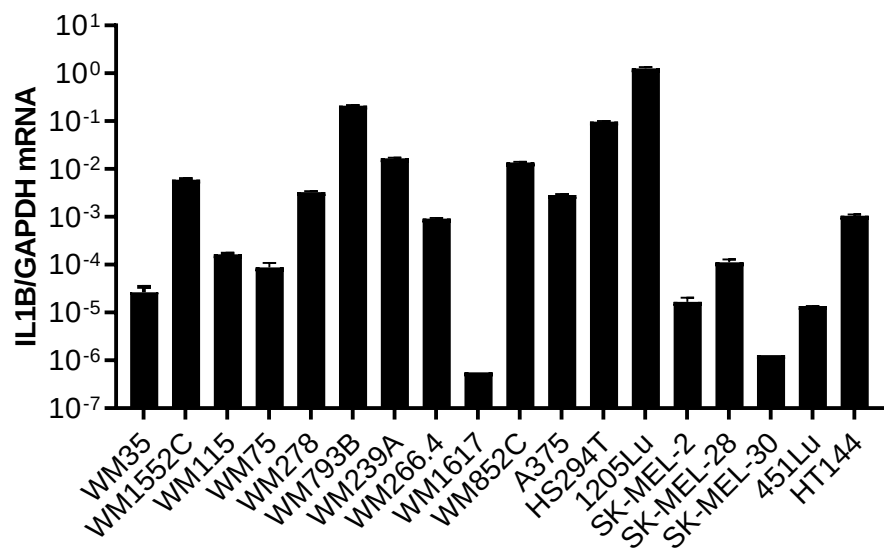
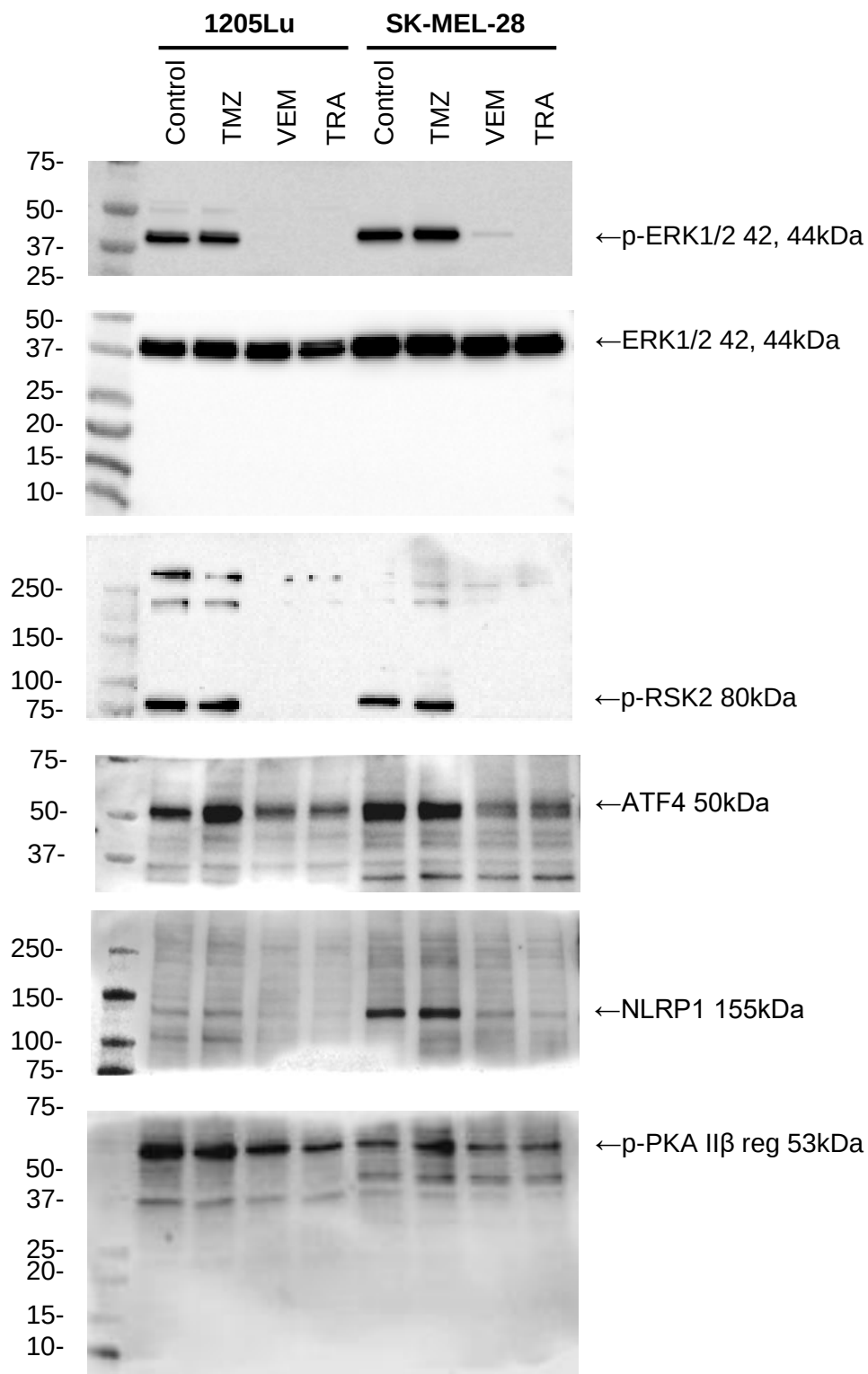


