## Supporting Information

## Designed DNA Nanostructure grafting Erlotinib for Non-Small-Cell

## Lung Cancer Therapy

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## Materials and methods

## Materials

All oligonucleotides were purchased from Sangon Biotech (Shanghai, China). The single strands were stored in 96-well plates with concentration of $100 \mu \mathrm{M}$ and used without further purification. The concentration of each strand was estimated by measuring the UVVis absorption at 260 nm with Nanodrop (Thermo Fisher Scientific, USA). Erlotinib and Cuprous Bromide were purchased from Sigma Aldrich Co. Ltd. (China). Tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl] amine (TBAB), tert-Butanol (t-BuOH), Dimethyl sulfoxide (DMSO), 2-(4-Amidinophenyl)-6-indolecarbamidine dihydrochloride (DAPI) and 3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyltetrazolium Bromide (MTT) were purchased from J\&K Scientifc Ltd. (Shanghai, China). The Lyso Tracker Green DND-26 was purchased from (Thermo Fisher Scientific, USA). The RPMI 1640 medium, Dulbecco's modified Eagle's medium (DMEM), phosphate buffered saline (PBS), antibiotics (penicillin/streptomycin) and fetal bovine serum (FBS) were purchased from Gibco BRL (Grand Island, USA). The Annexin V-FITC/PI apoptosis detection kit was purchased from Invitrogen (China). Other chemical reagents were purchased from Servicebio Ltd. (Shanghai, China). The ultrapure water was used in all experiments.

## Measurements

Ultraviolet-Visible absorption (UV-Vis). The concentrations of each DNA strand were quantified by measuring the UV-Vis absorption of samples at 260 nm with Nanodrop (Thermo Fisher Scientific, USA). The slit-width was set as 1 nm with a scan speed of 480 $\mathrm{nm} \min ^{-1}$.

Dynamic light scattering (DLS). DLS measurements were conducted by a Zetasizer Nano ZS90 with 125 mW laser (Malvern Instruments Ltd., UK). The scattering angle was kept at $173^{\circ}$ and the wavelength was kept at 633 nm during the measurements.

Mass spectrometry (MS). Liquid chromatography-mass spectrometry of Erlotinib anchored T15 strand (T15-Er) was obtained using UPLC-Q plus ion-trap mass spectrometer through electron spray ionization (Thermo Electron, San Jose, USA). Exact mass spectrometry of the $\mathrm{T} 15-\mathrm{Er}$ was performed on a matrix assisted laser desorption/ionization time of flight mass spectrometer (MALDI-7090 TOF-TOF Mass Spectrometer, Shimadzu).

Transmission electron microscopy (TEM). TEM images were obtained by using a Tecnai G2 Spirit Biotwin transmission electron microscope (FEI, USA) at 120 KV .

Atomic force microscopy (AFM). AFM images were obtained by using a Dimension FastScan Bio AFM in peak force tapping mode to evaluate height.

## Methods

## Synthesis of Erlotinib anchored T15 DNA strand (T15-Er).

Erlotinib, Cuprous Bromide and TBAB were dissolved in DMSO solutions ( 10 mM ) and mixed with azide modified T15 DNA single strand ( $5^{\prime}$ - $\mathrm{N}_{3}$-TTTTTTTTTTTTTTT-3') solution $(100 \mu \mathrm{M})$ under gently shaking for 48 h at room temperature. ${ }^{1}$ Then the mixture was centrifuged under 3000 rpm at room temperature for three times to wash the free Erlotinib and other reactants out. After centrifuging, the concentration of the T15-Er strand was quantified by measuring the absorption at 260 nm by Nanodrop (Thermo Fisher Scientific, USA). Finally, the T15-Er strand was dissolved in $1 \times$ TE buffer to form a stock solution ranging from 100 to $500 \mu \mathrm{M}$.

## Synthesis of free 6x6x64nt DNA nanostructures.

This $6 \times 6 \times 64 n t$ DNA nanostructure was designed using Cadnano software and assembled by our previous reports. ${ }^{2,3}$ The specific DNA sequences and schematic illustrations were shown in the Supporting Information and Figure S1. All oligonucleotides were purchased from Sangon (Shanghai, China). For $6 x 6 x 64 n t$, all DNA strands were mixed with the concentration of 200 nM in the buffer solution of $0.5 \times \mathrm{TE}(5 \mathrm{mM}$ Tris- $\mathrm{HCl}, \mathrm{pH}=8.0,0.5$ mM EDTA) and 40 mM of $\mathrm{MgCl}_{2}$. The solution was then subjected to the following thermal annealing program: $95^{\circ} \mathrm{C}$ for $5 \mathrm{~min}, 85^{\circ} \mathrm{C}$ to $65^{\circ} \mathrm{C}$ for 1 h , then slowly cooling from $65{ }^{\circ} \mathrm{C}$ to $25{ }^{\circ} \mathrm{C}$ during a period of 36 h . For purification, MWCO 100 kDa ultrafiltration filter was used under the centrifuging speed of 3000 G for three times to remove the free DNA strands. The assembled nanostructure was characterized by agarose gel electrophoresis, TEM and AFM imaging. The concentrations of DNA nanostructure were determined by the UV absorption at 260 nm .

## Synthesis of Erlotinib-grafted 6x6x64nt DNA nanostructures (6x6x64nt-Er).

The DNA nanostructures with protruding handles were designed based on the free $6 \times 6 \times 64 \mathrm{nt}$ nanostructures. Some of the strands in the original design were extended with AAAAAAAAAAAAAAA (A15), so that the Erlotinib anchored T15 strand (T15-Er) can be hybridized via base-pairing. The DNA sequences and schematic illustrations used to
assemble $6 \times 6 \times 64 \mathrm{nt}-\mathrm{Er}$ DNA nanostructures with protruding handles were shown in the Supporting Information and Figure S1. The number of handle strands were 42. All oligonucleotides were purchased from Sangon (Shanghai, China). The synthesis procedures were same with the procedures of free $6 \times 6 \times 64 \mathrm{nt}$ nanostructure. Notably, the $\mathrm{T} 15-\mathrm{Er}$ strand was added to the mixture solutions before thermo annealing program (T15Er : Handle strands = 1:1). The loading efficiency of T15-Er was determined by UV-Vis absorption measurements at 332 nm .

## Non-denaturing PAGE gel analysis.

$17 \%$ non-denaturing PAGE gel was prepared by using the $3.75 \mathrm{~mL} 40 \%$ acrylamide (29:1, acrylamide/bisacrylamide) solution, $1 \times \mathrm{TAE}, 10 \mathrm{mM} \mathrm{Mg}{ }^{2+}$ buffer, 5.25 mL ultrapure water, $75 \mu \mathrm{~L}$ ammonium persulfate and $7.5 \mu \mathrm{~L}$ tetramethyl ethylenediamine (TEMED). Each sample was mixed with loading dye $(2 \mu \mathrm{~L})$ and then analyzed at $4^{\circ} \mathrm{C}(100 \mathrm{~V})$ for about 30 min . The bands were stained with EB, visualized by UV exposure ( 254 nm ), and photographed by UVP Bio-Imaging Systems.

