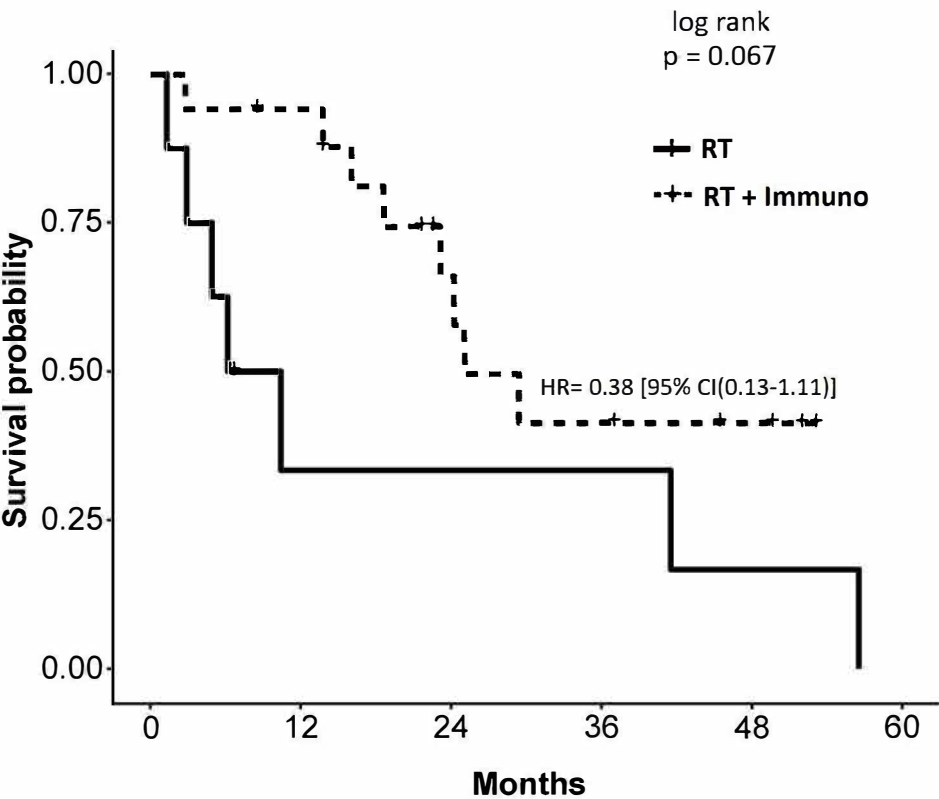


Supplementary Material



	0	12	24	36	48	60
RT	8	2	2	2	1	0
RT + Immuno	17	15	8	5	3	0

Months

Fig S1. Impact of timing. Kaplan-Meier curve of patients with melanoma brain metastases (MBM) who received radiation therapy (RT) ('no' group; solid line, n=8) or RT and immunotherapy ('yes' group; broken line, n=17) (Log rank p-value, 0.067) (Source file for Table 1). Hazard ratios based on Cox proportionality hazards models are reported as: hazard ratio (95% CI): HR for 'yes' vs 'no' group 0.38 (0.13-1.11), type 3 p-value= 0.078, log rank p-value = 0.067.

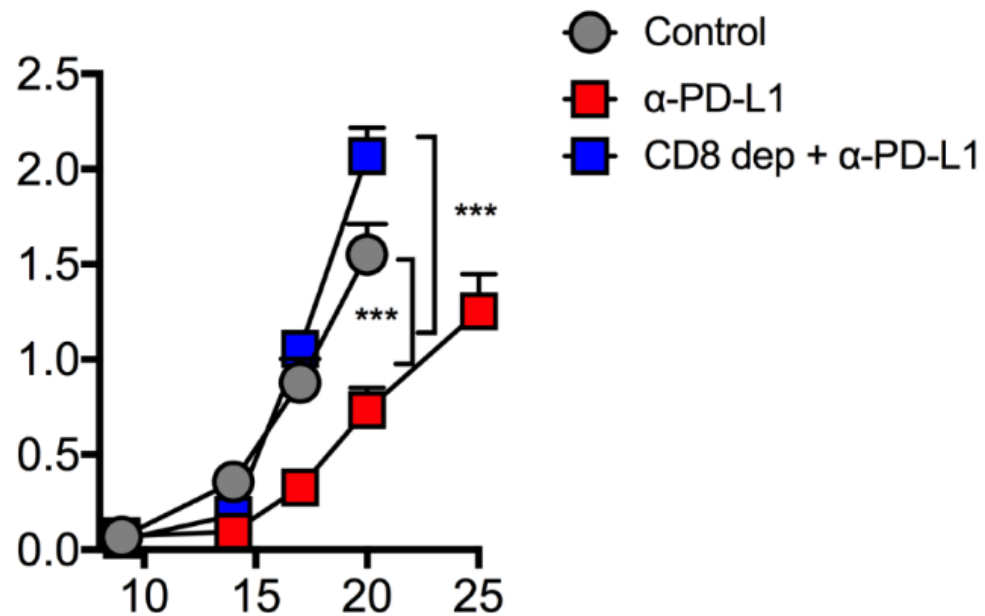


Fig. S2. Antibody depletion and drug treatment. Mice were injected with 500 μ g of α -CD8 (clone 2.43) for depletion of CD8 T cells, one day before irradiation and one day after radiation and weekly thereafter. α -PD-L1 (200 μ g; clone 29F.1A12) antibody in phosphate buffer saline (500 μ L) was injected i.p. every third day. Each error bar is \pm standard error of the mean.

