Supporting Information

A Bioswitchable siRNA Delivery System: RNAi Therapy Based on Tetrahedral Framework Nucleic Acids for Bone Defect Repair

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Oligonucleotides Name	Sequence (5'-3')
BiRDS	
S1	ggacuuggAGGATGGGCATGCTCTTCCCGACGGTATTGGACCCTCGCATGAgcaaggaaTAAG
S2	ggacuuggACATGCGAGGGTCCAATACCGACGATTACAGCTTGCTACACGAgcaaggaaTAAG
S3	ggacuuggACGTGTAGCAAGCTGTAATCGACGGGAAGAGCATGCCCATCCAgcaaggaaTAAG
siRNA	uuccuugcuaccaagucccuua
Cy5-siRNA	Cy5- uuccuugcuaccaagucccuua
Cy5-siRNA-BHQ	Cy5- uuccuugcuaccaagucccuua-BHQ
tFNA	
S1	ATTTATCACCCGCCATAGTAGACGTATCACCAGGCAGTTGAGACGAACATTCCTAAGTCTGAA
S2	ACATGCGAGGGTCCAATACCGACGATTACAGCTTGCTACACGATTCAGACTTAGGAATGTTCG
S3	ACTACTATGGCGGGTGATAAAACGTGTAGCAAGCTGTAATCGACGGGAAGAGCATGCCCATCC
S4	ACGGTATTGGACCCTCGCATGACTCAACTGCCTGGTGATACGAGGATGGGCATGCTCTTCCCG

Table S1. Sequences of the Oligonucleotides used in this study

Primer Name		Sequences from 5' to 3'
CKIP-1	Forward	AGAGCGGACTCAGACAGGAT
	Reverse	TGGGTAACTTCTTCAGTGCTTG
GAPDH	Forward	ACAGCAACAGGGTGGTGGAC
	Reverse	TTTGAGGGTGCAGCGAACTT

Table S2. The primer sequences used in this study.

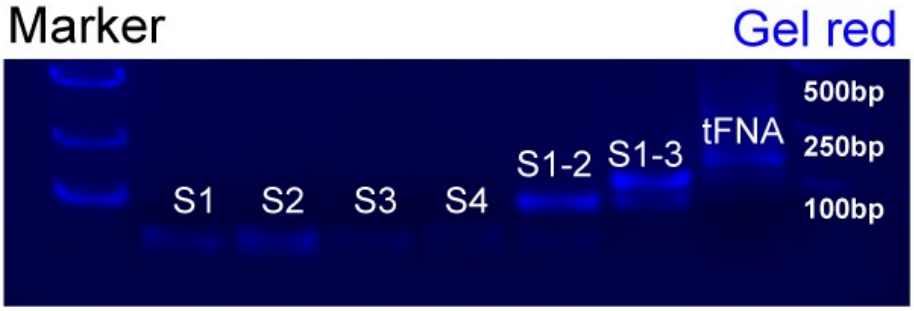

Figure S1. Verification of the stepwise loading process of tFNA in AGE. As shown in the gel images, the lanes 1-8 (from left to right) represent S1, S2, S3, S4, S1-2, S1-3 and tFNA, respectively.

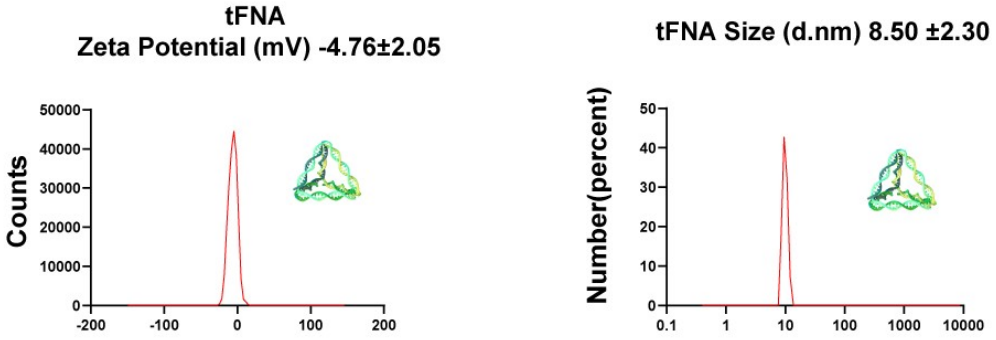

Figure S2. Zeta potential and molecular size of tFNA.

