Mitochondrion-targeted NIR therapeutic agent suppresses melanoma by inducing apoptosis and cell cycle arrest *via* E2F/Cyclin/CDK pathway

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Table S1. Primer sequences for RT-qPCR assay.

	Primer Name	Sequence (5'-3')
108961	***E2f8-F***	GCTCTGAAGGAGGATTGACAGG
	E2f8-R	ATGCAGGGGGCTTTTCATCA
52679	***E2f7-F***	GATGCGTTCGTGAACTCCCTG
	E2f7-R	CCGACGACACGGTCTTCAAAGA
12544	***Cdc45-F***	CCGGCAACAAGGAACCAATC
	Cdc45-R	GGCGGATACCTAGAACTGGC
12428	***Ccna2-F***	GAGCTCCCAAGCTCTACTGC
	Ccna2-R	TTTTCATGGGCAGTCCTGGT
12534	***Cdk1-F***	AAGTGTGGCCAGAAGTCGAG
	Cdk1-R	TCGTCCAGGTTCTTGACGTG
20135	***Rrm2-F***	TGATGCCGGGCCTTACATTT
	Rrm2-R	CCTGCTCTATCCTAACGGCG
12433	***Ccnd1-F***	CAGCCCCAACAACTTCCTCT
	Ccnd1-R	CAGGGCCTTGACCGGG
12567	***Cdk4-F***	CTTAGCCGAGCGTAAGGCTG
	Cdk4-R	CCAGGCCGCTTAGAAACTGA
12447	***Ccne1-F***	GACACAGCTTCGGGTCTGAG
	Ccne1-R	CTGGAGCGGACTGAAAGGTC

12566	***Cdk2-F***	CGGCTCGACACTGAGACTG
	Cdk2-R	TTCTTGAGGTCCTGGTGCAG
12575	***P21-F***	CAGAATAAAAGGTGCCACAGGC
	P21-R	CGTCTCCGTGACGAAGTCAA
12576	***P27-F***	CAGACGTAAACAGCTCCGAATTA
	P27-R	GGCAGATGGTTTAAGAGTGCC

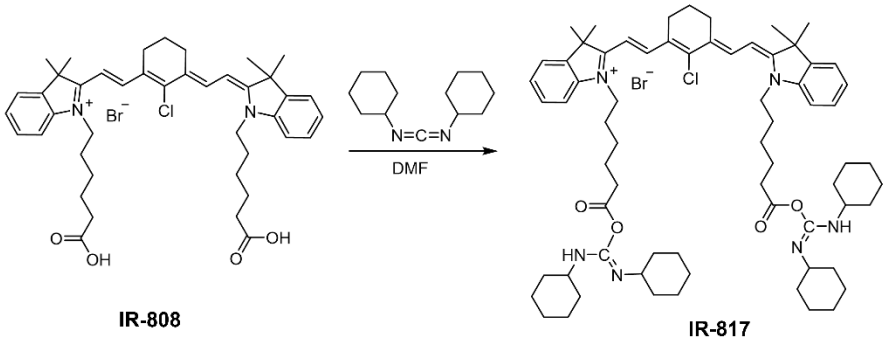

Figure S1. The synthetic route of IR-817.

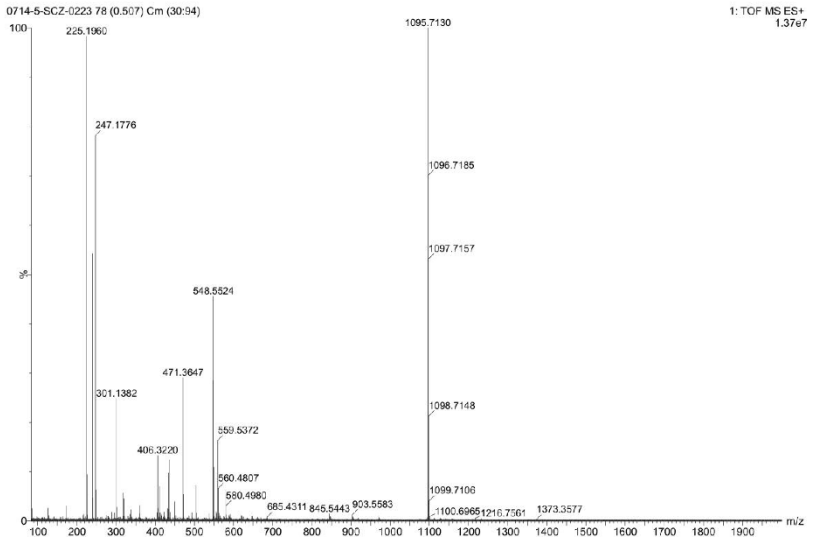

Figure S2. HRMS spectrum of IR-817.

