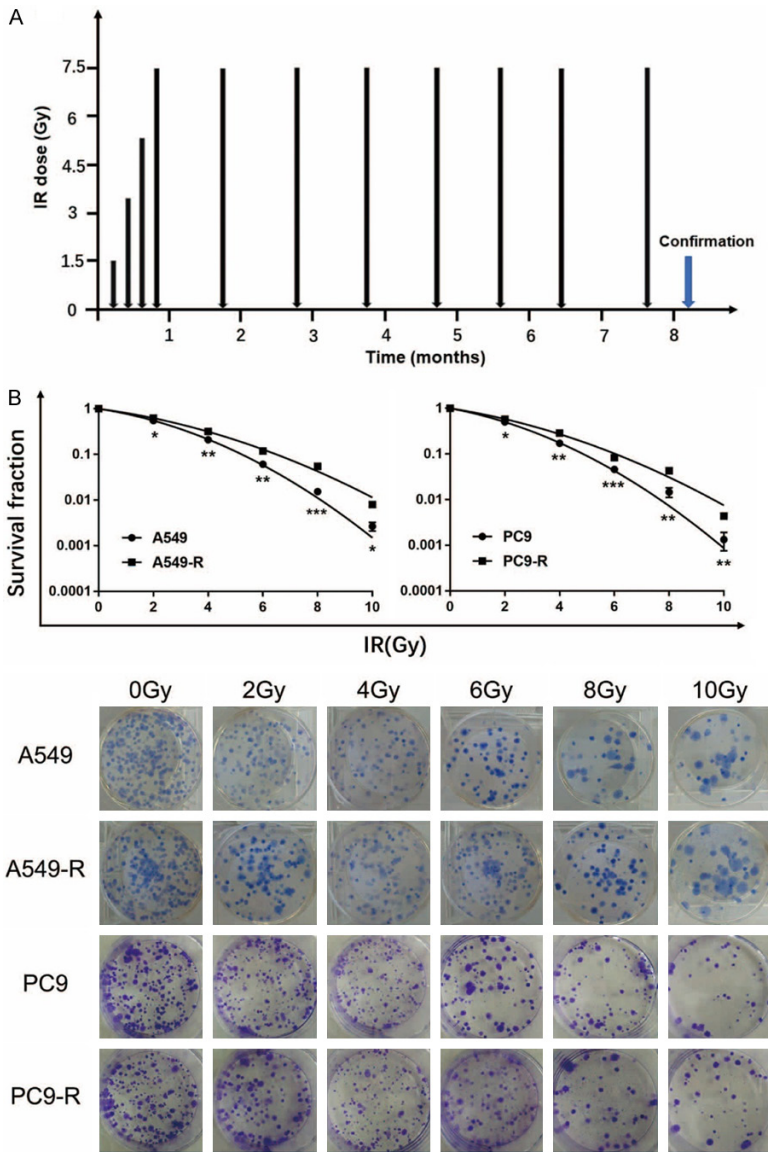

Figure S1. Establishment and verification of radioresistant NSCLC cell lines. A. Both A549 and PC9 cells were irradiated according to procedure described in the Method part and sublines were renamed as A549-R and PC9-R respectively. B. The survival curves of RR and their parental cell lines after irradiation (n=3). They were irradiated with 0, 2, 4, 6, 8, 10 Gy and colonies formed after 14 days. *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$. IR: irradiation. Gy: grayunit.