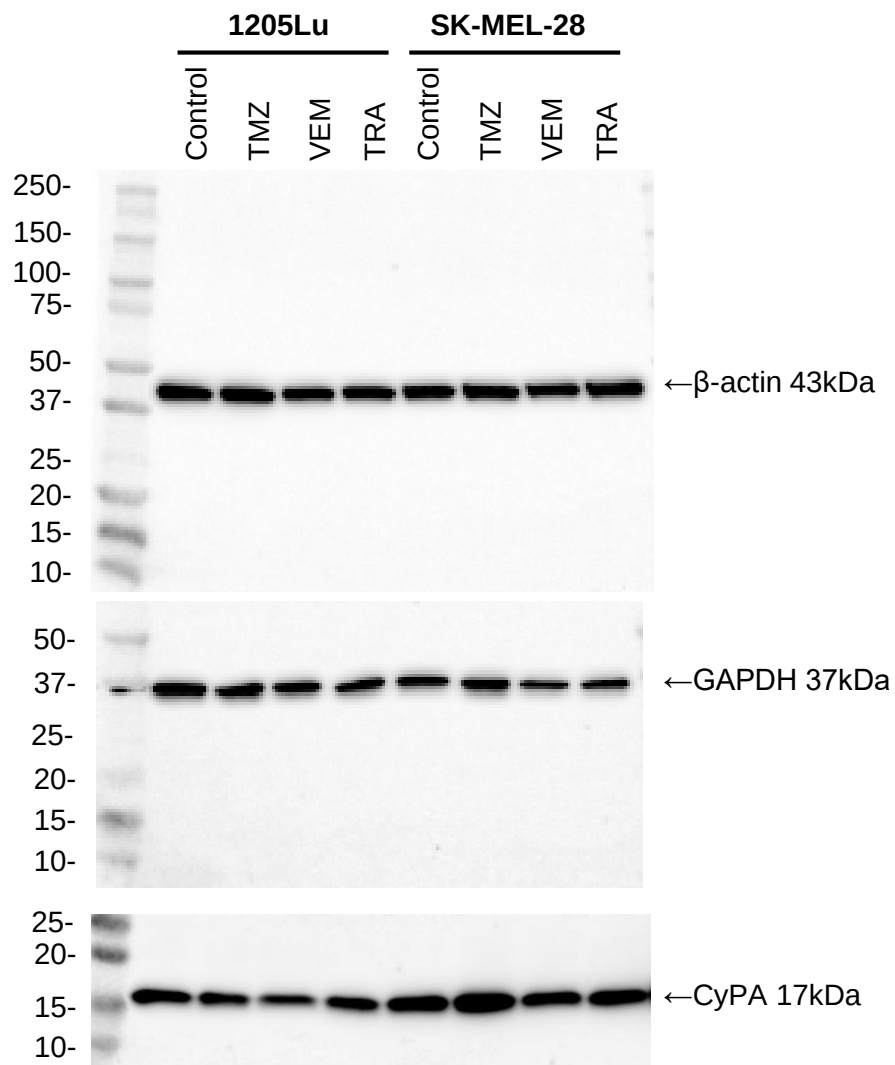
Supplemental data



**Figure S1.** The mRNA expression levels of *IL1B* in human melanoma cell lines.



**Figure S2.** Original blots of Figure 1c, 2b, and 4e.



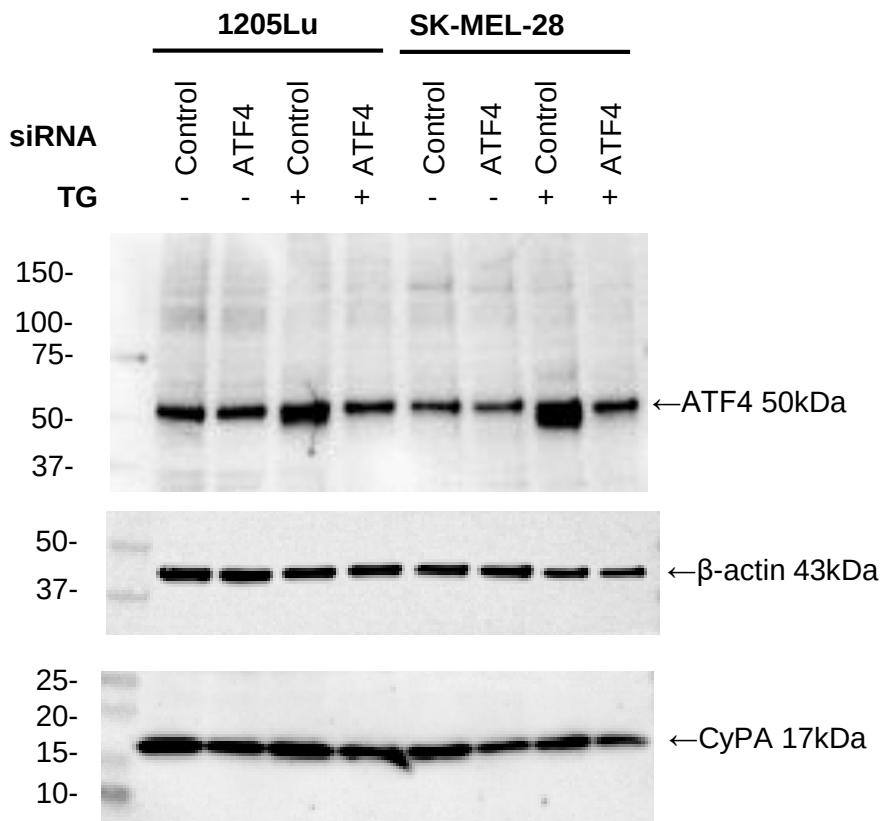
β-actin, GAPDH and CyPA were used as loading control.