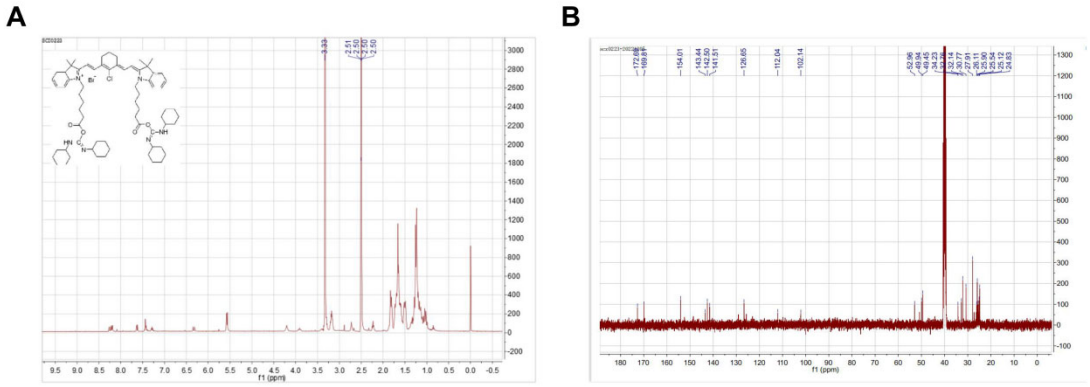

Figure S3. ^{1}H NMR and ^{13}C NMR spectrum of IR-817.

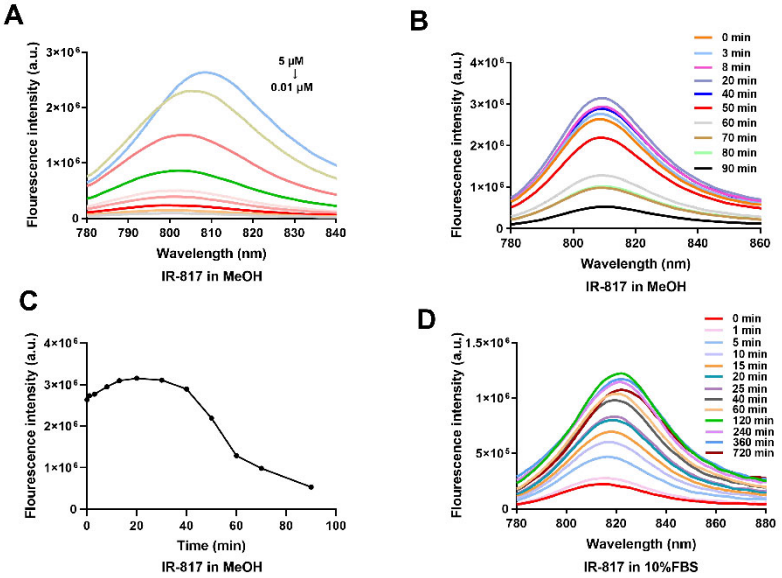

Figure S4. (A) The fluorescence intensity was plotted versus with different concentration (0.01-5 μM) of IR-817 in MeOH. (B) Fluorescence intensity of 5 μM IR-817 in MeOH over time. (C) Fluorescence instability of IR-817 in MeOH. (D) Fluorescence intensity of 5 μM IR-817 in 10% FBS over time.

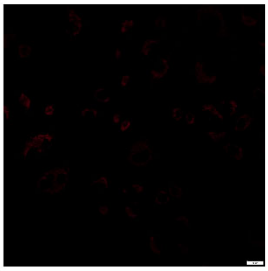

Figure S5. Fluorescence image of 5 μM IR-817 co-incubated with A549 cells for 1 h. Scale.

bars, 20 μm.