Table S1. Radiosensitive Parameters of Respective Cell Lines

Parameter	D0	SF2	SER10
A549	2.75	0.52	1
A549-R	3.52	0.61	0.77
PC9	2.55	0.47	1
PC9-R	3.27	0.57	0.79
A549-ago-nc	2.86	0.51	1
A549-ago	3.39	0.65	0.82
PC9-ago-nc	2.65	0.48	1
PC9-ago	3.07	0.63	0.76
A549-R-anta-nc	3.68	0.63	1
A549-R-anta	2.61	0.50	1.25
PC9-R-anta-nc	3.00	0.55	1
PC9-R-anta	2.58	0.46	1.18
A549-ago-nc+ctrl	2.84	0.53	1
A549-ago-nc+rapamicin	3.43	0.65	0.89
A549-ago+ctrl	3.52	0.63	0.88
A549-ago+rapamicin	4.25	0.74	0.75
PC9-ago-nc+ctrl	2.39	0.47	1
PC9-ago-nc+rapamicin	3.32	0.60	0.79
PC9-ago+ctrl	3.33	0.61	0.78
PC9-ago+rapamicin	4.25	0.71	0.65
A549-R-anta-nc+ctrl	3.49	0.60	1
A549-R-anta-nc+CQ	2.72	0.48	1.20
A549-R-anta+ctrl	2.50	0.43	1.26
A549-R-anta+CQ	2.39	0.38	1.41
PC9-R-anta-nc+ctrl	3.98	0.75	1
PC9-R-anta-nc+CQ	2.84	0.54	1.22
PC9-R-anta+ctrl	2.77	0.48	1.27
PC9-R-anta+CQ	2.17	0.41	1.53
A549-ago-nc	2.94	0.56	1.22
A549-ago	3.56	0.65	1
A549-ago+mTOR	2.94	0.56	1.19
A549-ago+CQ	3.00	0.50	1.28
PC9-ago-nc	2.69	0.48	1.28
PC9-ago	3.26	0.55	1
PC9-ago+mTOR	2.70	0.49	1.21
PC9-ago+CQ	2.48	0.46	1.39

ago: agomir, anta: antagomir; D0, dose to reduce survival to 37% of its value; SF2, surviving fraction at 2 Gy; SER10, sensitizer enhancement ratio at 10% survival.

Table S2. Probe and primer information

Name	Sequence (5'-3')
Primers for qRT-PCR	
miRNA universal R	GTGCAGGGTCCGAGGT
miR-1246-F	CGCAGAATGGATTTTTGGAG
miR-1246-RT	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGAC
miR-1908-5p-F	ATAATAACGGCGGGGACGG
miR-1908-5p-RT	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGAC
miR-1915-3p-F	GCGCTGGAAGACTAGTGATTTTG
miR-1915-3p-RT	CTCAACTGGTGTCGTGGAGTCGGCAATTCAGTTGAGCCCGCCGC
miR-25-5p-F	CGCCTCTTTGGTTATCTAGCTGT
miR-25-5p-RT	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGAC
miR-638-F	ATCCAGTGCGT G TCGTG
miR-638-RT	GTCGTATCCAGTGCGTGTCGTGGAGTCGGCAATTGCACTGGATA
miR-762-F	CGGGGCAGGGACAGAG
miR-762-RT	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGAC
miR-7977-F	TATAGATAGTGTGGCCGGCAG
miR-7977-RT	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGAC
miR-4485-F	AGUAACGGCCGCGGUAC
miR-4485-RT	GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGAC
U6-F	CTCGCTTCGGCAGCACA
U6-R	AACGCTTCACGAATTTGCGT
mTOR-F	AAGCCGCGCGAACCTC
mTOR-R	GGCATCTGAGCTGGAAACCA
ATG2B-F	GTGGATCTGAGGAGGAGAC
ATG2B-R	ACACTTCGGATTTGTAAACC
DRAM-F	GTCCCCTTCCTCTTGGTGACCTG
DRAF-R	CTGTCCATTCACAGATCGCACTCA
ATG12-F	GATGTCTCCCCAGAAACAAC
ATG12-R	CACCCCTACTCGGATGC
ATG10-F	TACGCAACAGGAACATCCA
ATG10-R	AACAACTGGCCCTACAATGC
ATG4D-F	GAGGAAATTGAGGTATAGAGAGGC
ATG4D-R	AACGCCCAAATAAAACTAACTACG
YY1-F	CCTGGCATTGACCTCTCAGATCCCA
YY1-R	GGGCAAGCTATTGTTCTTGGAGCA
GAPDH-F	GGGAGCCAAAAGGGTCATCATCTC
GAPDH-R	CCATGCCAGTGAGCTTCCCGTTC
Primers for ChIP-PCR	
Site A-F	CATTTTATTTTTAATCTGAGTCCATG
Site A-R	GGATACAACAAAGCCATCAGTGT
Site B-F	AACCTGAGTGGTTTGTCTGAACC
Site B-R	ATGTGATGATTTATTGCTTTGGAG
Site C-F	CGAAAACTATGAATAAGGATAAGG
Site C-R	CAAGATTCAGAAAATGGTGGC
Site D-F	TGAATCTTGGAAGAGATGGAAGA
Site D-R	ACACTCTAGGTCTCCTCTGGCC
Site E-F	CAGTGTAGCGTGACTGAGAAGCA
Site E-R	CCTCTTTGTGGAGCAACTTTTCT
Site F-F	GCAAAGCAGGAAATGGAAAATC
Site F-R	GTTCCCTTGATGTGGATTATTCTC

