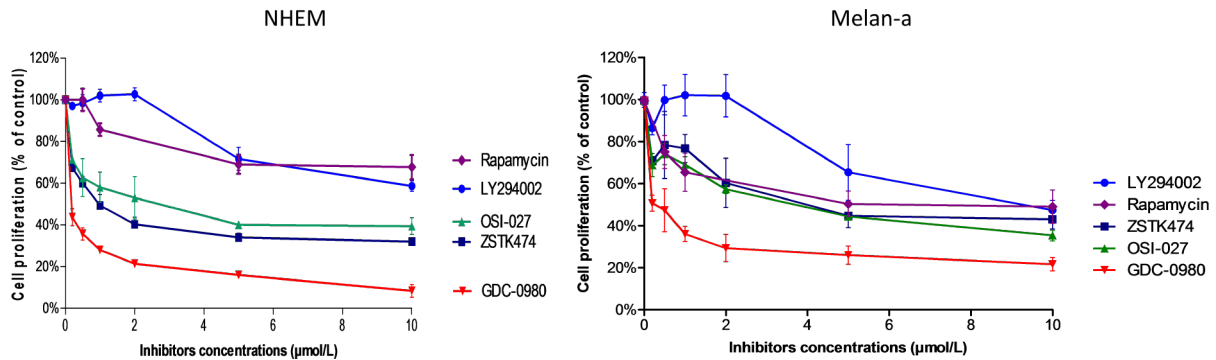
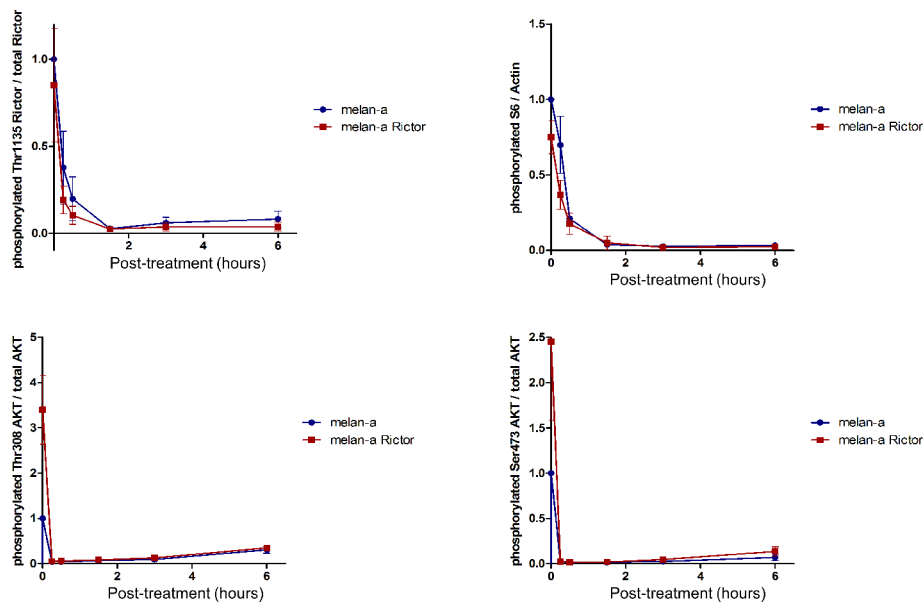


SUPPLEMENTARY FIGURES AND SUPPLEMENTARY DATA

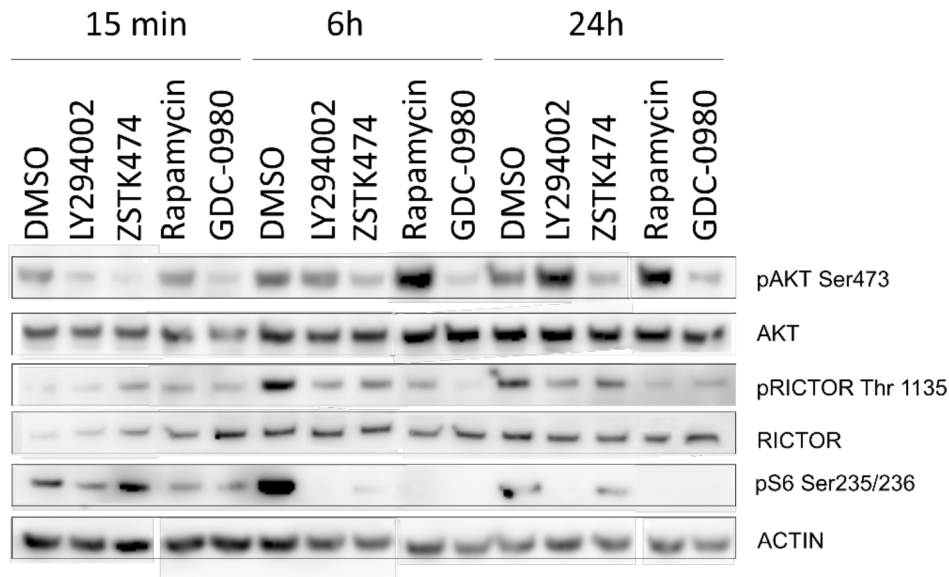


Supplementary Figure S1: Melanocytes are more sensitive to dual PI3K/mTOR inhibition than single PI3K inhibition. NHEM or Melan-a were treated for 3 days with different concentrations of LY294002, ZSTK474, rapamycin, OSI-027 or GDC-0980 in their respective growing medium and proliferation was analyzed with CellTiter.