## Agarose gel electrophoresis.

Each DNA sample was mixed with loading dye ( $2 \mu \mathrm{~L}$ ) and analyzed using $1 \%$ agarose gel at $4{ }^{\circ} \mathrm{C}(70 \mathrm{~V})$ for about 90 min in $1 \times \mathrm{TAE}, 10 \mathrm{mM} \mathrm{Mg}{ }^{2+}$ buffer. The bands were stained with EB, visualized by UV exposure ( 254 nm ), and photographed by UVP Bio-Imaging Systems. For sample purification, the target gel bands were excised and centrifuged at 5000 G for 5 min , the liquid phase was collected and stored at $4^{\circ} \mathrm{C}$ for TEM or AFM imaging.

## TEM imaging.

$10 \mu \mathrm{~L}$ solution of sample purified by agarose gel was spotted and absorbed for 10 min onto glow-discharged, carbon-coated copper grids. The grids were then stained for 1 min using the $1 \%$ aqueous uranyl acetate solution containing 20 mM NaOH . Imaging was performed using a FEI Tecnai G2 Spirit BioTwin electron microscope with a Gatan 832 CCD camera at 120 kV .

## AFM imaging.

$10 \mu \mathrm{~L}$ solution of sample purified by agarose gel was spotted and absorbed for 10 min onto freshly cleaved mica surface substrate (Electron Microscopy Sciences). Subsequently, the sample drop was washed off by $30 \mu \mathrm{~L}$ buffer solution containing $1 \times$ TE, magnesium chloride ( 2 mM ) and nickel chloride ( 1 mM ), then dried by compressed air. AFM imaging was performed using a Multimode System under peak force tapping
mode (Bruker).

## The stability of DNA nanostructures.

DNA nanostructures ( $200 \mathrm{~nm}, 20 \mu \mathrm{~L}$ ) were mixed with $10 \%$ fetal bovine serum (FBS) and incubated at $37{ }^{\circ} \mathrm{C}$ for predetermined time (from 0 to 48 h ). ${ }^{3}$ After incubation, all samples were analyzed by $1 \%$ agarose gel electrophoresis and TEM imaging.

## In vitro drug release behaviors.

In vitro Erlotinib release from the $6 x 6 x 64 \mathrm{nt}-\mathrm{Er}$ was measured by dialysis method. ${ }^{4}$ Briefly, $500 \mu \mathrm{~L}$ sample solutions were transferred into dialysis bags (MWCO: 1 kDa ) and then dialyzed against 20 mL different appointed buffer solutions PBS ( $\mathrm{pH}=7.4$ ) and PBS ( pH $=5.4$ ), respectively. The release process was conducted at $37^{\circ} \mathrm{C}$ with gentle shaking. At predetermined timepoints, aliquots ( $200 \mu \mathrm{~L}$ ) of the solution were taken out and equal volumes of corresponding fresh buffer solutions were added back into outside dialysate. The release contents of Er were evaluated by UV-Vis measurement at 332 nm on a microplate reader (TECAN, InfiniteM200, Switzerland).

## The intracellular degradation.

The A549 cells were incubated with Cy3 and Cy5 dual-labeled $6 \times 6 \times 64 n t-E r$ DNA nanostructures at concentration of 200 nM with the equal amount of Cy 3 and Cy 5 for 2 h , $4 \mathrm{~h}, 8 \mathrm{~h}$ and 12 h , respectively. Subsequently, the cells were stained with DAPI fluorescence dye for 15 min . Thereafter, the culture medium was removed and the cells were washed three times with PBS and the co-localization of Cy 3 and Cy 5 was visualized using confocal microscopy (Leica TCS SP8 STED $2.5 \times$ ) immediately.

## Cell culture.

A549 cells (human lung adenocarcinoma cell line), Helf (human embryonic lung fibroblast cell line), HeLa (cervical cancer cell line) and MCF-7 (pancreatic cancer cell line) were purchased from Chinese Academy of Sciences Institute of Cell Resource Center (Shanghai, China). A549 and Helf cells were cultured in RPMI 1640 (Roswell Park Memorial Institute 1640, Gibco BRL) medium; Hela and MCF-7 cells were cultured in Dulbecco's modified Eagle's medium (DMEM) containing 10\% FBS and antibiotics (50 units $\mathrm{mL}^{-1}$ penicillin and 50 units $\mathrm{mL}^{-1}$ streptomycin) in a humidified atmosphere containing $5 \% \mathrm{CO}_{2}$ at $37^{\circ} \mathrm{C}$ environment.

## In vitro cytotoxicity assay.

The cytotoxicity of different formulations of drug against A549 cell lines was investigated by MTT assay. Cells were seeded in 96-well plates and incubated for 24 h . The different formulations of drug were adjusted to equal Er concentration before they were added, then the cells were incubated with series concentration for 44 h . After that, $15 \mu \mathrm{~L}$ MTT solution ( $5 \mathrm{mg} \mathrm{mL}^{-1}$ in PBS) was added to each well and incubated for 4 h . Finally, the medium was carefully removed, then the formazan product was dissolved in DMSO ( $150 \mu \mathrm{~L}$ per well). The absorbance at 490 nm was measured by microplate reader (TECAN, InfiniteM200, Switzerland) to evaluate the cell viability. Each experiment was repeated at least three times.

## Immunogenic response assay.

The RAW 264.7 cells were seeded in 24 -well plates and cultured for 24 h . Then the RAW 264.7 cells were incubated with free $6 \times 6 \times 64 n t, 6 x 6 x 64 n t-A 15$ and $6 \times 6 \times 64 n t-E r$ at the concentration of DNA $(1 \mu \mathrm{M})$ for 24 h . The gene expression of TNF- $\alpha$, CD86, Arg-1 and CD206 were evaluated by the real-time PCR. Total mRNAs were extracted from RAW 264.7 cells and cDNAs were generated by using $5 \times$ PrimeScript RT Master Mix (Takara, China) according to the instructions from manufacturers. Real-time PCR was performed using TB Green Premix Ex Taq Kit (Takara).

## Cellular uptake studies of 6x6x64nt-Er DNA nanostructures.

Confocal laser scanning microcopy (CLSM) and flow cytometry were used to investigate the cell uptake behaviors of $6 \times 6 \times 64 \mathrm{nt}-\mathrm{Er}$ DNA nanostructures. For CLSM imaging, A549 and Hela cells were seeded in 24 -well culture plates and cultured for 24 h . Then the cells were incubated with Cy5 labeled T15-Er and $6 \times 6 \times 64 \mathrm{nt}-\mathrm{Er}$ DNA nanostructures at concentration of Cy5 with 250 nM with (equal amount of Cy5) for $2 \mathrm{~h}, 4 \mathrm{~h}, 8 \mathrm{~h}$ and 12 h , respectively. Subsequently, the cells were stained with DAPI fluorescence dye and Lyso Tracker Green DND-26 for 15 min . Thereafter, the culture medium was removed and the cells were washed three times with PBS and visualized using confocal microscopy (Leica TCS SP8 STED $2.5 \times$ ) immediately. For flow cytometry, A549 cells were seeded in 12well culture plates and cultured for 24 h . Then the cells were incubated with Cy5 labeled $\mathrm{T} 15-\mathrm{Er}$ and $6 \times 6 \times 64 \mathrm{nt}-\mathrm{Er}$ at concentration of Cy 5 with 250 nM (equal amount of Cy 5 ) for $2 \mathrm{~h}, 4 \mathrm{~h}, 8 \mathrm{~h}$ and 12 h , respectively. Thereafter, the culture medium was removed and the cells were washed three times with PBS. The amounts of intracellular fluorescent signal were quantified using flow cytometry system (LSRFortessa, BD, USA). Finally, the cell
populations were analyzed with FlowJo software (Tree Star, OR, USA).