Table S1. Annotation/pathway enrichment analysis using MetaCore of differentially expressed genes between treatment groups.

#	Maps	Total	pValue	Min FDR	p-value	FDR	In Data	Network Objects from Active Data
1	Stellate cells activation and liver fibrosis	70	8.795E-05	1.038E-02	8.795E-05	1.038E-02	3	RIPK1, DAB2, NIK(MAP3K14)
2	Apoptosis and survival Anti-apoptotic TNFs/NF-kB/IAP pathway	27	5.259E-04	2.390E-02	5.259E-04	2.390E-02	2	RIPK1, NIK(MAP3K14)
3	Activation of ACTH production in pituitary gland in major depressive disorder	32	7.404E-04	2.390E-02	7.404E-04	2.390E-02	2	RIPK1, NIK(MAP3K14)
4	Signal transduction PTMs (phosphorylation) in TNF-alpha-induced NF-kB signaling	41	1.216E-03	2.390E-02	1.216E-03	2.390E-02	2	RIPK1, NIK(MAP3K14)
5	Signal transduction PTMs (phosphorylation and acetylation) in TNF-alpha-induced NF-kB signaling	41	1.216E-03	2.390E-02	1.216E-03	2.390E-02	2	RIPK1, NIK(MAP3K14)
6	Apoptosis and survival Anti-apoptotic TNFs/NF-kB/Bcl-2 pathway	42	1.276E-03	2.390E-02	1.276E-03	2.390E-02	2	RIPK1, NIK(MAP3K14)
7	Immune response Inhibitory action of Lipoxins on pro-inflammatory TNF-alpha signaling	46	1.529E-03	2.390E-02	1.529E-03	2.390E-02	2	RIPK1, NIK(MAP3K14)
8	Activation of TNF-alpha-dependent pro-tumoral effect in colorectal cancer	49	1.733E-03	2.390E-02	1.733E-03	2.390E-02	2	RIPK1, NIK(MAP3K14)
9	Signal transduction NF-kB activation pathways	51	1.877E-03	2.390E-02	1.877E-03	2.390E-02	2	RIPK1, NIK(MAP3K14)
10	TLRs-mediated IFN-alpha production by plasmacytoid dendritic cells in SLE	53	2.025E-03	2.390E-02	2.025E-03	2.390E-02	2	NIK(MAP3K14), CDC37
11	Immune response T regulatory cell-mediated modulation of antigen-presenting cell functions	66	3.122E-03	3.349E-02	3.122E-03	3.349E-02	2	DAB2, NIK(MAP3K14)
12	Immune response OX40L/ OX40 signaling pathway	69	3.407E-03	3.351E-02	3.407E-03	3.351E-02	2	RIPK1, NIK(MAP3K14)
13	T follicular helper cell dysfunction in SLE	90	5.728E-03	5.199E-02	5.728E-03	5.199E-02	2	RIPK1, NIK(MAP3K14)
14	Stem cells CD30 signaling in transformed embryonic stem cells	18	2.278E-02	9.324E-02	2.278E-02	9.324E-02	1	NIK(MAP3K14)
15	Development Degradation of beta-catenin in the absence of WNT signaling	19	2.404E-02	9.324E-02	2.404E-02	9.324E-02	1	DAB2
16	DNA damage Inhibition of telomerase activity and cellular senescence	20	2.529E-02	9.324E-02	2.529E-02	9.324E-02	1	TEP1
17	Stem cells Putative pathways of telomerase regulation in glioblastoma stem cells	20	2.529E-02	9.324E-02	2.529E-02	9.324E-02	1	TEP1
18	wtCFTR and deltaF508-CFTR traffic / Clathrin coated vesicles formation (normal and CF)	20	2.529E-02	9.324E-02	2.529E-02	9.324E-02	1	DAB2
19	Cell cycle Chromosome condensation in prometaphase	21	2.653E-02	9.324E-02	2.653E-02	9.324E-02	1	INCENP
20	wtCFTR traffic / Sorting endosome formation (normal)	22	2.778E-02	9.324E-02	2.778E-02	9.324E-02	1	DAB2
21	Stem cells Aberrant Wnt signaling in medulloblastoma stem cells	23	2.903E-02	9.324E-02	2.903E-02	9.324E-02	1	DAB2
22	Development Cross-talk between VEGF and Angiopoietin 1 signaling pathways	25	3.151E-02	9.324E-02	3.151E-02	9.324E-02	1	RIPK1
23	Transcription Transcription regulation of aminoacid metabolism	25	3.151E-02	9.324E-02	3.151E-02	9.324E-02	1	MAFG