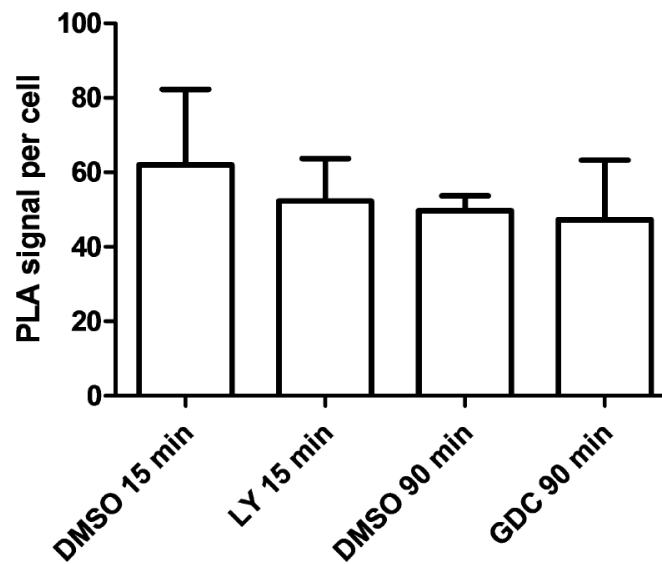
Traitement with GDC-0980 at 0.5 μM



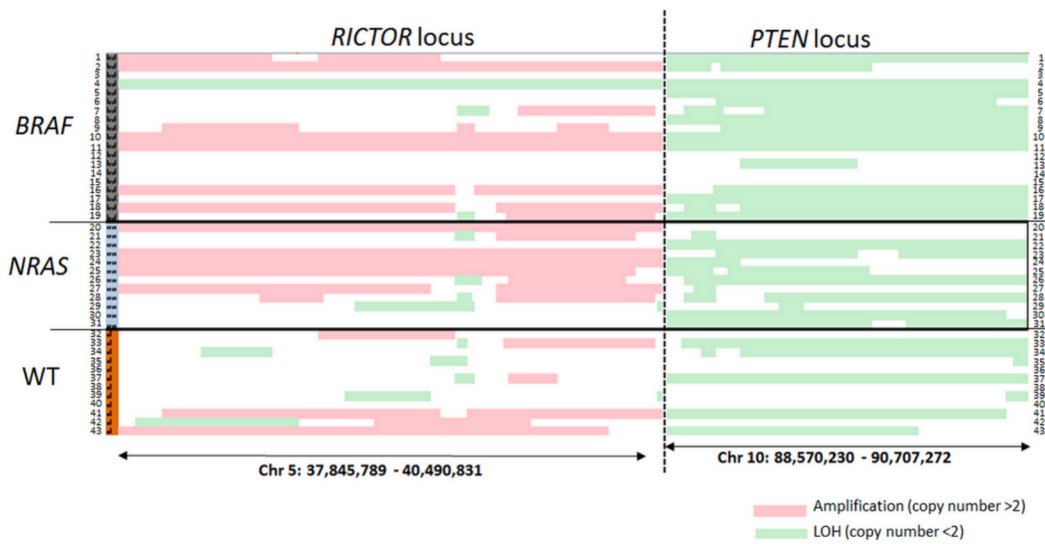
Supplementary Figure S2: Melan-a transfected with RICTOR and controls both have a stable inhibition of AKT Ser473, RICTOR Thr1135, S6 Ser235/236 phosphorylation upon GDC-0980 treatment. Melan-a and Melan-a transfected with RICTOR were treated with DMSO (control 0 min) or GDC-0980 at 5 μM for 15 min, 30 min, 1 h30, 3 h or 6 h. Levels of phosphorylated proteins and total proteins were analyzed by Western Blotting and quantified (data are represented as mean +/- SD).



Supplementary Figure S3: PI3K and mTOR inhibitors inhibits of AKT phosphorylation transiently. NHEMs were treated for 15 min, 6 hours or 24 hours with DMSO (control), LY294002, ZSTK474, rapamycin or GDC-0980 at respectively 5 μ M, 0.2 μ M, 5 μ M and 0.5 μ M in growing medium. Level of phosphorylated protein or total protein were analyzed by Western Blotting.



Supplementary Figure S4: Interaction of AKT with RICTOR is independent of their phosphorylation status. Melan-a were treated for 15 min or 1 h30 with LY294002 or GDC-0980. Interaction between RICTOR and AKT was determined by PLA and red dots per cell were quantified (data are represented as mean \pm SD).



MUTATION	AMPLIFICATION AT RICTOR LOCUS	LOH AT PTEN LOCUS
BRAF	9 / 19 (47%)	15 / 19 (79%)
NRAS	8 / 12 (67%)	7 / 12 (58%)
WT	5 / 12 (42%)	5 / 12 (42%)
TOTAL	19 / 43 (44%)	27 / 43 (63%)

Supplementary Figure S5: In BRAF mutated melanoma cell lines, amplification at *RICTOR* locus is associated with LOH at *PTEN* locus. Short term melanoma cell lines were analysed for amplification or deletion at *RICTOR* and *PTEN* loci. Numbers 1 to 43 indicate cell line number. Red lines correspond to amplification (copy number > 2) and green lines to loss of heterozygosity (copy number < 2).

Supplementary Table S1: copy number (CN) details on *RICTOR* and *PTEN* loci