## Cell apoptosis assay.

A549 cells were seeded in 24 -well plates and cultured for 24 h . Then the A549 cells were incubated with free Er, T15-Er and $6 \times 6 \times 64 n t-E r$ at the concentration of $\operatorname{Er}(15 \mu \mathrm{M})$ for 48 h. The different formulations of drug were adjusted to equal Er concentration before they were added. The untreated A549 cells were used as control. The apoptosis assays were performed using a combined staining with FITC-Annexin V/PI (FITC, fluorescein isothiocyanate, PI, propidium iodide) flow cytometry assay. Briefly, untreated and treated cells were suspended in annexin binding buffer, with the addition of FITC-labeled Annexin V and PI, and incubated at room temperature for 15 min . After incubation, the samples were analyzed by BD LSRFortessa ${ }^{\text {TM }}$ flow cytometry system. Finally, the cell populations were analyzed with FlowJo software (Tree Star, OR, USA).

## Western Blot assay.

A549 cells were seeded in 12-well plates and cultured for 24 h . Then the A549 cells were incubated with free Er, T15-Er and $6 \times 6 \times 64 n t-E r$ at the concentration of $\operatorname{Er}(15 \mu \mathrm{M})$ for 48 h. The different formulations of drug were adjusted to equal Er concentration before they were added. The cell lysates were separated by SDS-PAGE gel and proteins in the gel were transferred by the polyvinylidene difluoride (PVDF) membranes. Then, the membranes were incubated with primary antibodies against p-EGFR and GAPDH overnight at $4{ }^{\circ} \mathrm{C}$ and secondary antibodies for 2 h at room temperature. The binding of antibody was evaluated using ECL Prime Western Blotting Detection Reagent (GE Healthcare UK Ltd., UK) and the images were obtained by ChemiDoc XRS system. The expressions of proteins were examined by using Image Lab analysis.

## Tumor implantation.

Animal studies were conducted in accordance with the guidelines for the care and use of laboratory animals proved by the Animal Ethics Committee of Shanghai Jiao Tong University. All 6-week-old BALB/c female nude mice were purchased from Chinese Academy of Sciences (Shanghai, China). The suspensions of A549 cells were subcutaneously injected in flanks of female nude mice with $200 \mu \mathrm{~L}$ to established A549 xenograft-tumor model. The tumors were allowed to grow for a mean volume from 50 $\mathrm{mm}^{3}$ to $500 \mathrm{~mm}^{3}$ for in vivo biodistribution imaging experiments and antitumor studies, respectively. Tumor volumes were calculated by the following formula: tumor volume $=$ $0.5 \times \mathrm{ab}^{2}$, where a and b were the longest and the shortest diameters of the tumor.

## In vivo biodistribution studies.

In vivo biodistribution imaging was performed and analyzed using Bruker In-Vivo F PRO imaging system (Billerica, MA, USA) with 630 nm excitation wavelength and 680 nm emission wavelength. The A549 tumor-bearing nude mice were anesthetized with isoflurane and images were taken at predetermined timepoint with $1 \mathrm{~h}, 2 \mathrm{~h}, 4 \mathrm{~h}, 6 \mathrm{~h}, 8 \mathrm{~h}$, 12 h and 24 h after intravenous injection with Cy5 labeled T15-Er-Cy5 and 6x6x64nt-ErCy5 nanostructures. For the biodistribution studies, mice were sacrificed at 12 h and 24 h post-injection. Then the major organs and tumor tissues were harvested, washed with PBS and imaged using the same system.

## In vivo antitumor evaluation.

The A549 xenograft-bearing nude mice were randomly divided into four groups of three mice each when the tumor volume reached $50 \mathrm{~mm}^{3}$. PBS, free Er (dissolved in Tween 80/ethanol mixed solution and diluted with physiologic saline), T15-Er and $6 \times 6 \times 64 \mathrm{nt}-\mathrm{Er}$ were intravenously injected via the tail vein of the mice at the dose of $\operatorname{Er}\left(2.5 \mathrm{mg} \mathrm{kg}^{-1}\right.$, $200 \mu \mathrm{~L}$ ) every three days for 18 days. Tumor sizes and body weight were measured once every 3 days. The length (a) and width (b) of the tumors were measured by using the digital caliper every 3 days and calculated according to the formula: $\mathrm{V}\left(\mathrm{mm}^{3}\right)=1 / 2 \times \mathrm{a}(\mathrm{mm}) \times$ $\mathrm{b}(\mathrm{mm}) \times \mathrm{b}(\mathrm{mm})$. The body weight of mice was measured using an electronic balance at the time of each treatment. Mice were sacrificed on day of 18th and the tumor tissues, major organs were harvested for further hematoxylin and eosin (H\&E) staining, terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) staining and immunohistochemical assay.

## Serum biochemistry analysis.

All blood samples were collected and centrifuged at 5000 rpm for 15 min after the last treatment, then the supernatant of serum was harvested and analyzed by the serum biochemistry analysis according to the instructions from manufacturers.

## Histological studies and immunohistochemical analysis.

For histological and immunohistochemical analysis, major organs and tumor tissues were fixed in 4\% paraformaldehyde, then embedded in paraffins. Then the slices were stained with hematoxylin solution and eosin Y solution (H\&E), TUNEL and p-EGFR according to the instructions from manufacturers.

## Statistical analysis.

The experimental data were statistically analyzed by using the Student's t -test. $p$-values $<$ 0.05 were considered with the statistically significant. Besides, experimental data were reported as the mean $\pm$ standard deviations (SD) from at least 3 individual experiments.

## Supplementary Figures



Figure S1. Schematic illustration of the design of the three DNA nanostructures. Arrows indicated 3'-end of DNA. Functional strands colored in red were for fluorescent dye Cy5 loading, the number of red strands was 5. Functional strands colored in blue for Er loading. The single stranded DNA handles were extended from the $3^{\prime}$ ends of the blue strands, the number of blue strands (handle strands) was 42. In addition, to investigate the structure stability of $6 \times 6 \times 64 \mathrm{nt}$ inside of cells, fluorescent dye Cy 5 and Cy 3 were directly labeled at 5 '-ends of the strands colored in red and green, respectively.


Figure S2. LC-MS profiles of Erlotinib anchored T15 strand (T15-Er) in water solution. The retention time of T15-Er was 0.34 min . High purity of T15-Er was shown in the LCMS profiles.


Figure S3. MALDI-TOF spectrum of Er anchored T15 strand (T15-Er). MALDI-TOF spectrum was characterized on a MALDI-7090 TOF-TOF Mass Spectrometer. The target mass of $\mathrm{T} 15-\mathrm{Er}\left(\left[\mathrm{C}_{182} \mathrm{H}_{238} \mathrm{~N}_{37} \mathrm{O}_{111} \mathrm{P}_{15}+\mathrm{H}\right]^{+}\right)$was 5185.660 , which is consistent with the theoretical value of 5185.581. MALDI-TOF results demonstrated that azide modified T15 strand successfully conjugated with Erlotinib molecule.


Figure S4. TEM images, AFM images and DLS analysis of the series of $6 \times 6 \times 64 n t-b a s e d$ DNA nanostructures. (A) free $6 x 6 x 64 n t$ DNA nanostructure. (B) $6 x 6 x 64 n t-A 15$ DNA nanostructure. Scale bars: 25 nm .