Probes for EMSA	
mut-A	TTAATCTGAGTCCATGTTGGCA
mut-B	GTAAAAAAAATGGGTCCATAG
mut-C	CTTCTTGGCCACCATTTTCTGA
mut-D	TGGAAGAGATGGAAGAAA
mut-E	GATTCACAATGGCCATGCG
mut-F	CAGATGGCCATCATTCGTC
Probes for ISH	
miR-1246	DIG-CCTGCTCCAAAAATCCATT-DIG
Probes for FISH	
CDR1as	DIG-GGTGCCATCGGAAACCCTGGATATTGCAGACACTG-DIG.

F: forward, R: reverse, RT, reverse-transcription, mut: mutant.

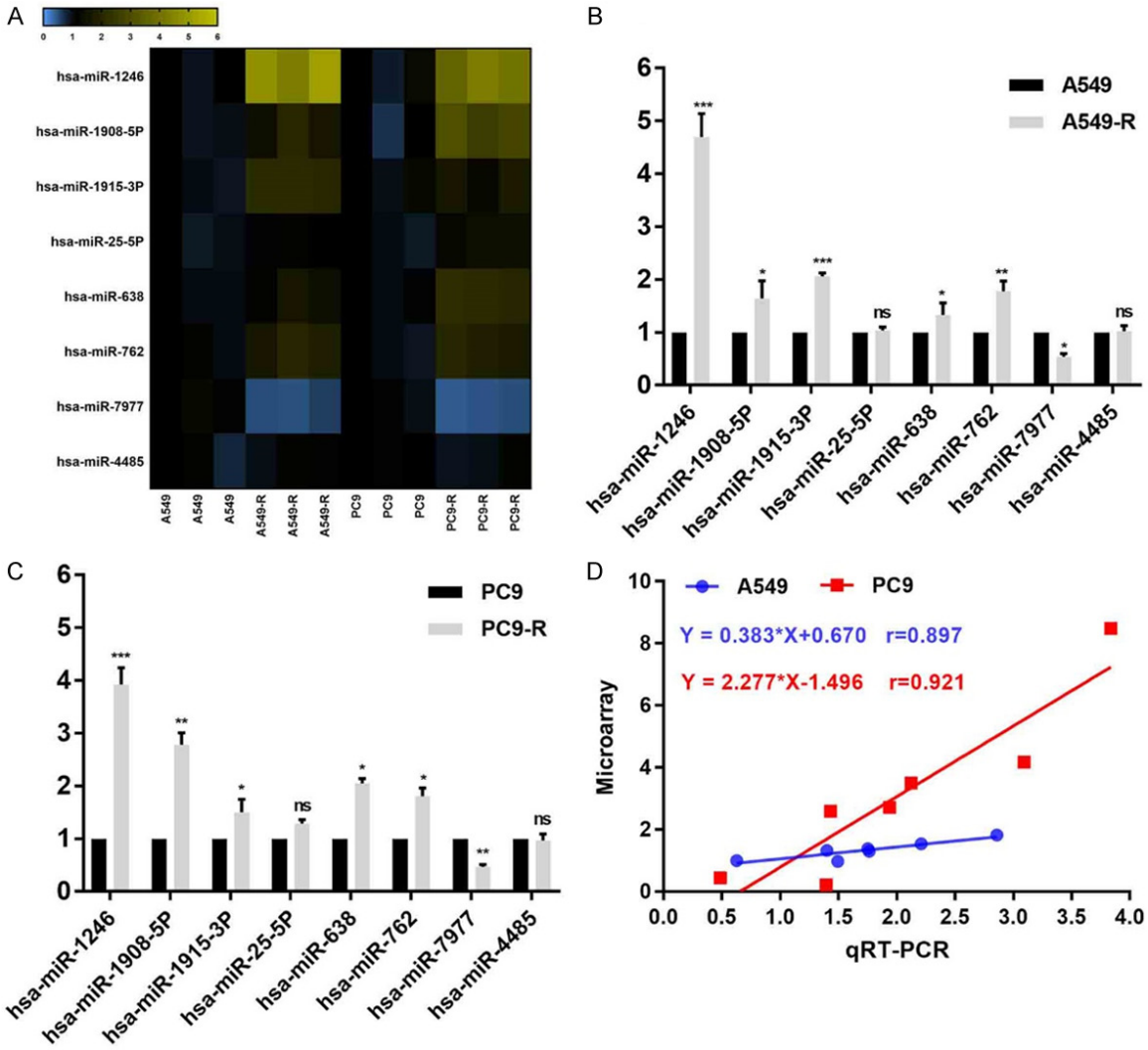

Figure S2. Verification of differential expressed miRNA by qRT-PCR. A. Heat map of eight miRNAs (5 up-regulated, 2 down-regulated, and 1 non-significant) based on the miRNA microarray results by qPCR (n=3). Yellow represented relatively high expression while blue represented relatively low expression. B, C. Relative expression of these eight miRNAs in both A549 and PC9 cell lines. Data were shown as the means ± SD. *, p<0.05; **, p<0.01; ***, p<0.001; ns, no significant. D. The correlation of qRT-PCR and microarray results. Red represented the results in A549 and A549-R cell lines (Pearson r=0.897, p=0.04) while blue represented the results in PC9 and PC9-R cell lines (Pearson r=0.921, p=0.01).

