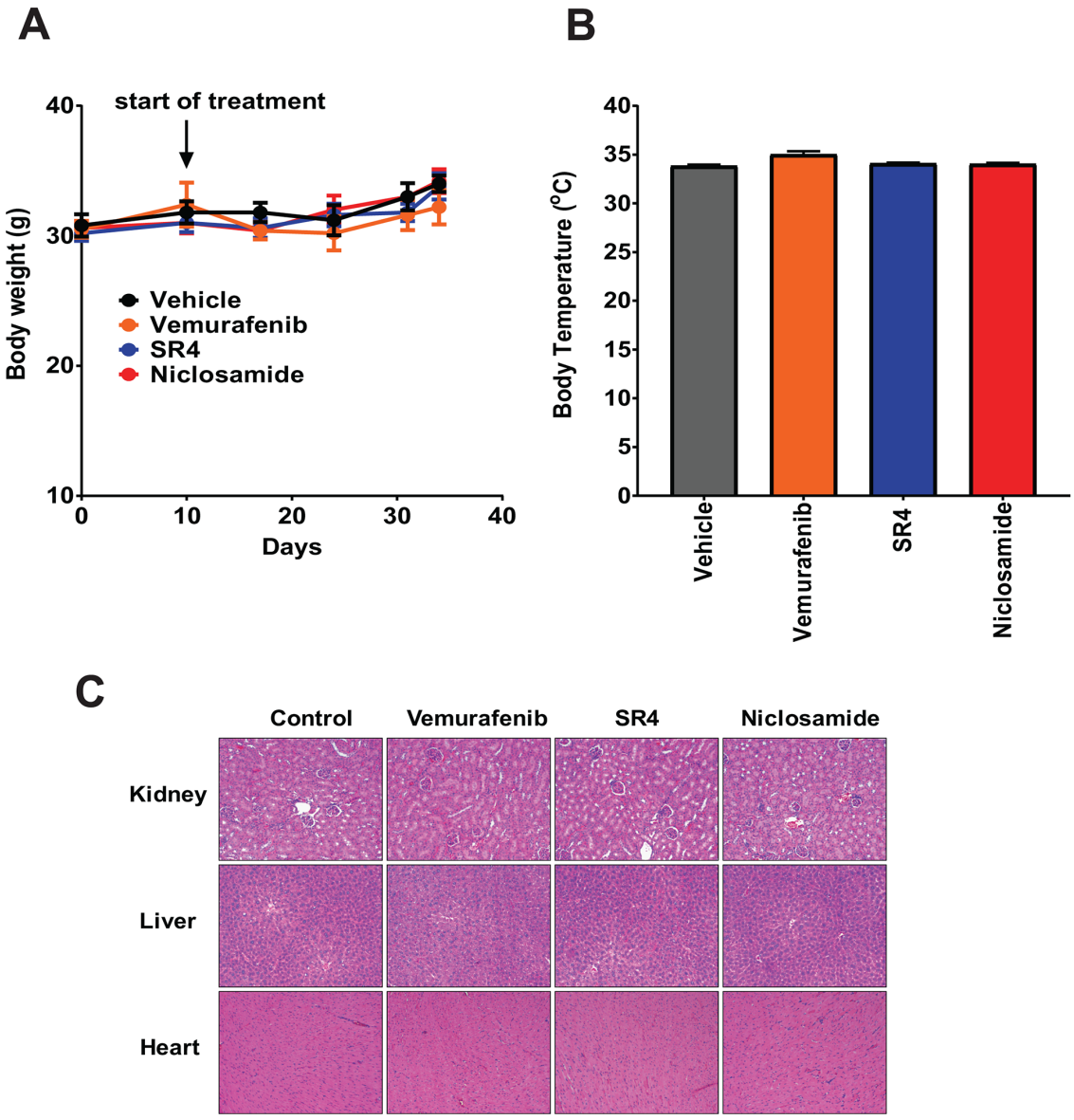
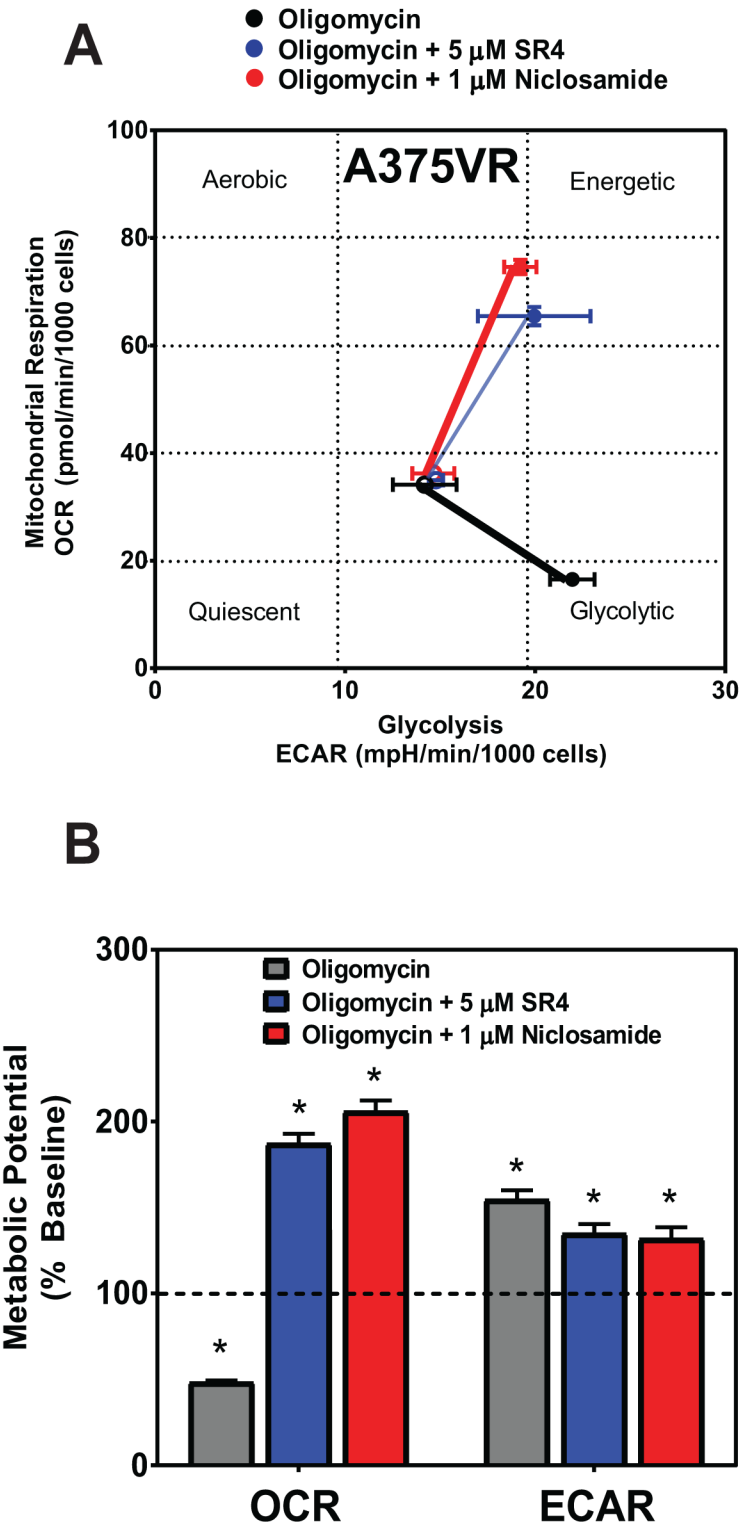
Bioenergetic modulation with the mitochondria uncouplers SR4 and niclosamide prevents proliferation and growth of treatment-naïve and vemurafenib-resistant melanomas