Figure S5. The UV/Vis spectra of free Erlotinib and 6x6x64nt-Er nanostructures. The maximum absorption peak was shown at $332 \mathrm{~nm}\left(\lambda_{\max }=332 \mathrm{~nm}\right)$, which was not interfered with the characteristic absorption of 260 nm from DNA strands.


Figure S6. Cellular cytotoxicity of free $6 \times 6 \times 64 n$ DNA nanostructures against A549, Helf, HeLa and MCF-7 cells. Cells were incubated with DNA nanostructures at different concentrations with $100 \mathrm{nM}, 1 \mu \mathrm{M}$ and $2 \mu \mathrm{M}$ under $5 \% \mathrm{CO}_{2}$ at $37^{\circ} \mathrm{C}$ for 48 h .


Figure S7. Immunogenic gene expression of RAW 264.7 cells induced by the series of 6x6x64nt-based DNA nanostructures. RAW 264.7 Cells were incubated with DNA nanostructures at concentration of $1 \mu \mathrm{M}$ under $5 \% \mathrm{CO}_{2}$ at $37^{\circ} \mathrm{C}$ for 24 h .


Figure S8. Electrophoretic analysis of the stability of $6 \times 6 \times 64 n t-E r$. The $6 \times 6 \times 64 n t-E r$ nanostructures were incubated under $10 \% \mathrm{FBS}$ at $37{ }^{\circ} \mathrm{C}$ conditions for $2-48 \mathrm{~h}$ and analyzed by $1 \%(\mathrm{w} / \mathrm{w})$ agarose gel electrophoresis. The $6 \times 6 \times 64 \mathrm{nt}-\mathrm{Er}$ was relatively stable after incubation with $10 \%$ FBS for the first 4 h , while partially degraded after 8 h incubation, completely degraded after 24 h incubation. The control sample is the $6 \times 6 \times 64 n t-E r$ without FBS incubation.


Figure S9. TEM images of the $6 \times 6 \times 64 n t-E r$ nanostructures after incubation with $10 \%$ FBS collected at different reaction time. The results were in agreement with the electrophoresis analysis. Scale bars: 50 nm .


Figure S10. CLSM images of the intracellular integrity of $6 \times 6 \times 64 \mathrm{nt}-\mathrm{Er}$ dual-labeled with Cy5 (on the surface of DNA structure) and Cy3 (inside of DNA structure) at different timepoints. Scale bars: $5 \mu \mathrm{~m}$.


Figure S11. CLSM images of A549 cells incubated with Cy5-labeled DNA nanostructure ( $6 \times 6 \times 64 n t-E r-C y 5$ ) at different timepoints, as well as further stained with Lyso Tracker Green DND-26. The images demonstrated that $6 \times 6 \times 64 n t-E r$ were mainly distributed in cytoplasm of A549 cells. Scale bars: $5 \mu \mathrm{~m}$.


Figure S12. CLSM images of Hela cells incubated with Cy5-labeled DNA nanostructure (6x6x64nt-Er-Cy5) at different timepoints. Scale bars: $10 \mu \mathrm{~m}$.


Figure S13. Representative photographs of the A549 xenograft-bearing nude mice during the antitumor treatments.


Figure S14. Histological studies for the toxicity with different drug formulations in vivo.
Representative optical images of H\&E staining of heart, liver, spleen, lung and kidney.
Scale bar: $50 \mu \mathrm{~m}$.


Figure S15. Liver function related index (AST), and kidney function related indexes (UA and BUN). NS (no significant).

## DNA strands for 6x6x64nt-Er

| Name | Sequence (5'-3') | Note |
| :---: | :---: | :---: |
| [1,23] | CCAGGTTAAGTGGCTCAATCATACTCACGGTTAACTGTTGTGTCCTATAAAAAAAAAAAAAAA | Er handle |
| [1,39] | GTTTACTTAGGGATGGTACGAACTCAACGCACAAAAAAAAAAAAAAA | Er handle |
| [1,55] | GCTCGGGTAGTCTCAAGAAGATAGAGAGCATAAATTCGCTAAACCGGAAAAAAAAAAAAAAAA | Er handle |
| [1,71] | AAAGTATCCGCATCTCACTCAGTGATCGAGTAAAAAAAAAAAAAAAA | Er handle |
| [3,23] | TTCATGTCGCCTTTTCGAACGGTGACACACTTAAAAAAAAAAAAAAA | Er handle |
| [3,39] | GTGTTCATTCAGAGTAGCGGAAATATGGCCGCAAAAAAAAAAAAAAA | Er handle |
| [3,55] | TTCGGTGCGCAGCGGGCCGCCTGTAACGCTTAAAAAAAAAAAAAAAA | Er handle |
| [3,71] | ATCAGCCCGGGCTTTTGCTAATACGCTGAGCGAAAAAAAAAAAAAAA | Er handle |
| [5,39] | ATGCTGTTGTTGCGGGGTTTCTGAACCGGAACCCGGGCTAATGAAGCCAAAAAAAAAAAAAAA | Er handle |
| [5,71] | GTGACCCCAGAGACTGTCTGATGCACCGGGAGCCAGCCACTTAGCTGTAAAAAAAAAAAAAAA | Er handle |
| [6,8] | GTCAGTGTGATCGCGAAAAAAAAAAAAAAAA | Er handle |
| [7,23] | GTTCCCTCTAGCTAGGGTGATGCCAAAAGGGT | Core |
| [7,39] | GGATATGGAGCTGGAACGGCTCTGATTTCTAGTGACCTGGTATAATGGAAAAAAAAAAAAAAA | Er handle |
| [7,55] | CGGAGCTACCTGACCTCAATCATACGTCCCAC | Core |
| [7,71] | GGAAGGATTCATCCCCTTTAAGAATGATCGCAAAAAAAAAAAAAAAA | Er handle |
| [9,23] | CAGTCTTTGAGATGTTGAACATCTTTTGGTTG | Core |
| [9,39] | GCGTAAAGATCTCGCATTCTGGTGCCAAAACT | Core |
| [9,55] | GCCGACTCGTTCAAGCACTATTATCTGGCTAT | Core |
| [9,71] | AAAAGATGTCTGTCAGCCCAAGCTTAGCATAAAAAAAAAAAAAAAAA | Er handle |
| [11,23] | GCGGCTGGACGACCCCAAAAAAAAAAAAAAA | Er handle |
| [11,55] | GCCGTGCGACGACTGACCGTCGAGCCCTGCGCGACAAACGCATATCCT | Core |
| [11,71] | CGGCCCGCCAAATTAATAGTCGATTACGCTTCAAAAAAAAAAAAAAA | Er handle |
| [13,23] | GCCTAAAGGTCCTTCCACGGTAATCGGGGGTGACTCCGGCCTCCTTGGAAAAAAAAAAAAAAA | Er handle |
| [13,39] | TATATTAGCTTACCCACTCGCGTGGCACGTCT | Core |
| [13,55] | ACGACTCGTCGAACGAGGACTGTTCTACATAGTGACTTGGACGAGGTTAAAAAAAAAAAAAAA | Er handle |
| [13,71] | TCACTGGGCGCTATACAGGAAACTCGAGGGGCAAAAAAAAAAAAAAA | Er handle |
| [15,23] | TCCCTGTCTGTCGAGCCCAGCGACCACTTCTG | Core |
| [15,39] | GAGAAAGATGCGGTGGCAGTAGTTGTGATTAG | Core |
| [15,55] | CTTGGGGGTGATATACCTCACTAAACTCCTTC | Core |
| [15,71] | TAATGTGACTAAGCGTTAACTCCAAAGGAAACAAAAAAAAAAAAAAA | Er handle |
| [17,39] | CAGCTATCCCATATTCGATGTAAGCGGACATCTATGCGCCCGATATCC | Core |
| [17,71] | GTTCAAACTAGGGGGCTTCTGACCAAAGCTCATGAGAATTGTAAACAG | Core |
| [18,8] | GAACAGCTTAGAGCAGAAAAAAAAAAAAAAA | Er handle |
| [19,23] | TCAAGTTCGGATACGCTACCTATGGACGGGGA | Core |
| [19,39] | TATGCGACACCATGATCCGGATGAGTTATGAAGATCGTCATTGGGATAAAAAAAAAAAAAAAA | Er handle |
| [19,55] | TACAATCTCGAAGTAAAGCATAGCACCCTGCG | Core |
| [19,71] | AAGATAGGGTCACAGCAGTAATACCTCTACCTAAAAAAAAAAAAAAA | Er handle |
| [21,23] | TGTTGGACGTAAGCGTGAAATAACGACCAGAA | Core |
| [21,39] | AGCACGAGGATTATCACGTGTACCTCGAAATA | Core |
| [21,55] | ATCGTTAGTTTCTCGACTGTTCCGAAACAGGC | Core |