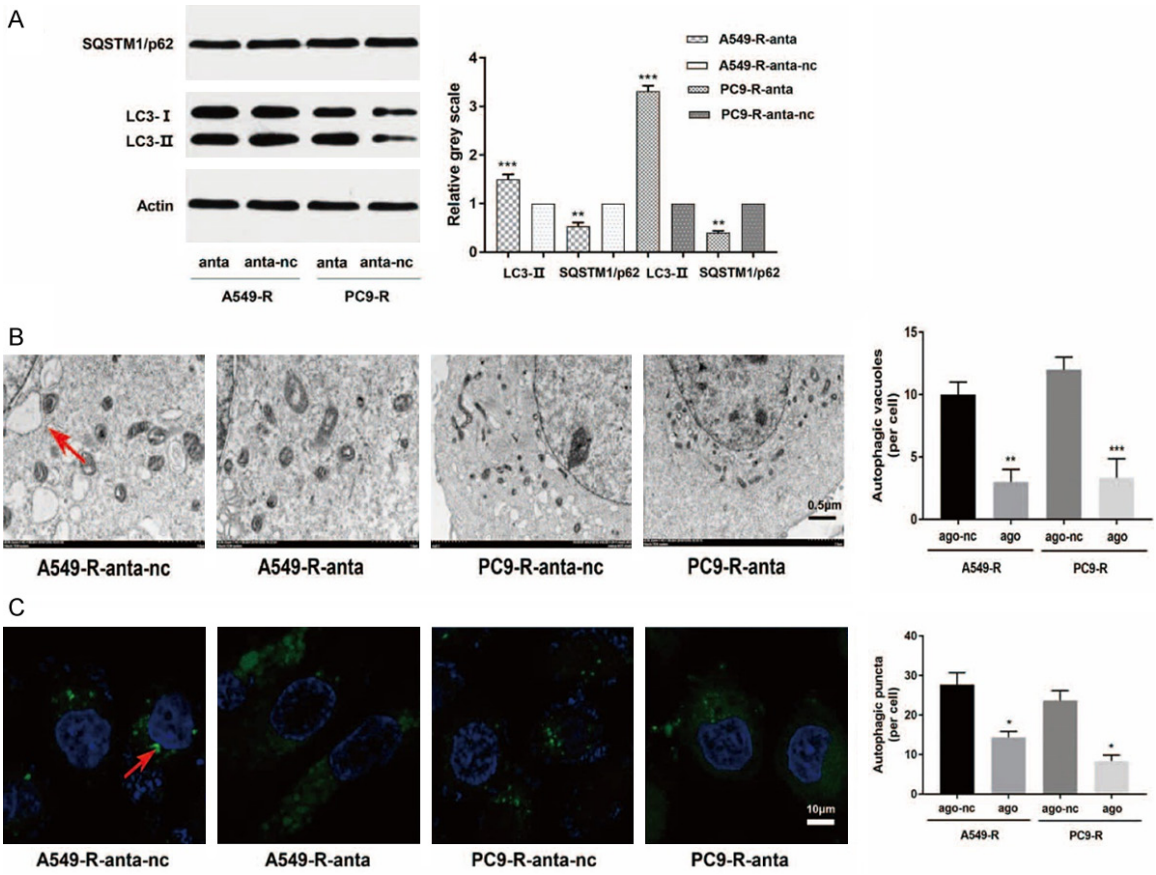

Figure S3. Downregulated miR-1246 inhibits autophagy in NSCLC cells. A. Downregulated miR-1246 decreased LC-II expression and increased SQSTM1/p62 expression. B. Downregulated miR-1246 decreased autophagic vacuoles accumulation under electron microscopy observations. Red arrow: autophagic vacuoles. C. Downregulated miR-1246 decreased