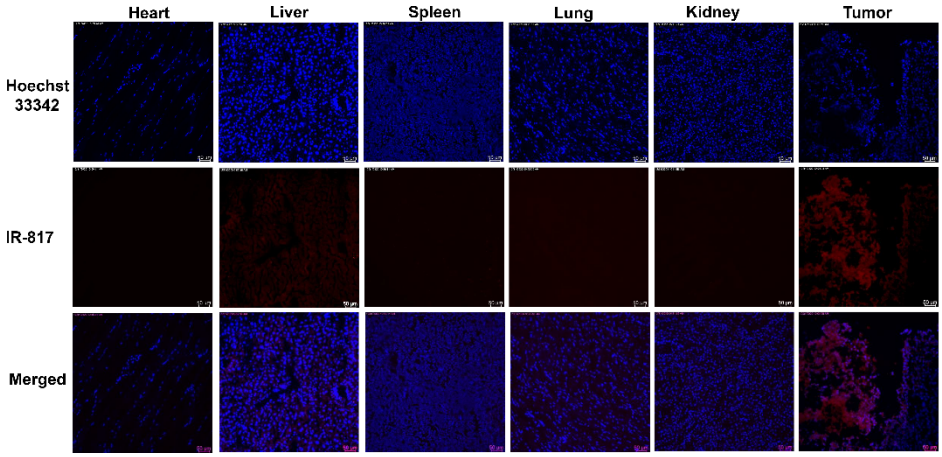

Figure S6. C57BL/6J mice with B16-F10 subcutaneous tumor xenografts were subjected to histopathologic analysis after a single-dose intravenous administration of IR-817 at 5 mg/kg for 12 h. Organs and xenografts were imaged by fluorescence microscope. Scale bars, 50 μm.

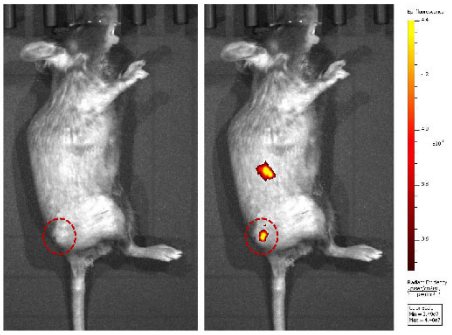

Figure S7. *In vivo* imaging of the subcutaneous tumor mice model after tail vein injection 48 h of IR-817 (5mg/kg).

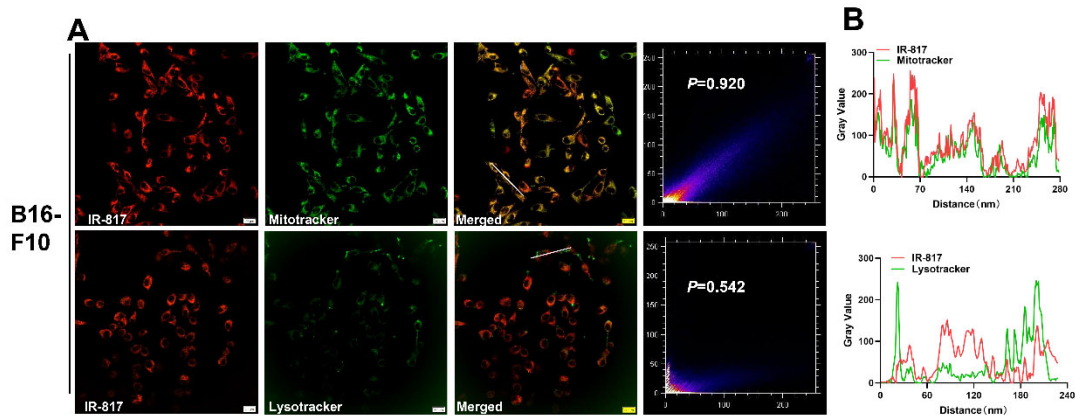

Figure S8. (A)Fluorescence co-localization of IR-817 and Mitotracker Green or Lysotracker Green in B16-F10 cells. (B) Normalized intensity profiles of co-localized image along the pixels marked by the solid line.