| [21,71] | AGCGGTAGCCTCCCACTTAACCTATGCCTTGGAAAAAAAAAAAAAAA | Er handle |
| :---: | :---: | :---: |
| [23,23] | TAACTGATTTTTCTCCTAAAAAAAAAAAAAAA | Er handle |
| [23,55] | GGTTCCGCTAGCTGATCTATGGTCCTTAATATAACCCTCGGAGGCAAG | Core |
| [23,71] | GGGAGAGGGTGAAACAGGCCACCTGGCTCGGGAAAAAAAAAAAAAAA | Er handle |
| [25,23] | GAGTGCCCCCTCGGCAGCCGCCTCGGTTATACTCGTCAAGCCTGCTTTAAAAAAAAAAAAAAA | Er handle |
| [ 25,39$]$ | CCATAGCTAACCCGATTGTGCATTCCACGTGA | Core |
| [ 25,55 ] | GTCGTACTTAAAGCAAACGTGGGAGTGCCCGAGCGTCTGAGGTATGGTAAAAAAAAAAAAAAA | Er handle |
| [25,71] | TTACCCACTATGTTGTCTCAAGTGCTAACAGTAAAAAAAAAAAAAAA | Er handle |
| [27,23] | ACTAATTATCCATAACTGTGCACGTCAGGGAT | Core |
| [27,39] | TCTCACCGGTGGCCGTTGCTACATCAGTTTCT | Core |
| [27,55] | TTGCACTCCTGGGGAAACTATACTTACGCACT | Core |
| [27,71] | GGTtTGGAGGGATTAGGCAATTGCTAGGTTGCAAAAAAAAAAAAAAA | Er handle |
| [29,39] | ATTGTAGGCACAATTTTTGATTCGATCACATACATGGGCAATAAAGCT | Core |
| [29,71] | GTAGCCTGAGGCGCGCAGCTGCACCGTGTCACCTTGATATTGAGGGAC | Core |
| [30,8] | ACCTCGTCATTCGGATAAAAAAAAAAAAAAA | Er handle |
| [31,23] | AAACCATACTGAGGGCAGTGGGCGAGATCGGCAAAAAAAAAAAAAAA | Er handle |
| [31,39] | TAATCATTAGTGCTCCCTTAGTTAGTTCATAGTTCATTAGGGGCGGAAAAAAAAAAAAAAAAA | Er handle |
| [31,55] | ATGGGCTGGTGCCCCACGTACAGTAACCAACCAAAAAAAAAAAAAAA | Er handle |
| [31,71] | GGTGTACCTGTGGGTAGGGCCGAGCGCTGGGCAAAAAAAAAAAAAAA | Er handle |
| [33,23] | TTACATGTGCAAGTGAAATATATGACTTGGTCAAAAAAAAAAAAAAA | Er handle |
| [33,39] | GACCAGATCTGCTAGAAACCACCAACATCCTCAAAAAAAAAAAAAAA | Er handle |
| [33,55] | CTTGACACCTTTCAATTTTTAGTAAACACCCAAAAAAAAAAAAAAAA | Er handle |
| [33,71] | ACAGAGCTGAACTTCCCATGGTCGTTCTACTGAAAAAAAAAAAAAAA | Er handle |
| [35,23] | TCGTATGATCATAGGAAAAAAAAAAAAAAAA | Er handle |
| [35,55] | TCAAACTAAATACAGCGTACCGCCAGTTCTTGTCCTTATTGGCGATCGAAAAAAAAAAAAAAA | Er handle |
| [35,71] | TGCATTCCAATGTTTGATGGCCGCGTGGCTTAAAAAAAAAAAAAAAA | Er handle |
| [0,15] | GTATGATTAAAA | Core |
| [0,47] | CTATCTTCATAGGACACAACAGTTAACCGTGACCAGCCGCGCGCAGGG | Core |
| [0,79] | AAAATCCGGTTTAGCGAATTTATGCTCTCGCACGGCTTAATTTG | Core |
| [2,15] | CACCGTTCAAAA | Core |
| [2,47] | ACAGGGGGGGTGCGTTGAGTTCGTAAAGTGTGTAAAGACTGTGCGAGAT | Core |
| [2,79] | AAAATACTCGATCACTGAGTTAAGCGTTGAGTCGGCCTGACAGA | Core |
| [4,15] | TAGCCCGGAAAA | Core |
| [4,47] | GTGGCTGGGCGGCCATATTTCCGCGGCTTCATGAGGGAACTTCCAGCT | Core |
| [4,79] | AAAACGCTCAGCGTATTAGCACAGCTAATAGCTCCGGGGGATGA | Core |
| [6,15] | ACACTGACAAAAAAAAGTTCCGGTTCAGAAACCCCGCAAC | Core |
| [6,31] | CAGAGCCGTCGCGATCCTTACATCGAATATGG | Core |
| [6,47] | CCAGGTCACTAGAAATAACAGCATCTCCCGGTGCATCAGACAGTCTCT | Core |
| [6,63] | TTCTTAAACCATTATAGGTCAGAAGCCCCCTA | Core |
| [6,79] | AAAATGCGATCAGGGGTCACAAAA | Core |


