

# Supporting Information

Remission of lymphoblastic leukaemia in an intravascular fluidic environment by pliable drug carrier with a sliding target ligand

Donghyun Jang<sup>1,2</sup>, Yeong Mi Lee<sup>1,2</sup>, Jaehyun Lee<sup>3</sup>, Junsang Doh<sup>3,4</sup> and Won Jong Kim<sup>1,2,\*</sup>

<sup>1</sup> Center for Self-Assembly and Complexity, Institute for Basic Science (IBS), Pohang 37673, Republic of Korea

<sup>2</sup> Department of Chemistry, Pohang University of Science and Technology (POSTECH), Pohang 37673, Republic of Korea

<sup>3</sup> School of Interdisciplinary Bioscience and Bioengineering (I-Bio), Pohang University of Science and Technology (POSTECH), Pohang, 37673, Republic of Korea

<sup>4</sup> Department of Mechanical Engineering, Pohang University of Science and Technology (POSTECH), Pohang, 37673, Republic of Korea

## Contents

### **1. Supplementary Figures .....S3**

#### **Supplementary Figure 1**

Synthetic schemes of DNA-CD and PRs.....S3

#### **Supplementary Figure 2**

Confirmation of  $\alpha$ CD-SH by <sup>1</sup>H NMR spectroscopy.....S4

#### **Supplementary Figure 3**

HPLC data of DNA-CD.....S4

#### **Supplementary Figure 4**

GPC data of PEG and PRs.....S5

#### **Supplementary Figure 5**

DLS size measurement of various PRNCs.....S6

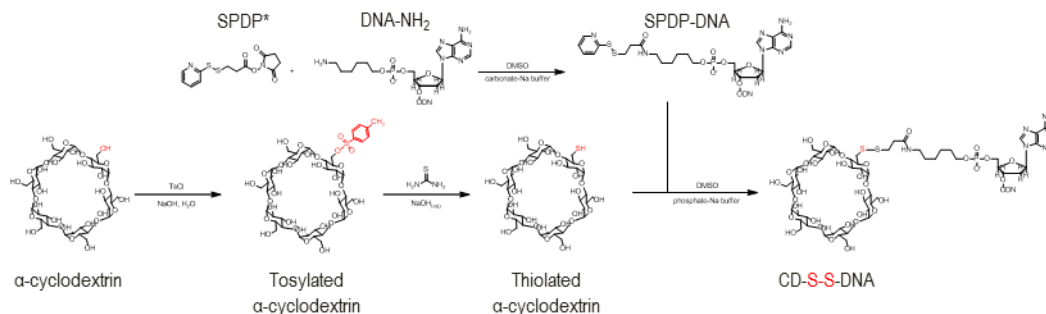
#### **Supplementary Figure 6**

Serum stability of PRNC.....S6

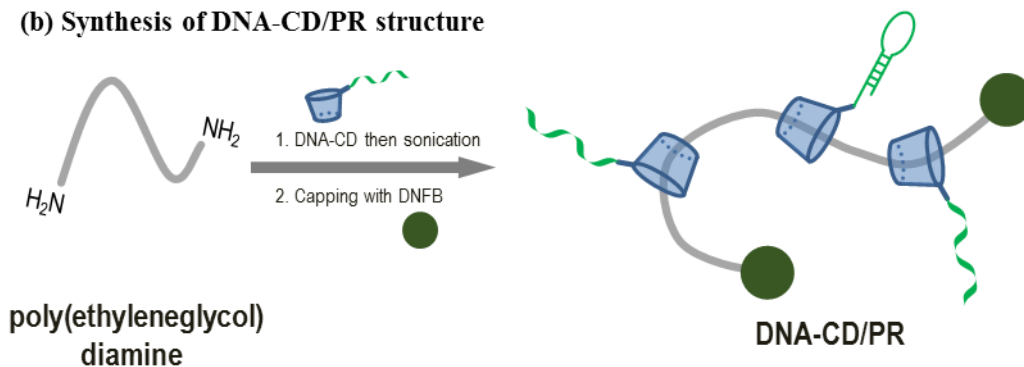
<b>Supplementary Figure 7</b>	
TEM image of various PRNCs.....	S7
<b>Supplementary Figure 8</b>	
CD spectra of i-motif DNA in different pH.....	S8
<b>Supplementary Figure 9</b>	
Drug loading properties of PRNC.....	S8
<b>Supplementary Figure 10</b>	
Haemolysis test of PRNC and control groups.....	S9
<b>Supplementary Figure 11</b>	
Release of DOX from S(+)/T(+)/P(-) PRNC in acidic condition .....	S9
<b>Supplementary Figure 12</b>	
Detailed flow cytometry data of <i>in vivo</i> targeting efficiency test.....	S10
<b>Supplementary Figure 13</b>	
Additional images of <i>in vivo</i> cytotoxicity evaluation .....	S11
<b>2. Supplementary Tables .....</b>	<b>S12</b>
<b>Supplementary Table 1</b>	
Sequences of DNAs used in this experiment.....	S12
<b>Supplementary Table 2</b>	
Types of PRNCs used in this experiment.....	S12
<b>Supplementary Table 3</b>	
IC <sub>50</sub> values of DOX and DOX loaded PRNCs.....	S13
<b>Supplementary Table 4</b>	
ROI fluorescence intensity calculation of microscopic images.....	S13