**Figure S2.** Original blots of Figure 1c, 2b, and 4e (cont'd).

**Putative ATF4 binding site  
within the NLRP1 promoter**

5'-G **T T A C A T C A** G-3'  
3'-C A A T G T A G T C-5'

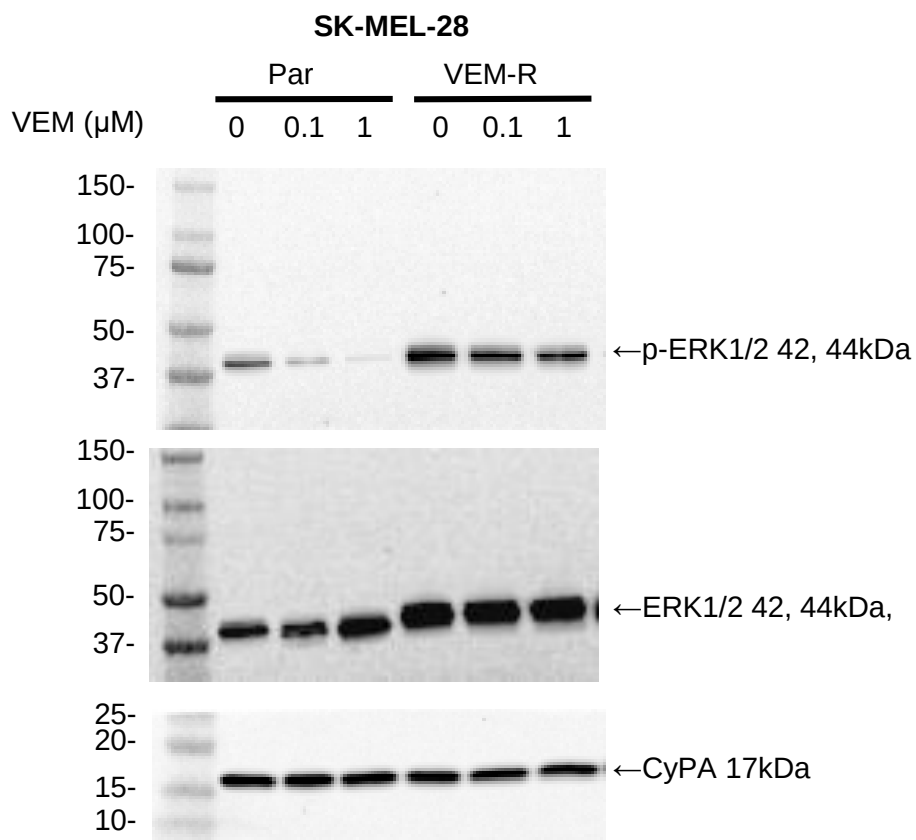
**Figure S3.** Putative ATF4 binding site within the *NLRP1* promoter.



