Supporting information:

Materials and Methods:

Table S1. Basic sequence of S1-S4 ssDNA

ssDNA	Base sequence（5'→3'）
S1	ATTTATCACCCGCCATAGTAGACGTATCACCAGGCAGTTGAGACGAACATTCCTAAGTCTGAA
S2	ACATGCGAGGGTCCAATACCGACGATTACAGCTTGCTACACGATTCAGACTTAGGAATGTTCG
S3	ACTACTATGGCGGGTGATAAAACGTGTAGCAAGCTGTAATCGACGGGAAGAGCATGCCCATCC
S4	ACGGTATTGGACCCTCGCATGACTCAACTGCCTGGTGATACGAGGATGGGCATGCTCTTCCCG

Table S2. sequences of the primers for q-PCR

mRNA	primer pairs (5′ → 3′)
Ho-1	Forward GTTCTGATCCTGCCTGTGCC
	Reverse GTCACCAACCGCATACCAGG
Nrf2	Forward GCAGGCAAGTCTGAGTGTCC
	Reverse GGAAGCTTGTCCACTGCTCC
SOD2	Forward AAGCCACCAGTGAGCATGTG
	Reverse GTTCAGTGGAGGCTAACGCC
IL-6	Forward GACAGCCACTCACCTCTTCAGAAC
	Reverse AAGCCTACCCACCTCCTTTCTCAG
IL-1β	Forward TTCGAGGCACAAGGCACAACAG
	Reverse CACACAAAGAGGCAGAGAGACAGAG
TNF-α	Forward ATGACAGACAGAGAGGACAGGAACC
	Reverse GGAGGGAGGGAGAGAGGGAGAG

TGF-β	Forward TACAGCAACAATTCCTGGCGATACC Reverse ATCCTCACCTCCACGGCTCAAC
P16^{INK4A}	Forward TAATAGCACCTCCTCCGAGCACTC Reverse ACCCTGTCCCTCAAATCCTCTGG
P21	Forward TCCAGCGACCTTCCTCATCCAC Reverse TCCATAGCCTCTACTGCCACCATC

Table S3. Parkin's scoring system

Edema score	0.5	Doubtful if any swelling
	1	Slight but definite swelling
	2	Severe swelling
Other score	0.5	Doubtful if abnormally pink
	1	Slight but definite reddening
	2	Severe reddening
	3	Focal desquamation
	4	Exudate or crusting involving about half of lip area
	5	Exudate or crusting involving about more than half of lip area

Table S4. Microscopical assessment system for histological score determination

Tissue	Region	Severity(score)
Keratin layer (Loss)	tip of the tongue	None (0), up to 1/4(1), up to 1/2(2)
	Rest of the tongue	Normal (0), thin (1), absent (2)
Epithelium(loss)	Near the base (dorsal surface)	Normal (0), thin (1), absent (2)
Lamina propria(thickness)	Near the base (dorsal surface)	Normal (0), slightly enlarged (1), notable (2)
Polymorphonuclear leukocytes	Near the base (dorsal surface)	Absent (0), a few cells (1), plenty (2)
Salivary glands (Glandular content)	Serous gland	Normal (0), slightly reduced (1), nearly empty (2)
	Mucous gland	Normal (0), slightly reduced (1), nearly empty

(2)

Results and Discussion:

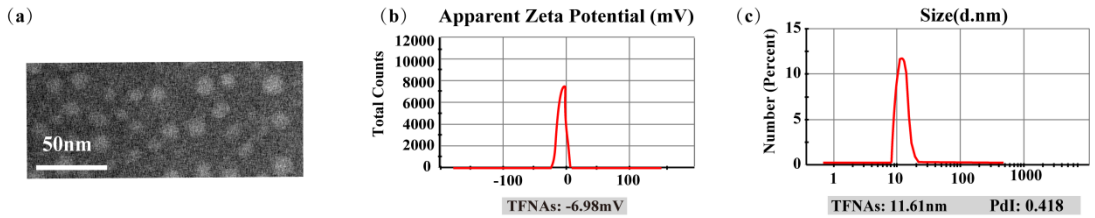

Figure S1：characterization of TFNAs (a) TEM images of the molecular structure of TFNAs. Scale bars: 50 nm. (b,c) Nanoparticle potentiometer detected the molecular size of TFNAs.