24	A proinflammatory phenotype of senescent alveolar epithelial cells in COPD	25	3.151E-02	9.324E-02	3.151E-02	9.324E-02	1	NIK(MAP3K14)
25	Role of keratinocytes and Langerhans cells in skin sensitization	25	3.151E-02	9.324E-02	3.151E-02	9.324E-02	1	NIK(MAP3K14)
26	Hedgehog signaling in prostate cancer	26	3.275E-02	9.324E-02	3.275E-02	9.324E-02	1	CDC37
27	Neurophysiological process Sweet taste signaling	27	3.399E-02	9.324E-02	3.399E-02	9.324E-02	1	Pannexin-1
28	Activation of TGF-beta signaling in pancreatic cancer	27	3.399E-02	9.324E-02	3.399E-02	9.324E-02	1	DAB2
29	DeltaF508-CFTR traffic / Sorting endosome formation in CF	27	3.399E-02	9.324E-02	3.399E-02	9.324E-02	1	DAB2
30	Immune response Innate immune response to RNA viral infection	28	3.523E-02	9.324E-02	3.523E-02	9.324E-02	1	RIPK1
31	Signal transduction PTMs in IL-17-induced CIKS-dependent NF-kB signaling and mRNA stabilization	28	3.523E-02	9.324E-02	3.523E-02	9.324E-02	1	NIK(MAP3K14)
32	Neurophysiological process Bitter taste signaling	28	3.523E-02	9.324E-02	3.523E-02	9.324E-02	1	Pannexin-1
33	Immune response CD137 signaling in immune cell	29	3.647E-02	9.324E-02	3.647E-02	9.324E-02	1	NIK(MAP3K14)
34	Cholesterol and Sphingolipid transport / Influx to the early endosome in lung (normal and CF)	29	3.647E-02	9.324E-02	3.647E-02	9.324E-02	1	DAB2
35	Signal transduction Additional pathways of NF-kB activation (in the nucleus)	30	3.770E-02	9.324E-02	3.770E-02	9.324E-02	1	NIK(MAP3K14)
36	IL-1 beta-dependent CFTR expression	31	3.894E-02	9.324E-02	3.894E-02	9.324E-02	1	NIK(MAP3K14)
37	Signal transduction PTMs in BAFF-induced non-canonical NF-kB signaling	32	4.017E-02	9.324E-02	4.017E-02	9.324E-02	1	NIK(MAP3K14)
38	The role of KEAP1/NRF2 pathway in skin sensitization	32	4.017E-02	9.324E-02	4.017E-02	9.324E-02	1	MAFG
39	Immune response TLR3 and TLR4 induced TICAM1-specific signaling pathway	33	4.140E-02	9.324E-02	4.140E-02	9.324E-02	1	RIPK1
40	The innate immune response to contact allergens	33	4.140E-02	9.324E-02	4.140E-02	9.324E-02	1	Pannexin-1
41	Role of Apo-2L(TNFSF10) in Prostate Cancer cell apoptosis	34	4.263E-02	9.324E-02	4.263E-02	9.324E-02	1	RIPK1
42	Apoptosis and survival Caspase cascade	34	4.263E-02	9.324E-02	4.263E-02	9.324E-02	1	RIPK1
43	Development Angiopoietin - Tie2 signaling	35	4.386E-02	9.324E-02	4.386E-02	9.324E-02	1	RIPK1
44	NF-kB pathway in multiple myeloma	35	4.386E-02	9.324E-02	4.386E-02	9.324E-02	1	NIK(MAP3K14)
45	Immune response Inflammasome in inflammatory response	35	4.386E-02	9.324E-02	4.386E-02	9.324E-02	1	Pannexin-1
46	Development Regulation of telomere length and cellular immortalization	35	4.386E-02	9.324E-02	4.386E-02	9.324E-02	1	TEP1
47	Extracellular matrix-regulated proliferation of airway smooth muscle cells in asthma	35	4.386E-02	9.324E-02	4.386E-02	9.324E-02	1	DAB2
48	Immune response Lipoxins and Resolvin E1 inhibitory action on neutrophil functions	35	4.386E-02	9.324E-02	4.386E-02	9.324E-02	1	NIK(MAP3K14)
49	Immune response IL-12-induced IFN-gamma production	36	4.508E-02	9.324E-02	4.508E-02	9.324E-02	1	NIK(MAP3K14)
50	Cell cycle The metaphase checkpoint	36	4.508E-02	9.324E-02	4.508E-02	9.324E-02	1	INCENP