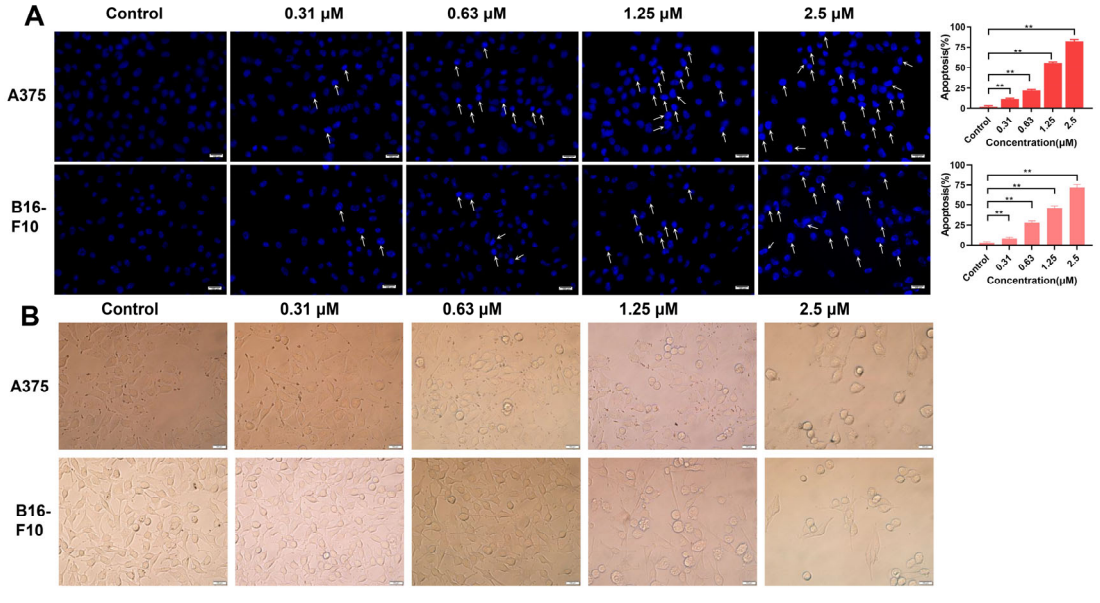

Figure S9. (A) The nuclear changes of A375, B16-F10 were observed after Hoechst 33342 staining (×400 magnification, scale bar =100 μm). The arrow refers to apoptotic cells. Each value was mean ± SD, n = 3. ** $p < 0.01$. (B) Photographs showing morphological changes in A375 and B16-F10 cells with different concentrations of IR-817 for 24 h.

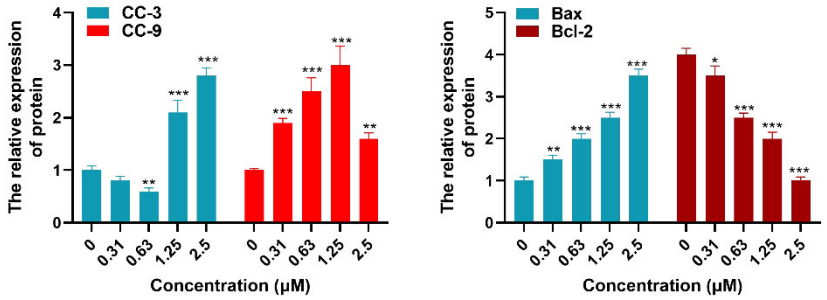

Figure S10. Relative protein expression levels of CC-3, CC-9 (35KDa), Bax and Bcl-2 in B16-F10 cells after different treatments analyzed from Western blotting were shown in each bar. Each value was mean ± SD, n = 3. *** $p < 0.001$,** $p < 0.01$, * $p < 0.05$.

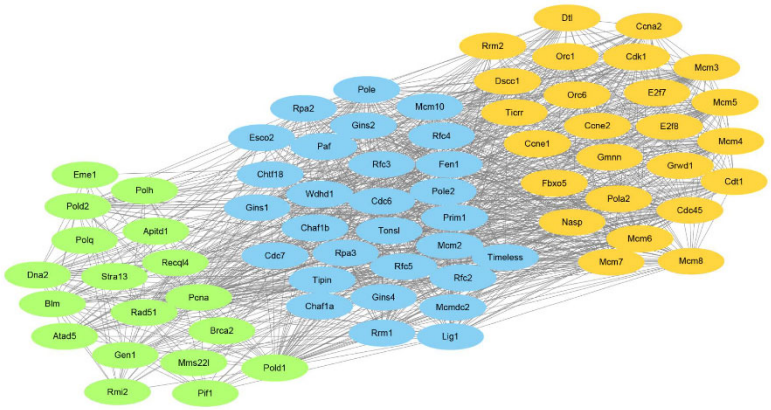

Figure S11. The PPI network complex of the 72 genes in the DNA repair pathway. The nodes meant proteins; the edges meant the interaction of proteins; three major clusters were identified by MCODE plug-in and labeled by green, blue and orange colors.

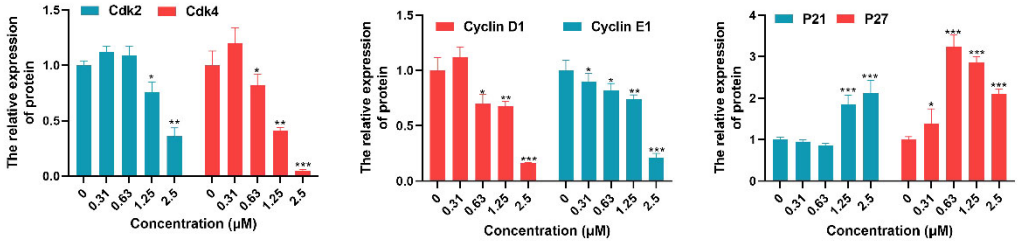

Figure S12. Relative protein expression levels of Cdk2, Cdk4, Cyclin D1, Cyclin E, P21 and P27 in B16-F10 cells after different treatments analyzed from Western blotting were shown in each bar. Each value was mean ± SD, n = 3. *** $p < 0.001$,** $p < 0.01$, * $p < 0.05$.