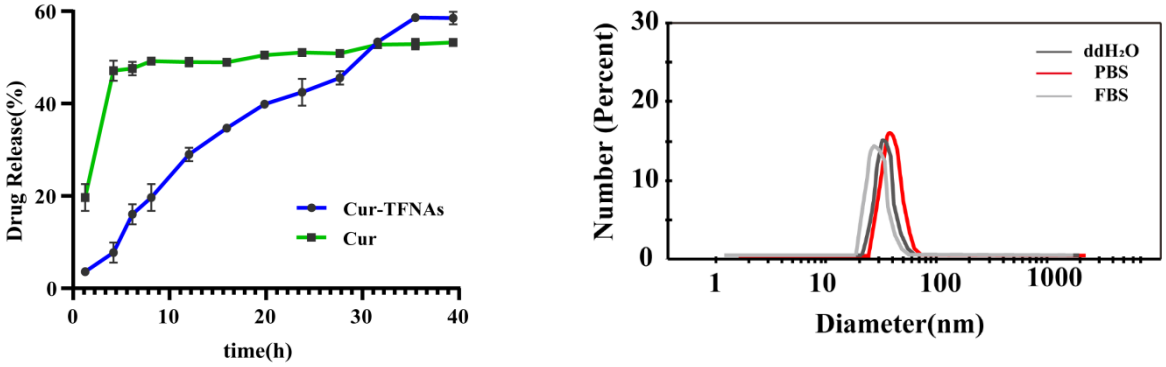

Figure S2: Release curve of Cur in Cur-TFNAs and free Cur solution at 37 °C *in vitro* (left). Colloidal stability of Cur-TFNAs in different conditions (right).Data is presented as mean ± SD (n=3).

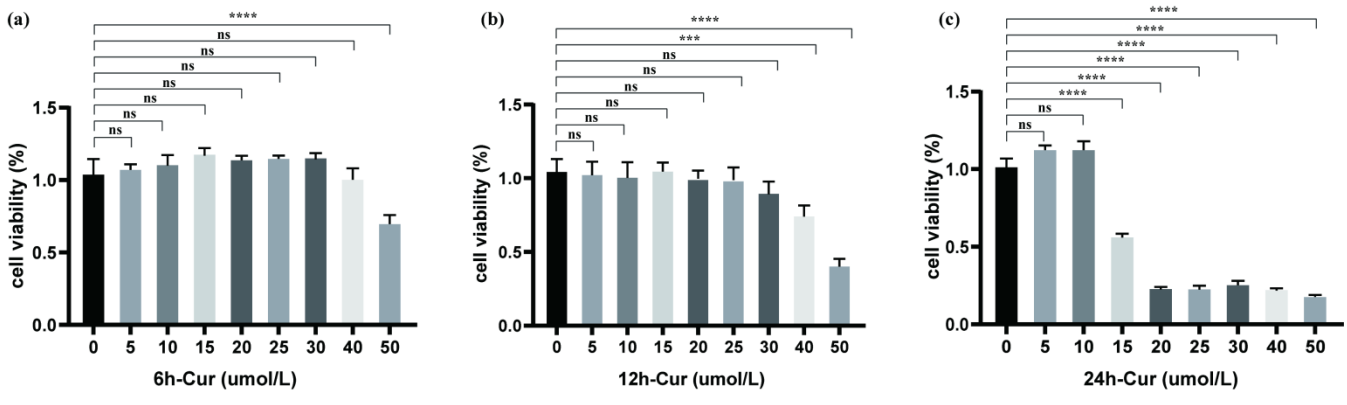

Figure S3: Results of CCK-8 experiments on normal HOK cells treated with different concentrations of curcumin at various time points.(a)HOK cell viability after 6h curcumin treatment (b)HOK cell viability after 12h curcumin treatment (c)HOK cell viability after 24h curcumin treatment. All data are presented as the mean ± standard deviation (SD) (n =3) and were analyzed using one-way ANOVA followed by Tukey's correction for multiple comparisons. Statistical analysis: *P < 0.05, **P < 0.01, ***P < 0.001; ****P<0.0001.