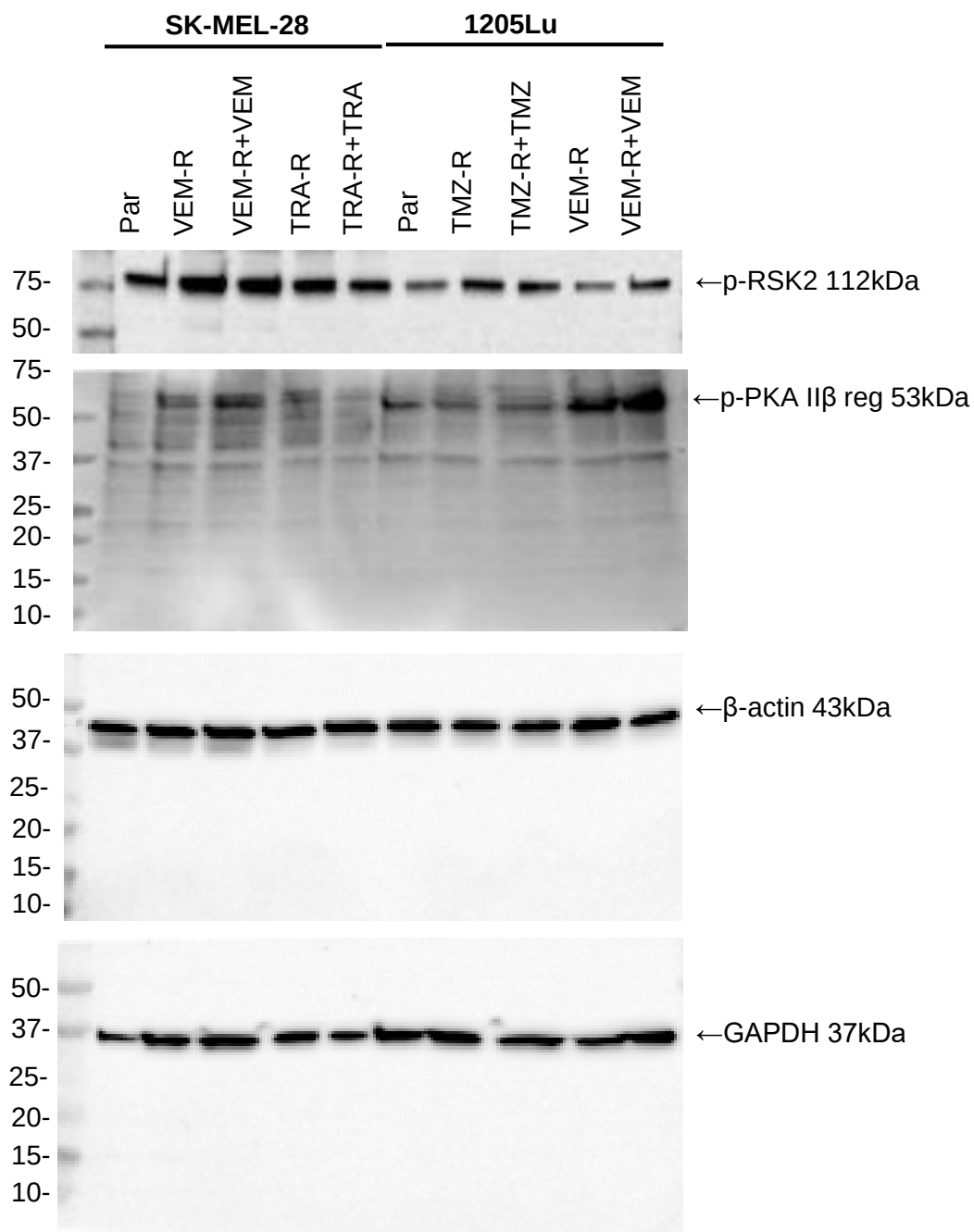
Both β-actin and CyPA were used as loading control.