# 1. Supplementary Figures

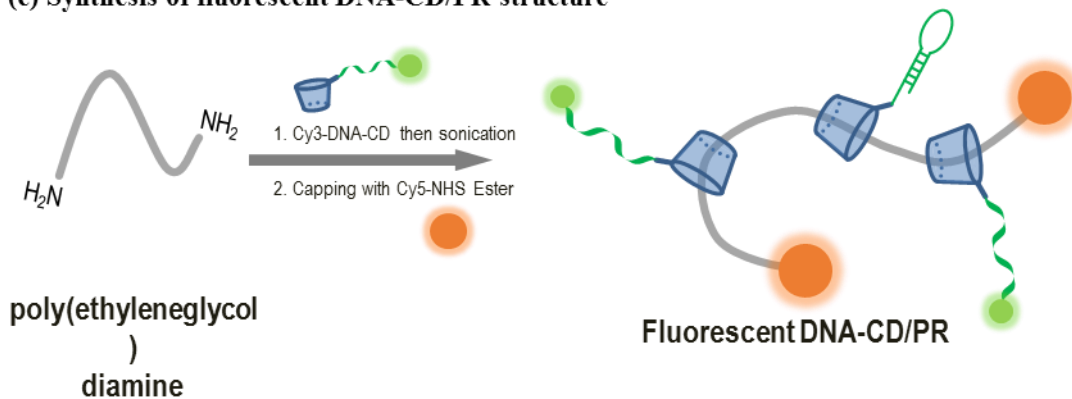
## (a) Synthesis of DNA-CD



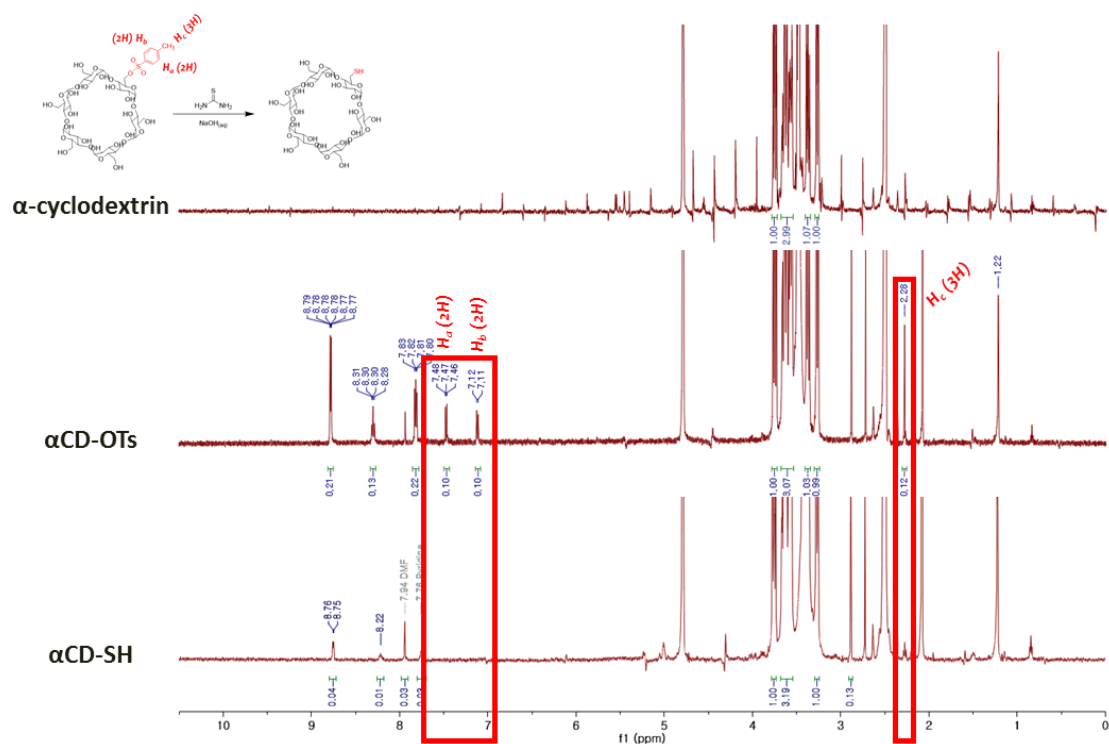