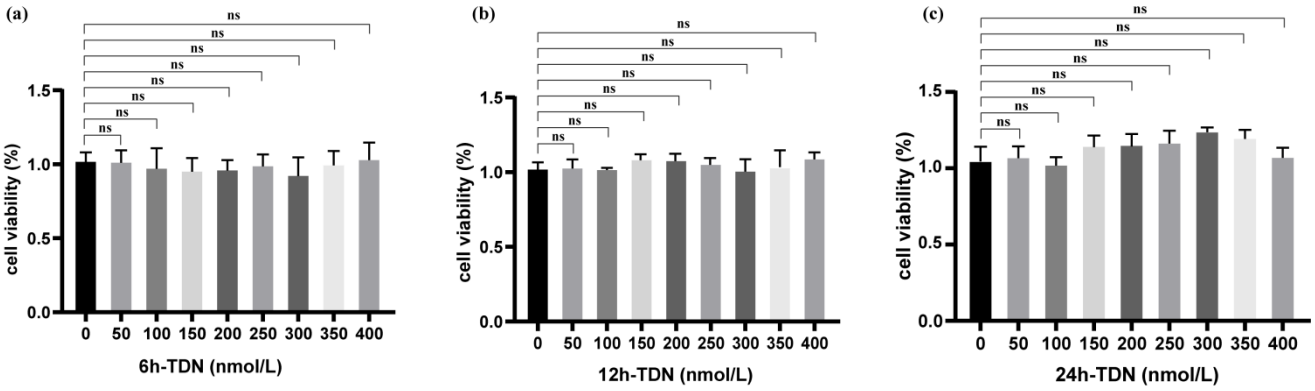

Figure S4: Results of CCK-8 experiments on normal HOK cells treated with different concentrations of TFNAs at various time points.(a)HOK cell viability after 6h TFNAs treatment (b)HOK cell viability after 12h TFNAs treatment (c)HOK cell viability after 24h TFNAs treatment. All data are presented as the mean ± standard deviation (SD) (n =3) and were analyzed using one-way ANOVA followed by Tukey's correction for multiple comparisons. Statistical analysis: *P < 0.05, **P < 0.01, ***P < 0.001; ****P<0.0001.

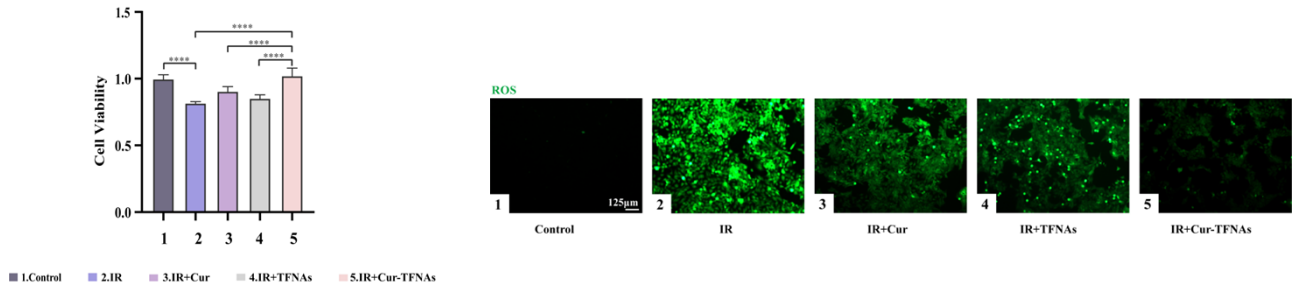

Figure S5: CCK-8 results of different pretreated HOK cells after IR (left) and ROS expression in different pretreated HOK cells after irradiation, Scale bars: 125μm (right). All data are presented as the mean ± standard deviation (SD) (n =3) and were analyzed using one-way ANOVA followed by Tukey's correction for multiple comparisons. Statistical analysis: *P < 0.05, **P < 0.01, ***P < 0.001; ****P<0.0001.