**Figure S4.** Original blots of Figure 1d.

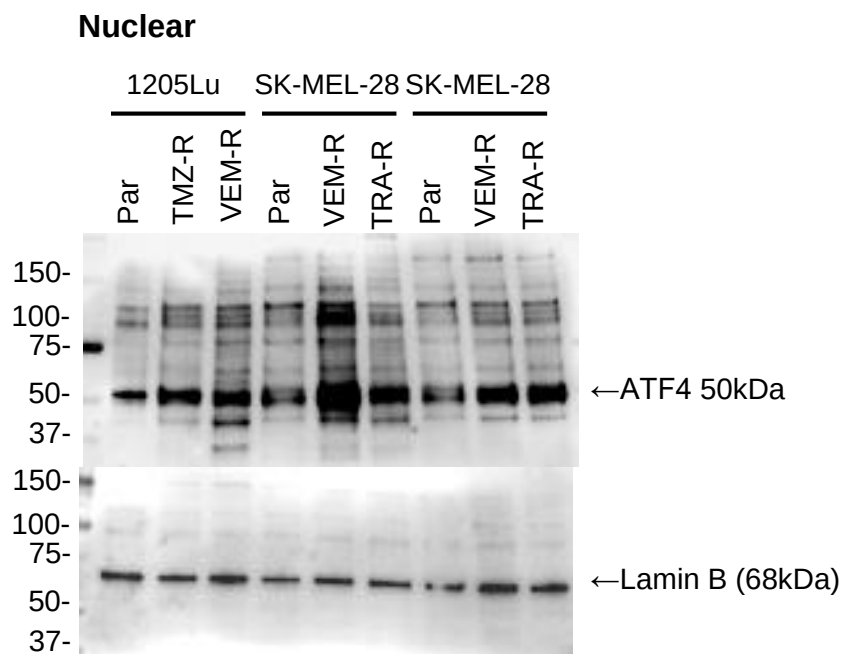
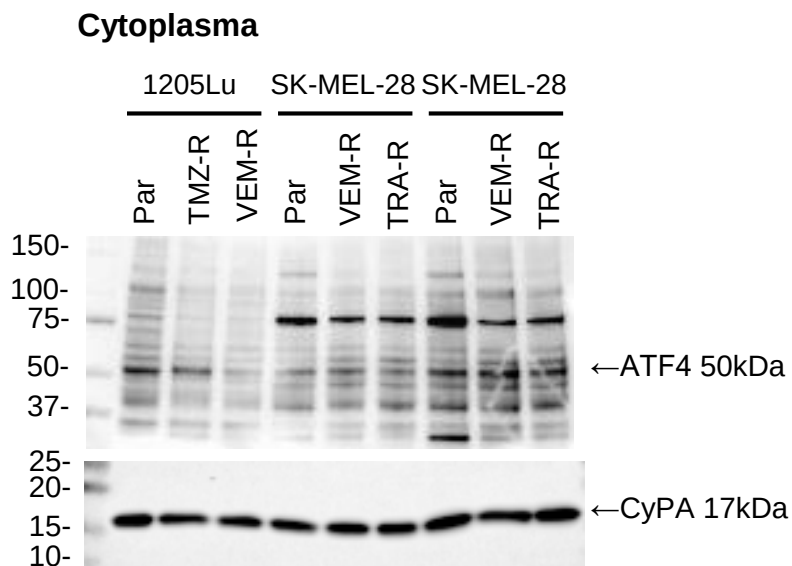




**Figure S7.** Original blots of Figure 3b.



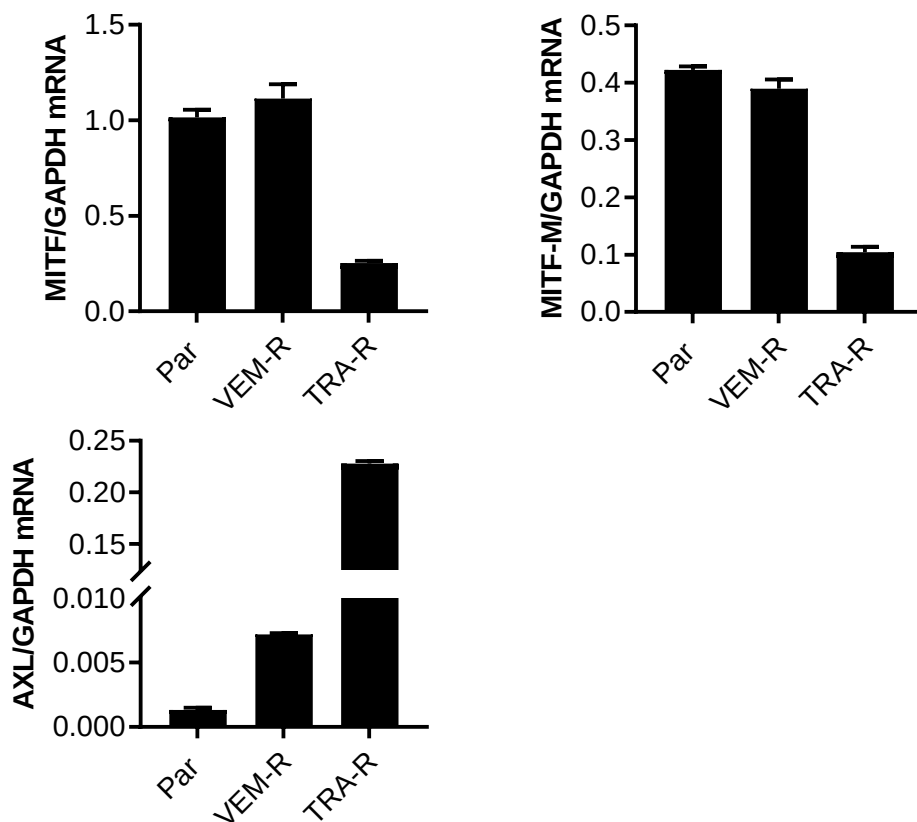
**Figure S8.** Original blots of Figure 3c, 4c and 4f.