| [8,15] | GGCATCACAAAAAAAAGAAAAGGCGACATGAATACTCTGA | Core |
| :---: | :---: | :---: |
| [8,31] | CACCAGAAACCCTTTTGACAGGGACCACCGCA | Core |
| [8,47] | TATGATTGAGTTTTGGATGAACACCCCGCTGCGCACCGAAAAAAGCCC | Core |
| [8,63] | AGCTTGGGGTGGGACGCCCCCAAGACGCTTAG | Core |
| [8,79] | AAAATTATGCTAGGGCTGATAAAA | Core |
| [10,15] | AGATGTTCAAAAAAAAGAGCCACTTAACCTGGCCATCCCT | Core |
| [10,31] | CGTTTGTCCAACCAAACTTTAGGCTGGGTAAG | Core |
| [10,47] | ATAATAGTAGGATATGAAGTAAACTTGAGACTACCCGAGCGAGATGCG | Core |
| [10,63] | ATCGACTAATAGCCAGCGAGTCGTGTATAGCG | Core |
| [10,79] | AAAAGAAGCGTAGATACTTTAAAA | Core |
| [12,15] | AtTACCGTAAAAAAAAGGGGTCGT | Core |
| [12,31] | GCCGGAGTCACCCCCGATCAGTTAATATTAAG | Core |
| [12,47] | AACAGTCCCCAAGGAGCTCGACGGTCAGTCGT | Core |
| [12,63] | CCAAGTCACTATGTAGGCGGAACCTGTTTCAC | Core |
| [12,79] | AAAAAACCTCGTGCGGGCCGAAAA | Core |
| [14,15] | GTCGCTGGAAAAAAAAAACATCTC | Core |
| [14,31] | CACGCGAGCAGAAGTGGTCCAACATGATAATC | Core |
| [14,47] | TTAGTGAGAGACGTGCCTTTACGCGCTTGAAC | Core |
| [14,63] | AGTTTCCTGAAGGAGTCTAACGATGTGGGAGG | Core |
| [14,79] | AAAAGCCCCTCGCATCTTTTAAAA | Core |
| [16,15] | GGCGCATAAAAAAAAACCTAGCTA | Core |
| [16,31] | AACTACTGGGATATCGGAACTTGAATCATGGT | Core |
| [16,47] | AATTCTCACTAATCACCCATATCCAGGTCAGG | Core |
| [16,63] | TGGAGTTACTGTTTACAGATTGTAGCTGTGAC | Core |
| [16,79] | AAAAGTTTCCTTATCCTTCCAAAA | Core |
| [18,15] | AGCTGTTCAAAAAAAAGATGTCCG | Core |
| [18,31] | TCATCCGGCTGCTCTACGAATCAAAAATTGTG | Core |
| [18,47] | TGACGATCTTCATAACGATAGCTGTGAGCTTT | Core |
| [18,63] | GTATTACTTATCCCAAGTGCAGCTGCGCGCCT | Core |
| [18,79] | AAAAAGGTAGAGGTTTGAACAAAA | Core |
| [20,15] | CATAGGTAAAAAAAAAGCTCGACA | Core |
| [20,31] | GGTACACGTCCCCGTCTAATTAGTACGGCCAC | Core |
| [20,47] | GCTATGCTTATTTCGATCTTTCTCGTATATCA | Core |
| [20,63] | TAGGTTAACGCAGGGTGAGTGCAACTAATCCC | Core |
| [20,79] | AAAACCAAGGCATCACATTAAAAA | Core |
| [22,15] | GTTATTTCAAAAAAAAGGAAGGAC | Core |
| [22,31] | CGAGGGTTTTCTGGTCGGGCACTCATCGGGTT | Core |
| [22,47] | CGGAACAGCTTGCCTCCTAATATATCGTTCGA | Core |


| [22,63] | AGGTGGCCGCCTGTTTAGTACGACACAACATA | Core |
| :---: | :---: | :---: |
| [22,79] | AAAACCCGAGCCCCCAGTGAAAAA | Core |
| [24,15] | GAGGCGGCAAAAAAAAAGGAGAAA | Core |
| [24,31] | CTTGACGAGTATAACCTCATACGACAAGAACTGGCGGTACGCTGTATT | Core |
| [24,47] | TCCCACGTAAAGCAGGGACCATAGATCAGCTA | Core |
| [24,63] | TCAGACGCTCGGGCACTAGTTTGACAAACATTGGAATGCAAAAA | Core |
| [24,79] | AAAAACCATACCCCTCTCCCAAAA | Core |
| [26,15] | CGTGCACAAAAAAAAAACGCTTAC | Core |
| [26,31] | AATGCACAATCCCTGAACATGTAATCTAGCAGATCTGGTCATTGAAAG | Core |
| [26,47] | AGTATAGTTCACGTGGCTCGTGCTTCGAGAAA | Core |
| [26,63] | CACTTGAGAGTGCGTAGTGTCAAGGGAAGTTCAGCTCTGTAAAA | Core |
| [26,79] | AAAAACTGTTAGCTACCGCTAAAA | Core |
| [28,15] | TGCCCATGAAAAAAAAGCGTATCC | Core |
| [28,31] | ATGTAGCAAGCTTTATTATGGTTTGGAGCACTAATGATTATGGGGCAC | Core |
| [28,47] | ATATCAAGAGAAACTGGTCGCATATTACTTCG | Core |
| [28,63] | GCAATTGCGTCCCTCACAGCCCATTACCCACAGGTACACCAAAA | Core |
| [28,79] | AAAAGCAACCTACCTATCTTAAAA | Core |
| [30,31] | TAACTAAGATCCGAATGACGAGGTAAAAAAAATATGTGAT | Core |
| [30,63] | CTCGGCCCTTCCGCCCCTAATGAACTATGAACCCTACAATGTGACACG | Core |
| [30,79] | AAAAGCCCAGCGCAGGCTACAAAA | Core |
| [31,0] | AAAAGCCCTCAG | Core |
| [32,31] | TGGTGGTTGCCGATCTCGCCCACTAAAAAAAAGTTATGGA | Core |
| [32,63] | CGACCATGGGTTGGTTACTGTACGGAGGATGTCGGTGAGATTCCCCAG | Core |
| [32,79] | AAAACAGTAGAATCCAAACCAAAA | Core |
| [33,0] | AAAATCACTTGC | Core |
| [34,31] | AATAAGGAGACCAAGTCATATATTAAAAAAAATGCCGAGG | Core |
| [34,63] | GCGGCCATTGGGTGTTTACTAAAACGATCGCCAGCTATGGTTGCTTTA | Core |
| [34,79] | AAAATAAGCCACGTGGGTAAAAAA | Core |
| [35,0] | AAAATCCTATGA | Core |
| Cy5 sin | rand Cy5-ATTTTATTTCGGAGCGAAGC | Cy5 |