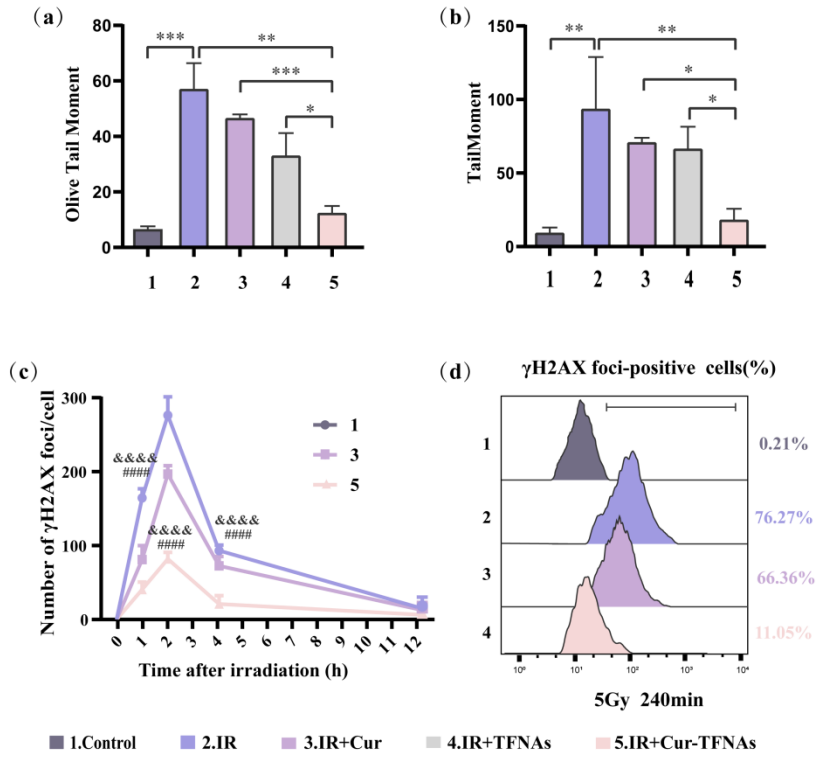

Figure S6: Cur-TFNAs protect DNA damage from IR. (a)(b) Data statistics of the neutral comet assay. The level of damaged DNA was also quantitated by measuring the Olive tail moment and tail moment. (c) The dynamic process of DNA DSBs was measured by detecting nuclear γH2AX foci at several time points after 5 Gy of X-ray irradiation. (&: IR,#: Cur) (d) The expression of γH2AX in different pretreated HOK cells after 240 min of irradiation was detected by flow cytometry. All data are presented as the mean ± standard deviation (SD) (n ≥3) and were analyzed using one-way ANOVA followed by Tukey's correction for multiple comparisons. Statistical analysis: *P < 0.05, **P < 0.01, ***P < 0.001; ****P<0.0001.