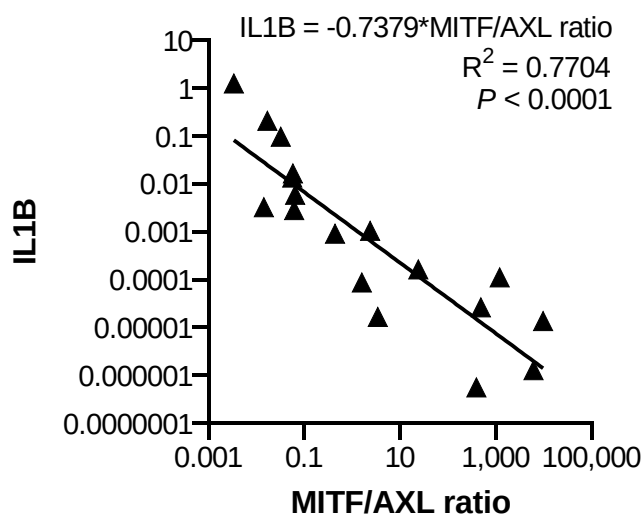
Note: Different passages of VEM-R and TRA-R SK-MEL-28 cells were tested. Left data of SK-MEL-28 cells were shown in the main text. 1205Lu data were not shown in the text.

**Figure S9.** Original blots of Figure 3e.

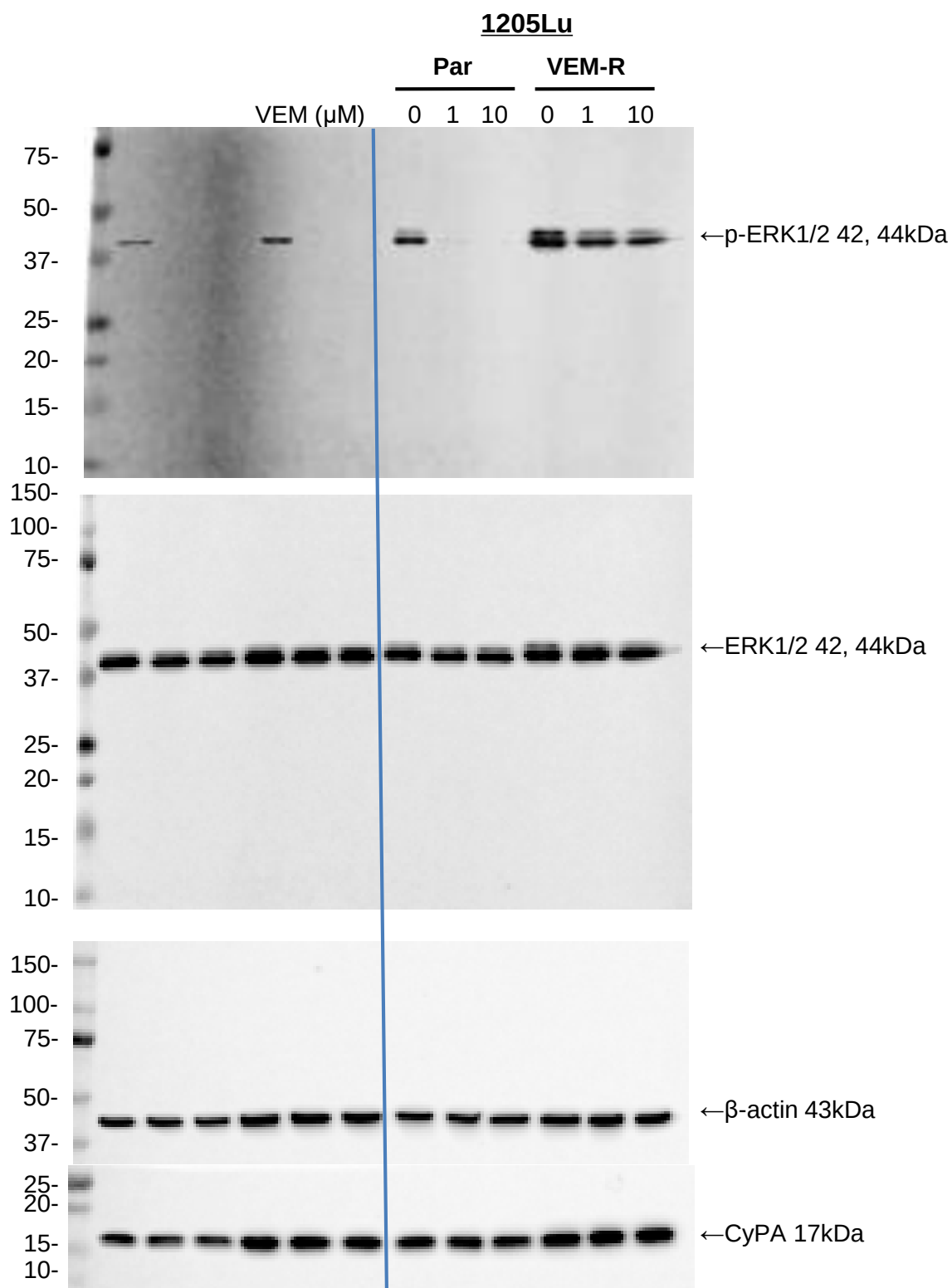




**Figure S10.** *MITF* and *AXL* gene expression in MAPK inhibitor-resistant SK-MEL-28 cells. *MITF-M* (*MITF* type M, exclusively expressed in melanocytes and melanoma cells) was also determined.