## (b) Synthesis of DNA-CD/PR structure



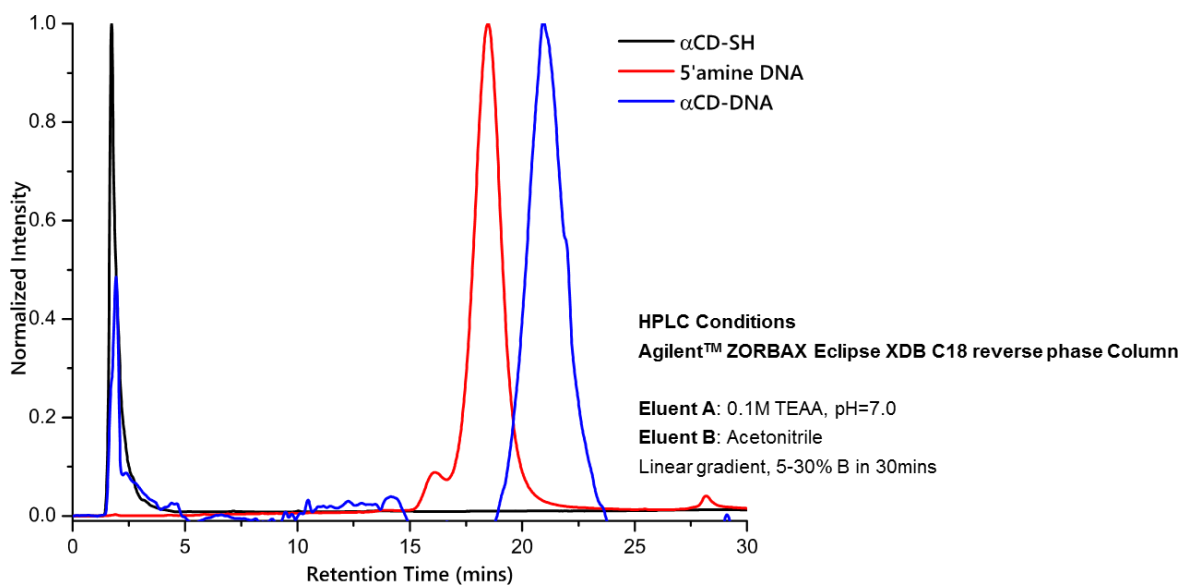
## (c) Synthesis of fluorescent DNA-CD/PR structure