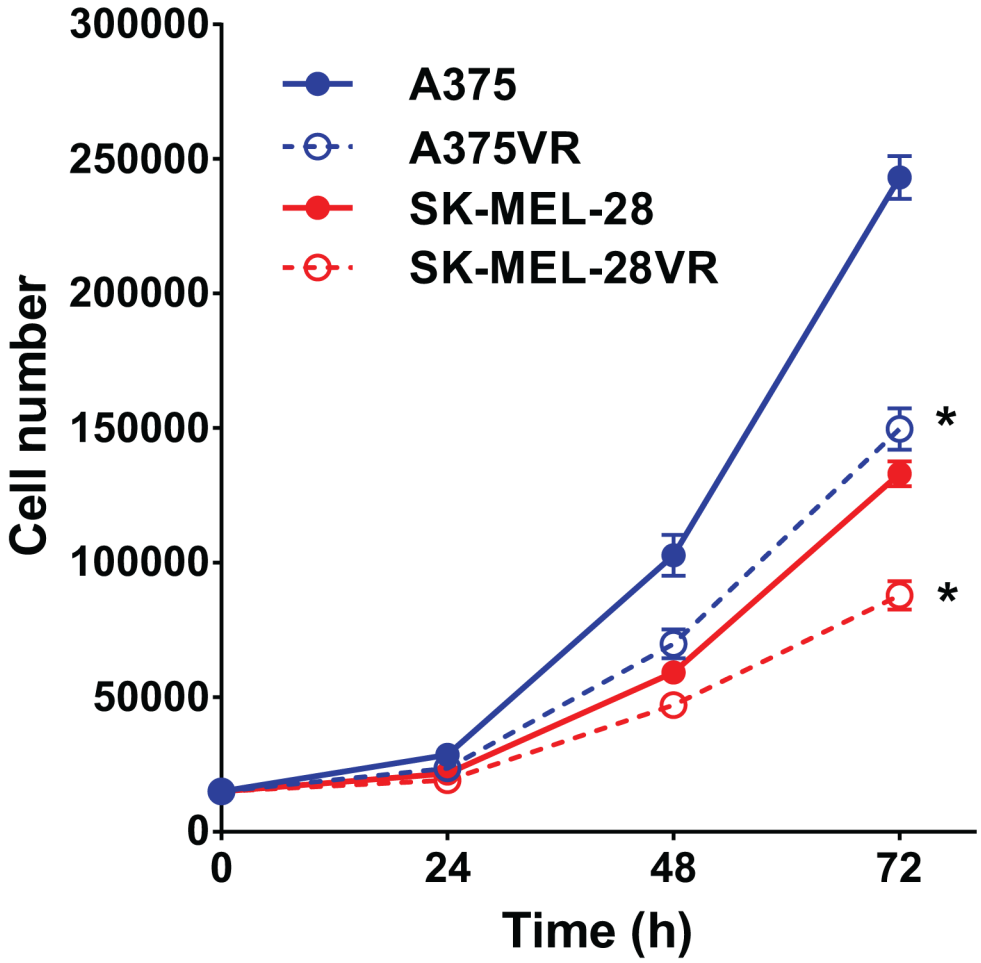
SUPPLEMENTARY MATERIALS



Supplementary Figure 1: Effects of SR4, niclosamide and vemurafenib on body weight, body temperature and key organs of nude mice bearing the A375 xenograft. (A) Body weights of mice during treatment of test compounds each administered orally at 10 mg/kg/day. Data are means ± SEM (n=6). **(B)** Body temperature of mice after 4 hr treatment of test compounds (10 mg/kg/day, p.o). Data are means ± SEM (n=6). **(C)** Representative H&E staining of kidney, heart and liver sections from xenograft mice in each treatment group.



Supplementary Figure 2: SR4 and niclosamide increase metabolic potential in vemurafenib-resistant melanoma. **(A)** Metabolic phenogram analysis of OCR and ECAR by Seahorse Cell Energy Phenotype test. A375VR cells were treated with 1 μM oligomycin with or without SR4 (5 μM) or niclosamide (1 μM) and the change in metabolic phenotype was assessed after 1 h treatment. **(B)** Metabolic OCR and ECAR potential of A375VR cells treated with oligomycin alone or oligomycin + SR4 or niclosamide as determined from the Cell Energy Phenotype test. Data in all three figures are means from 6-8 wells ± SEM, and are representative rates of 2 separate experiments. $^{*}P < 0.05$ vs. baseline levels.



Supplementary Figure 3: Cell growth comparison between parental and vemurafenib-resistant melanoma cell lines. Each cell line was plated at 15,000 cells/well at time=0. After 24, 48, and 72 h of incubation, the cell number in each well was measured using an automated cell counter (Coulter Z1, Beckman Coulter, Brea, CA). Data are means ± SEM from three replicates per time point. $^{*}P < 0.05$ vs. parental cell.

Supplementary Table 1: Comparison of growth inhibition (GI_{50}) data of niclosamide and SR4 from the NCI-DTP60 panel screening. Highlighted in *yellow* are the melanoma cell lines. In all cell panels, niclosamide had lower GI_{50} than SR4, except in the two colon cancer lines highlighted in *green*.

See Supplementary File 1