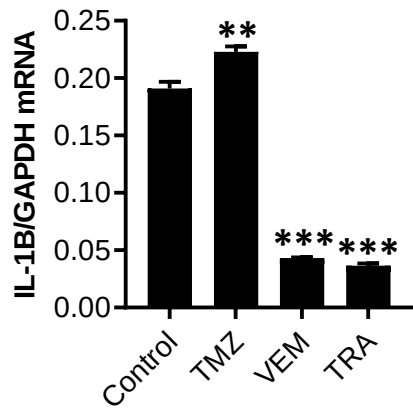


**Figure S11.** *IL1B* gene expression is inversely related to the expression ratio of *MITF/AXL* in melanoma cells as shows in Figure S1.

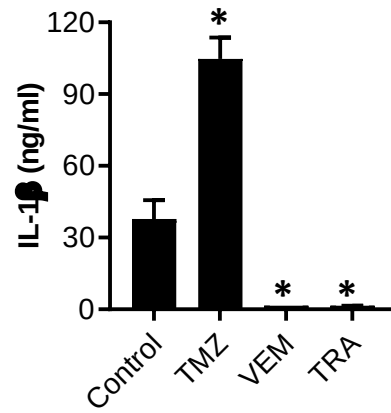


**Figure S12.** Original blots of Figure 4d.

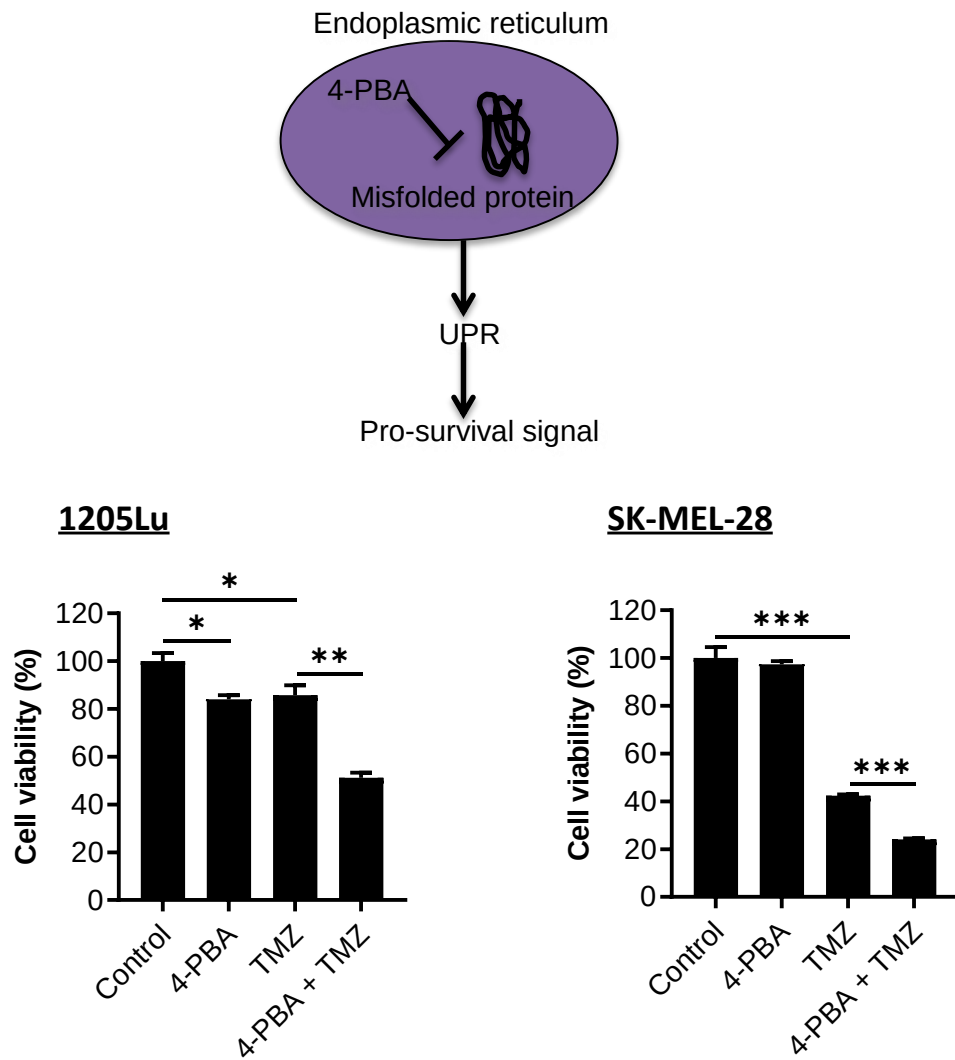
### *IL1B* mRNA



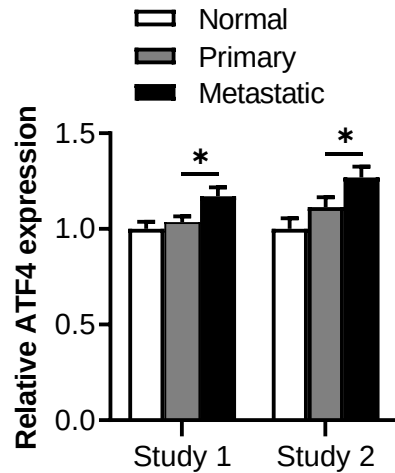
### IL-1 $\beta$ production



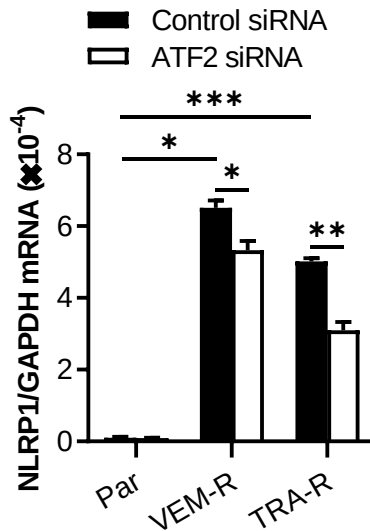
**Figure S13.** Decreased *IL1B* mRNA expression and IL-1 $\beta$  production in 1205Lu cells treated with 1  $\mu$ M vemurafenib (VEM) or 0.5  $\mu$ M trametinib (TRA).



**Figure S14.** Pretreatment of 1205Lu and SK-MEL-28 cells with 4-phenylbutyric acid (PBA, 2 mM), an ER stress inhibitor, sensitizes cells to temozolomide (TMZ, 100  $\mu$ M) and vemurafenib (VEM, 0.3  $\mu$ M), respectively.



**Figure S15.** Metastatic melanoma tissues display higher *ATF4* mRNA level than primary melanoma by examining *ATF4* mRNA expression in human melanoma tissues using two publicly available microarray data sets.



**Figure S16.** qRT-PCR analysis of *NLRP1* expression in parental and resistant SK-MEL-28 cells transfected with 50 nM control siRNA or ATF2 siRNA overnight. Mean  $\pm$  SEM,  $n = 2-3$ . \* $p < 0.05$ , \*\* $p < 0.01$ , and \*\*\* $p < 0.001$ .