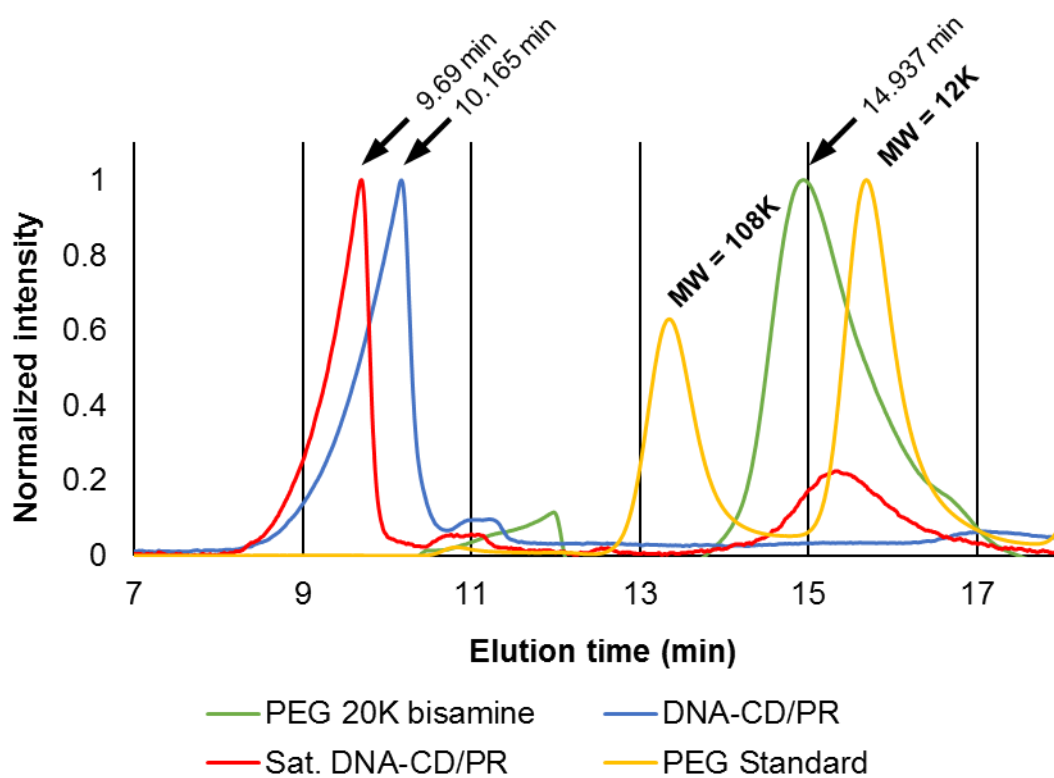
**Supplementary Figure 1** (a) Experimental schemes for synthesis of  $\alpha$ CD-SH and DNA-CD. (b) Preparation of DNA-CD/PR by capping strategy. (c) Preparation of the fluorescently labelled DNA-CD/PR.



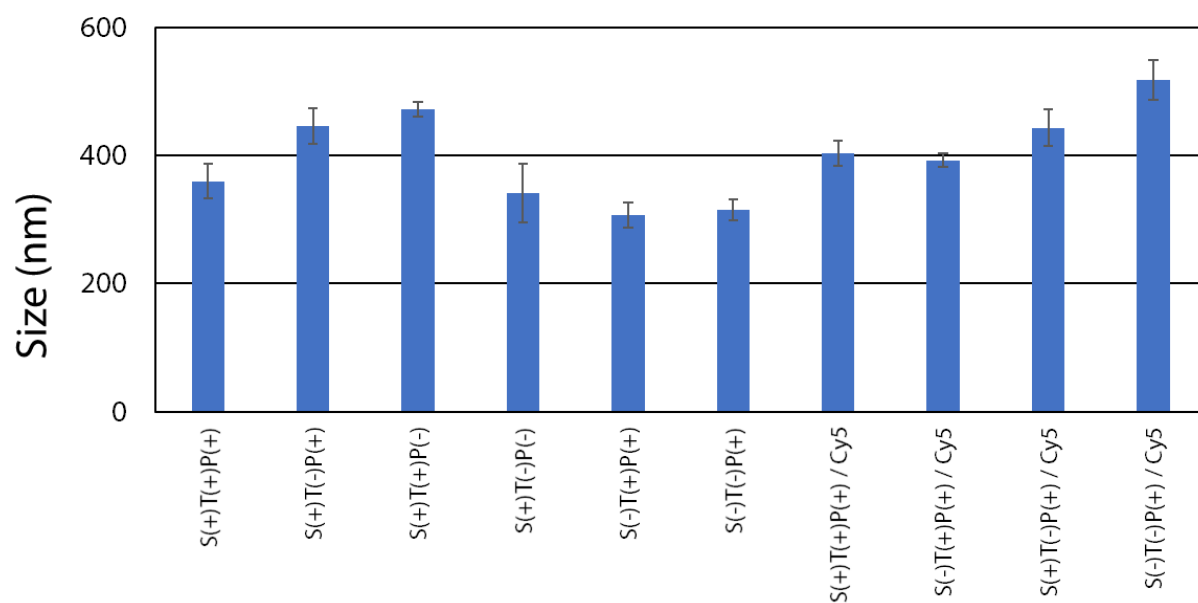
**Supplementary Figure 2** Confirmation of Mono-6-mercapto-6-deoxy- $\alpha$ -cyclodextrin by  $^1\text{H}$  NMR spectroscopy. Successful synthesis of  $\alpha\text{CD-SH}$  was confirmed by the disappeared tosylate peaks in final NMR spectra.