DNA strands for $\mathbf{6 x 6 x} \mathbf{6 4 n t}$

| Name | Sequence (5'-3') | Note |
| :---: | :---: | :---: |
| [1,23] | CCAGGTTAAGTGGCTCAATCATACTCACGGTTAACTGTTGTGTCCTAT | Core |
| [1,39] | GTTTACTTAGGGATGGTACGAACTCAACGCAC | Core |
| [1,55] | GCTCGGGTAGTCTCAAGAAGATAGAGAGCATAAATTCGCTAAACCGGA | Core |
| [1,71] | AAAGTATCCGCATCTCACTCAGTGATCGAGTA | Core |
| [3,23] | TTCATGTCGCCTTTTCGAACGGTGACACACTT | Core |
| [3,39] | GTGTTCATTCAGAGTAGCGGAAATATGGCCGC | Core |
| [3,55] | TTCGGTGCGCAGCGGGCCGCCTGTAACGCTTA | Core |
| [3,71] | ATCAGCCCGGGCTTTTGCTAATACGCTGAGCG | Core |
| [5,39] | ATGCTGTTGTTGCGGGGTTTCTGAACCGGAACCCGGGCTAATGAAGCC | Core |
| [5,71] | GTGACCCCAGAGACTGTCTGATGCACCGGGAGCCAGCCACTTAGCTGT | Core |
| [6,8] | GTCAGTGTGATCGCGA | Core |
| [7,23] | GTTCCCTCTAGCTAGGGTGATGCCAAAAGGGT | Core |
| [7,39] | GGATATGGAGCTGGAACGGCTCTGATTTCTAGTGACCTGGTATAATGG | Core |
| [7,55] | CGGAGCTACCTGACCTCAATCATACGTCCCAC | Core |
| [7,71] | GGAAGGATTCATCCCCTTTAAGAATGATCGCA | Core |
| [9,23] | CAGTCTTTGAGATGTTGAACATCTTTTGGTTG | Core |
| [9,39] | GCGTAAAGATCTCGCATTCTGGTGCCAAAACT | Core |
| [9,55] | GCCGACTCGTTCAAGCACTATTATCTGGCTAT | Core |
| [9,71] | AAAAGATGTCTGTCAGCCCAAGCTTAGCATAA | Core |
| [11,23] | GCGGCTGGACGACCCC | Core |
| [11,55] | GCCGTGCGACGACTGACCGTCGAGCCCTGCGCGACAAACGCATATCCT | Core |
| [11,71] | CGGCCCGCCAAATTAATAGTCGATTACGCTTC | Core |
| [13,23] | GCCTAAAGGTCCTTCCACGGTAATCGGGGGTGACTCCGGCCTCCTTGG | Core |
| [13,39] | TATATTAGCTTACCCACTCGCGTGGCACGTCT | Core |
| [13,55] | ACGACTCGTCGAACGAGGACTGTTCTACATAGTGACTTGGACGAGGTT | Core |
| [13,71] | TCACTGGGCGCTATACAGGAAACTCGAGGGGC | Core |
| [15,23] | TCCCTGTCTGTCGAGCCCAGCGACCACTTCTG | Core |
| [15,39] | GAGAAAGATGCGGTGGCAGTAGTTGTGATTAG | Core |
| [15,55] | CTTGGGGGTGATATACCTCACTAAACTCCTTC | Core |
| [15,71] | TAATGTGACTAAGCGTTAACTCCAAAGGAAAC | Core |
| [17,39] | CAGCTATCCCATATTCGATGTAAGCGGACATCTATGCGCCCGATATCC | Core |
| [17,71] | GTTCAAACTAGGGGGCTTCTGACCAAAGCTCATGAGAATTGTAAACAG | Core |
| [18,8] | GAACAGCTTAGAGCAG | Core |
| [19,23] | TCAAGTTCGGATACGCTACCTATGGACGGGGA | Core |
| [19,39] | TATGCGACACCATGATCCGGATGAGTTATGAAGATCGTCATTGGGATA | Core |
| [19,55] | TACAATCTCGAAGTAAAGCATAGCACCCTGCG | Core |
| [19,71] | AAGATAGGGTCACAGCAGTAATACCTCTACCT | Core |
| [21,23] | TGTTGGACGTAAGCGTGAAATAACGACCAGAA | Core |
| [21,39] | AGCACGAGGATTATCACGTGTACCTCGAAATA | Core |
| [21,55] | ATCGTTAGTTTCTCGACTGTTCCGAAACAGGC | Core |


| [21,71] | AGCGGTAGCCTCCCACTTAACCTATGCCTTGG | Core |
| :---: | :---: | :---: |
| [23,23] | TAACTGATTTTCTCCT | Core |
| [23,55] | GGTTCCGCTAGCTGATCTATGGTCCTTAATATAACCCTCGGAGGCAAG | Core |
| [23,71] | GGGAGAGGGTGAAACAGGCCACCTGGCTCGGG | Core |
| [25,23] | GAGTGCCCCCTCGGCAGCCGCCTCGGTTATACTCGTCAAGCCTGCTTT | Core |
| [ 25,39$]$ | CCATAGCTAACCCGATTGTGCATTCCACGTGA | Core |
| [25,55] | GTCGTACTTAAAGCAAACGTGGGAGTGCCCGAGCGTCTGAGGTATGGT | Core |
| [25,71] | TTACCCACTATGTTGTCTCAAGTGCTAACAGT | Core |
| [27,23] | ACTAATTATCCATAACTGTGCACGTCAGGGAT | Core |
| [27,39] | TCTCACCGGTGGCCGTTGCTACATCAGTTTCT | Core |
| [27,55] | TTGCACTCCTGGGGAAACTATACTTACGCACT | Core |
| [27,71] | GGTTTGGAGGGATTAGGCAATTGCTAGGTTGC | Core |
| [29,39] | ATTGTAGGCACAATTTTTGATTCGATCACATACATGGGCAATAAAGCT | Core |
| [29,71] | GTAGCCTGAGGCGCGCAGCTGCACCGTGTCACCTTGATATTGAGGGAC | Core |
| [30,8] | ACCTCGTCATTCGGAT | Core |
| [31,23] | AAACCATACTGAGGGCAGTGGGCGAGATCGGC | Core |
| [31,39] | TAATCATTAGTGCTCCCTTAGTTAGTTCATAGTTCATTAGGGGCGGAA | Core |
| [31,55] | ATGGGCTGGTGCCCCACGTACAGTAACCAACC | Core |
| [31,71] | GGTGTACCTGTGGGTAGGGCCGAGCGCTGGGC | Core |
| [33,23] | TTACATGTGCAAGTGAAATATATGACTTGGTC | Core |
| [33,39] | GACCAGATCTGCTAGAAACCACCAACATCCTC | Core |
| [33,55] | CTTGACACCTTTCAATTTTTAGTAAACACCCA | Core |
| [33,71] | ACAGAGCTGAACTTCCCATGGTCGTTCTACTG | Core |
| [35,23] | TCGTATGATCATAGGA | Core |
| [35,55] | TCAAACTAAATACAGCGTACCGCCAGTTCTTGTCCTTATTGGCGATCG | Core |
| [35,71] | TGCATTCCAATGTTTGATGGCCGCGTGGCTTA | Core |
| [0,15] | GTATGATTTTTTTTTTT | Core |
| [0,47] | CTATCTTCATAGGACACAACAGTTAACCGTGACCAGCCGCGCGCAGGG | Core |
| [0,79] | TTTTTTTTTTCCGGTTTAGCGAATTTATGCTCTCGCACGGCTTAATTTG | Core |
| [2,15] | CACCGTTCTtTttttt | Core |
| [2,47] | ACAGGCGGGTGCGTTGAGTTCGTAAAGTGTGTAAAGACTGTGCGAGAT | Core |
| [2,79] | TTTTTTTTTACTCGATCACTGAGTTAAGCGTTGAGTCGGCCTGACAGA | Core |
| [4,15] | TAGCCCGGTTTTTTTTT | Core |
| [4,47] | GTGGCTGGGCGGCCATATTTCCGCGGCTTCATGAGGGAACTTCCAGCT | Core |
| [4,79] | TTTTTTTTCGCTCAGCGTATTAGCACAGCTAATAGCTCCGGGGGATGA | Core |
| [6,15] | ACACTGACTTTTTTTTTTTTTTTTTGTTCCGGTTCAGAAACCCCGCAAC | Core |
| [6,31] | CAGAGCCGTCGCGATCCTTACATCGAATATGG | Core |
| [6,47] | CCAGGTCACTAGAAATAACAGCATCTCCCGGTGCATCAGACAGTCTCT | Core |