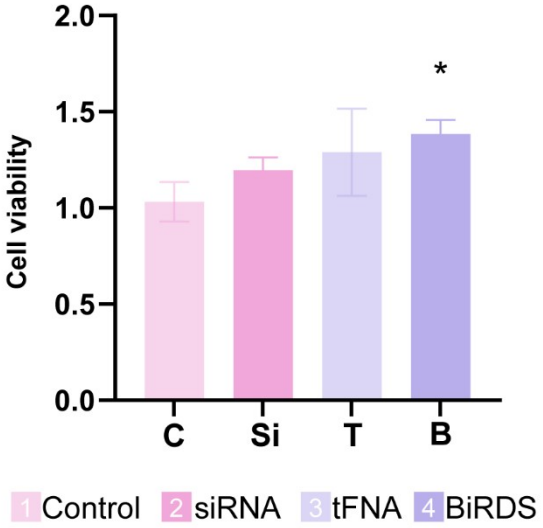

Figure S3. Cell viability assays by CCK-8 experiments. Data are presented as mean ± SD (n =3). Statistical method compared between groups involved one-way analysis of variance (ANOVA) and post-hoc analysis (Sidak. Test). Statistical analysis: *P < 0.05, **P < 0.01, ***P < 0.001, #P < 0.05, ##P < 0.01, ###P < 0.001. *: control group versus other groups, #: siRNA group versus other groups.

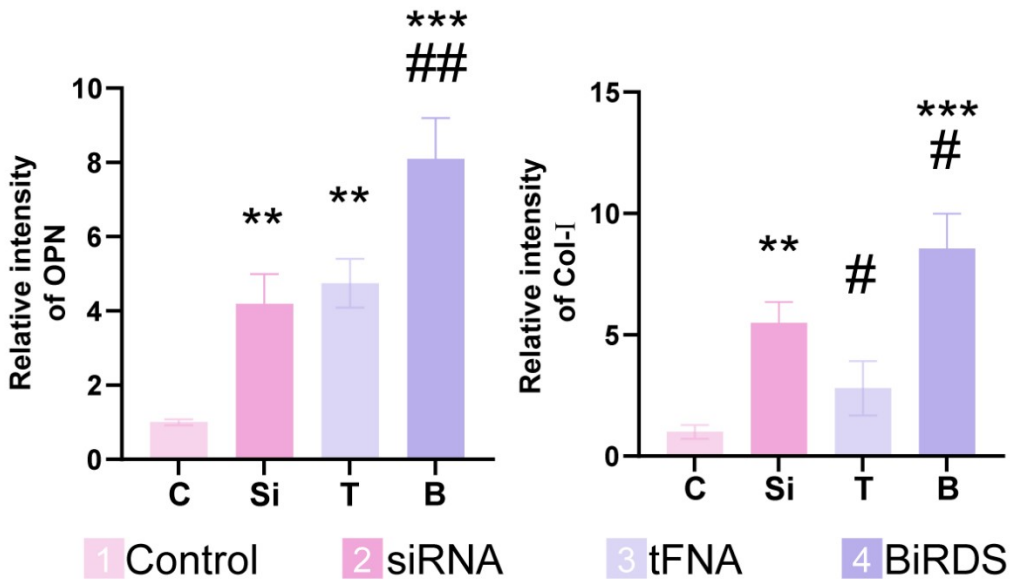

Figure S4. The semi-quantitative analysis of relative fluorescence intensity of OPN and Col-I. Data are presented as mean ± SD (n =3). Statistical method compared between groups involved one-way analysis of variance (ANOVA) and post-hoc analysis (Sidak. Test). Statistical analysis: *P < 0.05, **P < 0.01, ***P < 0.001, #P < 0.05, ##P < 0.01, ###P < 0.001. *: control group versus other groups, #: siRNA group versus other groups.

