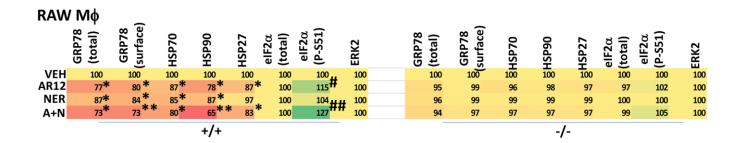
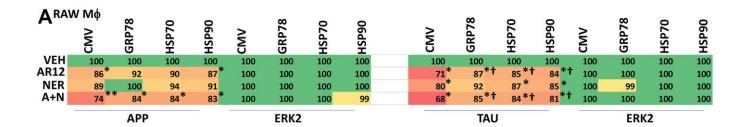
SUPPLEMENTARY FIGURES



Supplementary Figure 1. Deletion of Rubicon prevents the degradation of chaperones, Tau and APP in macrophages. RAW macrophages (+/+ and -/- for Rubicon) were treated with vehicle control, AR12 (2 μ M), neratinib (50 nM) or the drugs in combination for 6h. Cells were fixed in place and immunostaining performed to determine the expression of GRP78 (cell surface and total), HSP70, HSP90, HSP27, eIF2 α and ERK2, and the phosphorylation of eIF2 α S51. (n = 3 +/-SD) * p < 0.05 less than vehicle control; ** p < 0.05 less than corresponding neratinib value; # p < 0.05 greater than vehicle control; ## p < 0.05 greater than corresponding AR12 value.



B RAN	siscr M	siGRP78	siHSP70	siHSP90	siSCR	siGRP78	siHSP70	siHSP90	siSCR	siGRP78	siHSP70	siHSP90	siSCR	siGRP78	siHSP70	siHSP90
VEH	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
AR12	88	76	78*	81*	100	100	100	100	81*	67	76 *	73 *	100	100	100	100
NER	98	89	92	88	100	100	100	100	87*	72 †	76 +	74 🕇	100	100	99	99
A+N	77*	67	73*	75 *	100	100	100	100	71*	61	70*	71*	100	100	99	99
	APP				ERK2				TAU				ERK2			

Supplementary Figure 2. GRP78 plays a key role in regulating Tau and APP expression after drug exposure in macrophages. (A) RAW macrophages were transfected with an empty vector plasmid or with plasmids to express GRP78, HSP70 or HSP90, and in parallel co-transfected to express Tau or APP. After 24h, cells were treated with vehicle control, AR12 (2 μ M), neratinib (50 nM) or the drugs in combination for 6h. Cells were fixed in place and immunostaining performed to determine the expression of Tau, APP and ERK2. (n = 3 +/-SD) * p < 0.05 less than vehicle control; ** p < 0.05 less than corresponding AR12 value; ¶ p < 0.05 greater than corresponding value in CMV transfected cells. (B) RAW macrophages were transfected to express APP or Tau and co-transfected with a scrambled siRNA or with an siRNA molecules to knock down the expression of GRP78, HSP70 or HSP90. After 24h, cells were treated with vehicle control, AR12 (2 μ M), neratinib (50 nM) or the drugs in combination for 6h. Cells were fixed in place and immunostaining performed to determine the expression of Tau, APP and ERK2. (n = 3 +/-SD) * p < 0.05 less than vehicle control; † p < 0.05 less than corresponding value in siSCR cells.