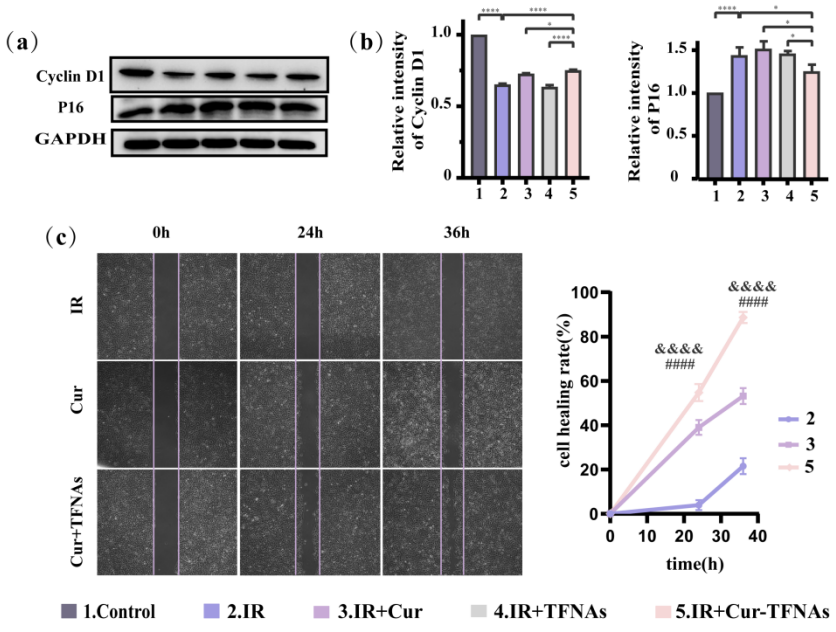

Figure S7: Cur-TFNAs alleviates cellular senescence and promotes cell migration. (a) Western blot analysis of the expression of Cyclin D1 and P16. (b) The expression levels of related proteins in (a) were quantitatively analyzed. (c) Images of the wound healing assay show the horizontal migration ability of different pretreated HOK cells after irradiation for 36 h. Statistical analysis of the wound healing assay. (&: IR,#: Cur) All data are presented as the mean ± standard deviation (SD) (n ≥3) and were analyzed using one-way ANOVA followed by Tukey's correction for multiple comparisons. Statistical analysis: *P < 0.05, **P < 0.01, ***P < 0.001; ****P<0.0001.