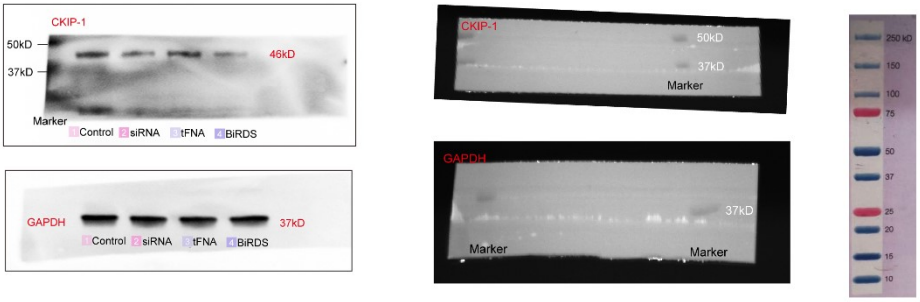

Figure S5. The raw data for the western blotting protein bands for Figure 2F (CKIP-1 and GAPDH).

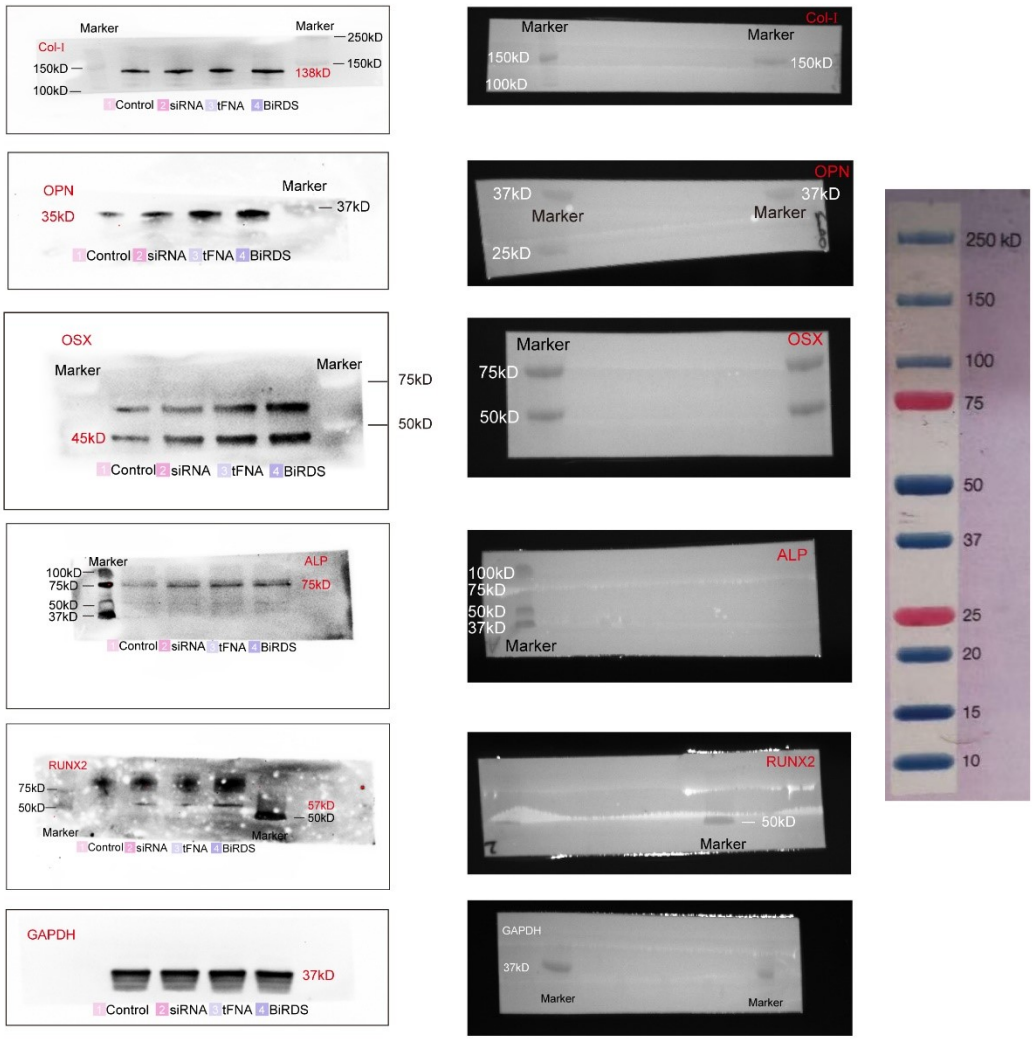

Figure S6. The raw data for the western blotting protein bands for Figure 3D (Col-I, OPN, OSX, ALP, RUNX2 and GAPDH).