**Table S1. Primers used for qRT-PCR and ChIP.**

**Primers for qRT-PCR (SYBR green)**

| Gene  | Gene ID | Forward                 | Reverse                    |
|-------|---------|-------------------------|----------------------------|
| IL1B  | 3553    | CAGGCTGCTCTGGGATTCTC    | GTCCTGGAAGGAGCACTTCAT      |
| ATF4  | 468     | ACCCAATTGGCCATCTCCCAGAA | ATCCACTTCACTGCCCAGCTCTAAAC |
| NLRP1 | 22861   | GCTGGACCAGACAACCTCTGA   | GGTTTCCGTCTGCTGAAGAT       |
| NLRP3 | 114548  | GATCTTCGCTGCGATCAACAG   | CGTGCATTATCTGAACCCAC       |
| MITF  | 4286    | CAGGCATGAACACACATTAC    | TCCATCAAGCCCAAGATTC        |
| AXL   | 558     | CAAGCACAGCCAGTCCACCA    | GTTCAAACACTTCTCCATAACGGG   |
| GAPDH | 2597    | CAGGGCTGCTTTTAACTCTGG   | TGGGTGGAATCATATTGGAACA     |

**Primers for ChIP (SYBR green)**

| Gene   | Gene ID | Forward               | Reverse                  |
|--------|---------|-----------------------|--------------------------|
| NLRP1  | 22861   | TCTGCCAGTCCAAGTGAAACC | TCCTCTTTCGTGGAATCTGCAA   |
| ATF3   | 467     | TGAGTGAGACTGTGGCTGGGA | ATTGGTAACCTGGAGTTAAGCGGG |
| NLRP1* | 22861   | ACTCACTGCAACCTCCACCT  | TGGTGAAACCCCGTCTCTAC     |

\*2 kb upstream of the binding site