autophagosome accumulation by immunofluorescence detection. Red arrow: autophagic vacuoles. anta: antagomir, nc: negative control. n=3 per group.

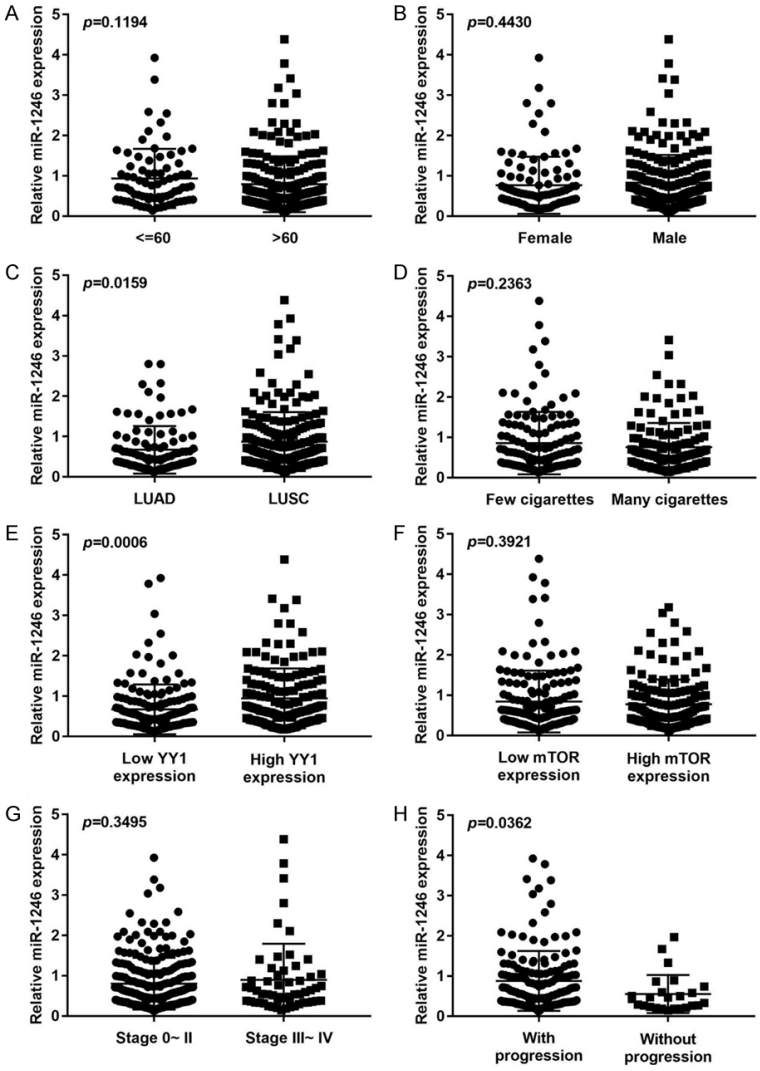

Figure S4. Correlation of miR-1246 with clinicopathologic factors and other key genes in TCGA dataset. LUAD: lung adenocarcinoma; LUSC: lung squamous cell carcinoma. Data were shown as the means ± SD.