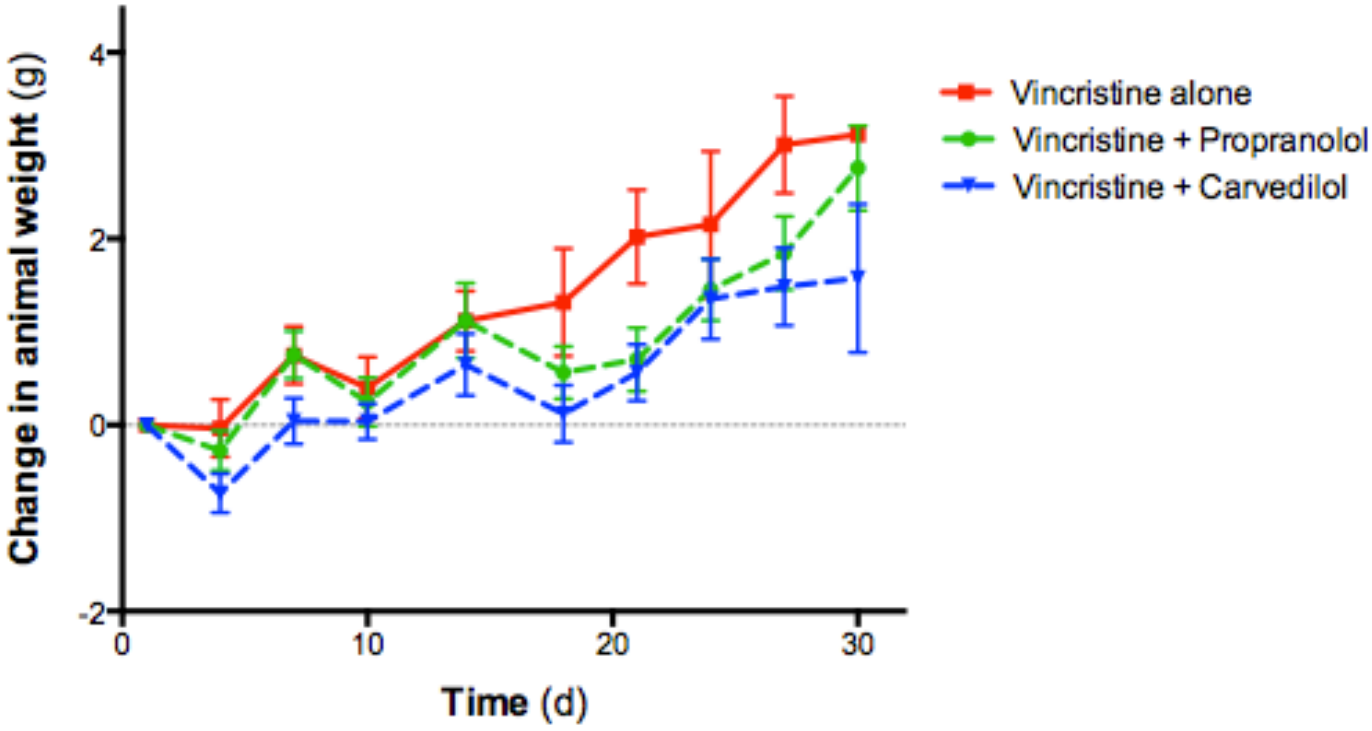

Figure S8. Change in animal weight during treatment

Points represent changes in animal weight over the course of treatment with vincristine alone or in combination with β-blockers, relative to animal weight at start of treatment (Day 1); *bars*, SEM.