| [6,63] | TTCTTAAACCATTATAGGTCAGAAGCCCCCTA | Core |
| :---: | :---: | :---: |
| [6,79] | TTTTTTTTTGGCGATCAGGGGTCACTTTTTTTTGCTTCGCTCCGAAATAAAAT | Cy5 handle |
| [8,15] | GGCATCACTTTTTTTTTTTTTTTTGAAAAGGCGACATGAATACTCTGA | Core |
| [8,31] | CACCAGAAACCCTTTTGACAGGGACCACCGCA | Core |
| [8,47] | TATGATTGAGTTTTGGATGAACACCCCGCTGCGCACCGAAAAAAGCCC | Core |
| [8,63] | AGCTTGGGGTGGGACGCCCCCAAGACGCTTAG | Core |
| [8,79] | TTTTTTITTTAATGCTAGGGCTGATTTTTTTTTT | Core |
| [10,15] | AGATGTTCTTTTTTTTTTTTTTTTGAGCCACTTAACCTGGCCATCCCT | Core |
| [10,31] | CGTTTGTCCAACCAAACTTTAGGCTGGGTAAG | Core |
| [10,47] | ATAATAGTAGGATATGAAGTAAACTTGAGACTACCCGAGCGAGATGCG | Core |
| [10,63] | ATCGACTAATAGCCAGCGAGTCGTGTATAGCG | Core |
| [10,79] | TTTTTTTTTGAAGCGTAGATACTTTTTTTTTTTT | Core |
| [12,15] | ATTACCGTTTTTTTTTTTTTTTTTGGGGTCGTGCTTCGCTCCGAAATAAAAT | Cy5 handle |
| [12,31] | GCCGGAGTCACCCCCGATCAGTTAATATTAAG | Core |
| [12,47] | AACAGTCCCCAAGGAGCTCGACGGTCAGTCGTGCTTCGCTCCGAAATAAAAT | Cy5 handle |
| [12,63] | CCAAGTCACTATGTAGGCGGAACCTGTTTCAC | Core |
| [12,79] | TTTTTTTTTAACCTCGTGCGGGCCGTTTTTTTTT | Core |
| [14,15] | GTCGCTGGTtTTTTTTTTTTTTTTTAACATCTC | Core |
| [14,31] | CACGCGAGCAGAAGTGGTCCAACATGATAATC | Core |
| [14,47] | TTAGTGAGAGACGTGCCTTTACGCGCTTGAAC | Core |
| [14,63] | AGTTTCCTGAAGGAGTCTAACGATGTGGGAGG | Core |
| [14,79] | TTTTTTTTGCCCCTCGCATCTTTTTTTTTTTT | Core |
| [16,15] | GGCGCATATTTTTTTTTTTTTTTTTCCTAGCTA | Core |
| [16,31] | AACTACTGGGATATCGGAACTTGAATCATGGT | Core |
| [16,47] | AATTCTCACTAATCACCCATATCCAGGTCAGG | Core |
| $[16,63]$ | TGGAGTTACTGTtTACAGATTGTAGCTGTGAC | Core |
| [16,79] | TTTTTTTTGTTTCCTTATCCTTCCTTTTTTTT | Core |
| [18,15] | AGCTGTTCTTTTTTTTTTTTTTTTTGATGTCCG | Core |
| [18,31] | TCATCCGGCTGCTCTACGAATCAAAAATTGTG | Core |
| [18,47] | TGACGATCTTCATAACGATAGCTGTGAGCTTT | Core |
| [18,63] | GTATTACTTATCCCAAGTGCAGCTGCGCGCCT | Core |
| [18,79] |  | Core |
| [20,15] | CATAGGTATTTTTTTTTTTTTTTTTGCTCGACA | Core |
| [20,31] | GGTACACGTCCCCGTCTAATTAGTACGGCCAC | Core |
| [20,47] | GCTATGCTTATTTCGATCTTTCTCGTATATCA | Core |
| [20,63] | TAGGTTAACGCAGGGTGAGTGCAACTAATCCC | Core |
| [20,79] | TTTTTTTTTCCAAGGCATCACATTATTTTTTTTT | Core |
| [22,15] | GTTATTTCTTTTTTTTTTTTTTTTTGGAAGGAC | Core |


| [22,31] | CGAGGGTTTTCTGGTCGGGCACTCATCGGGTT | Core |
| :---: | :---: | :---: |
| [22,47] | CGGAACAGCTTGCCTCCTAATATATCGTTCGA | Core |
| [22,63] | AGGTGGCCGCCTGTTTAGTACGACACAACATA | Core |
| [22,79] | TTTTTTTTCCCGAGCCCCCAGTGATTTTTTTT | Core |
| [24,15] | GAGGCGGCtTTTTTTTTTTTTTTTTAGGAGAAA | Core |
| [24,31] | CTTGACGAGTATAACCTCATACGACAAGAACTGGCGGTACGCTGTATT | Core |
| [24,47] | TCCCACGTAAAGCAGGGACCATAGATCAGCTAGCTTCGCTCCGAAATAAAAT | Cy5 handle |
| [24,63] | TCAGACGCTCGGGCACTAGTTTGACAAACATTGGAATGCATTTTTTTT | Core |
| [24,79] | TTTTTTTTACCATACCCCTCTCCCTTTTTTTT | Core |
| [26,15] | CGTGCACATTTTTTTTTTTTTTTTTACGCTTAC | Core |
| [26,31] | AATGCACAATCCCTGAACATGTAATCTAGCAGATCTGGTCATTGAAAG | Core |
| [26,47] | AGTATAGTTCACGTGGCTCGTGCTTCGAGAAA | Core |
| [26,63] | CACTTGAGAGTGCGTAGTGTCAAGGGAAGTTCAGCTCTGTtTTTTTTT | Core |
| [26,79] | Tttttittactattagctaccgettttittte | Core |
| [28,15] | TGCCCATGTTTTTTTITTTTTTTTTGGGTATCC | Core |
| [28,31] | ATGTAGCAAGCTTTATTATGGTTTGGAGCACTAATGATTATGGGGCAC | Core |
| [28,47] | ATATCAAGAGAAACTGGTCGCATATTACTTCG | Core |
| [28,63] | GCAATTGCGTCCCTCACAGCCCATTACCCACAGGTACACCTTTTTTTT | Core |
| [28,79] | TTTTTTTTGGAACCTACCTATCTTTTTTTTTT | Core |
| [30,31] | TAACTAAGATCCGAATGACGAGGTTTTTTTTTTTTTTTTTTTAATGTGAT | Core |
| [30,63] | CTCGGCCCTTCCGCCCCTAATGAACTATGAACCCTACAATGTGACACG | Core |
| [30,79] | TTTTTTTTTGCCCAGCGCAGGCTACTTTTTTTTT | Core |
| [31,0] | TTTTTTTTGCCCTCAG | Core |
| [32,31] | TGGTGGTTGCCGATCTCGCCCACTITTTTTTTTTTTTTTTTGTTATGGA | Core |
| [32,63] | CGACCATGGGTTGGTTACTGTACGGAGGATGTCGGTGAGATTCCCCAG | Core |
| [32,79] |  | Core |
| [33,0] | TTTTTTTTTTCACTTGC | Core |
| [34,31] | AATAAGGAGACCAAGTCATATATTTTTTTTTTTTTTTTTTTGCCGAGG | Core |
| [34,63] | GCGGCCATTGGGTGTTTACTAAAACGATCGCCAGCTATGGTTGCTTTA | Core |
| [34,79] | TTTTTTTTTTAAGCCACGTGGGTAATTTTTTTTGCTTCGCTCCGAAATAAAAT | Cy5 handle |
| [35,0] | Ttttttitticctatga | Core |
| Cy5 single strand | Cy5-ATtTTATTTCGGAGCGAAGC | Cy5 labeled strand |

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