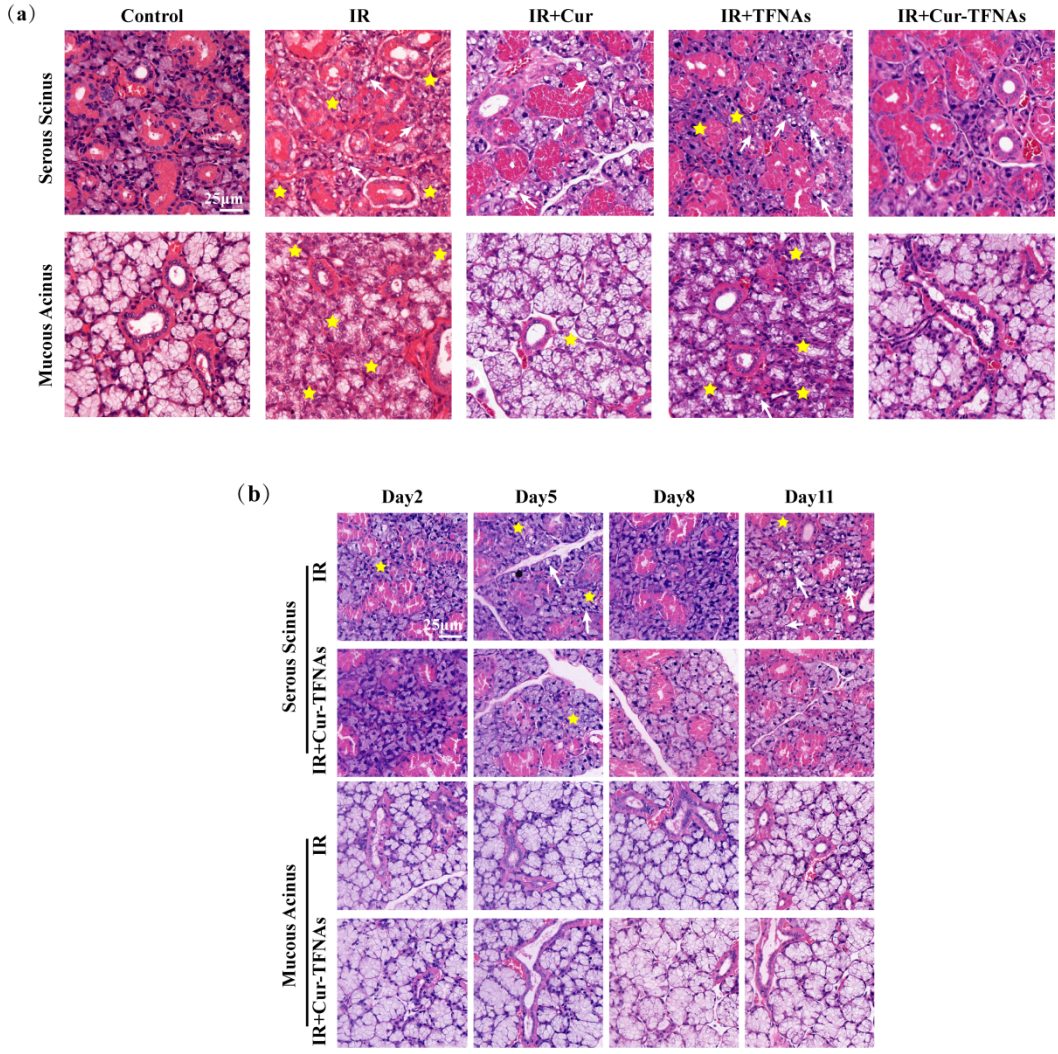

Figure S8: Cur-TFNAs protect salivary glands after radiation. (a) Histopathological changes in salivary glands after S-IR. (H&E staining). Histopathological changes in salivary glands after F-IR. (H&E staining) Yellow pentagram indicates acinar atrophy; White arrow indicates vacuolization.

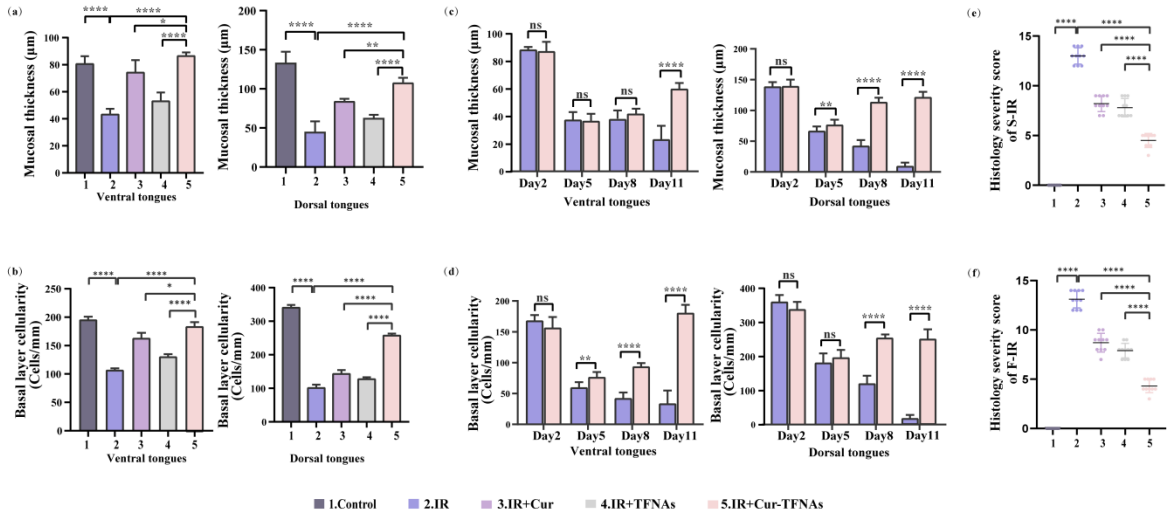

Figure S9: Cur-TFNAs alleviates the occurrence of RIOM in vivo. (a) Quantitative analysis of the mucosal thickness of the ventral and dorsal tongues after a single dose of irradiation. (b) Quantitative analysis of the cell quantity of ventral tongues and dorsal tongues after single-dose irradiation. (c) Quantitative analysis of the mucosal thickness of ventral tongues and dorsal tongues after fractional irradiation. (d) Quantitative analysis of the cell quantity of ventral tongues and dorsal tongues after fractional irradiation. (e) Severity of mucositis caused by single-dose irradiation evaluated using a microscopic assessment system for histological score determination. (f) Severity of mucositis caused by fractional irradiation evaluated using a microscopic assessment system for histological score determination.