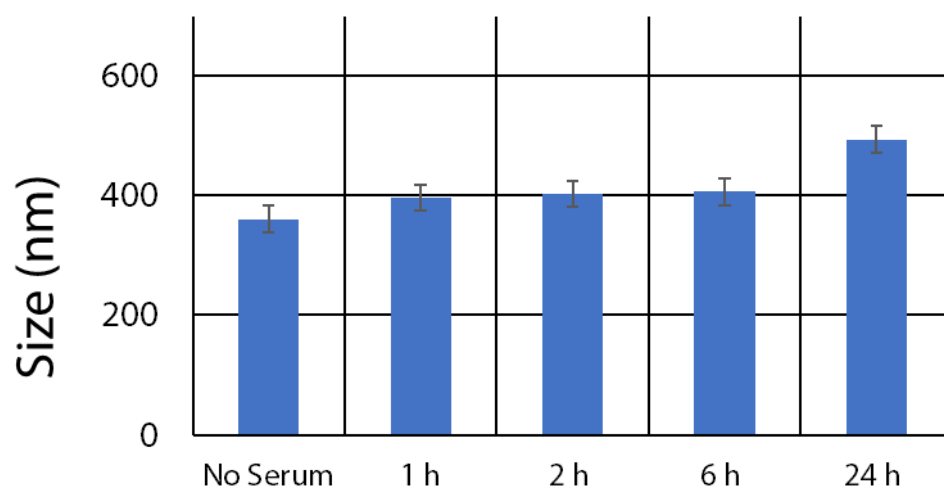
**Supplementary Figure 3** HPLC data of DNA-CD.



**Supplementary Figure 4** GPC data of 20K PEG-(AM)<sub>2</sub>, DNA-CD/PR and non-sliding Sat. DNA-CD/PR shown with calibration curve by PEG standards.

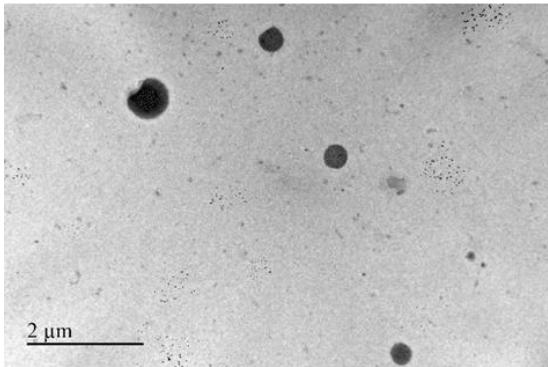


**Supplementary Figure 5** DLS size measurement of various PRNCs

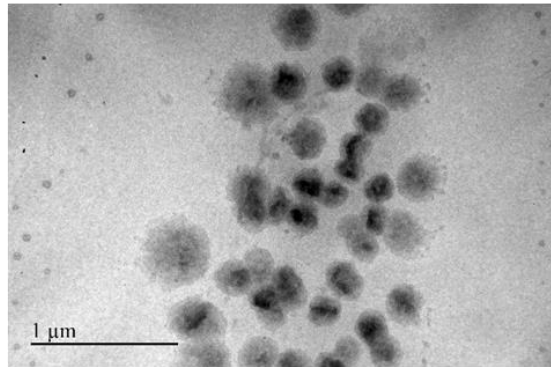


**Supplementary Figure 6** Serum stability of PRNC

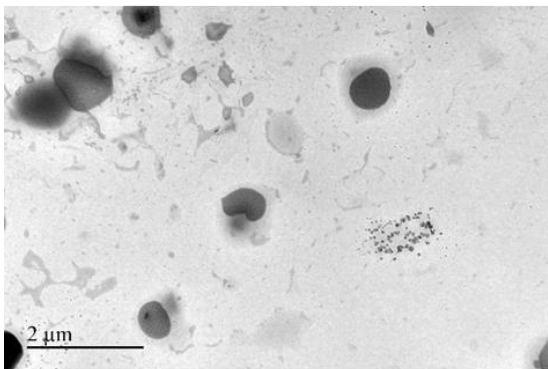
**(a) S(+)  
T(+)  
P(+)**



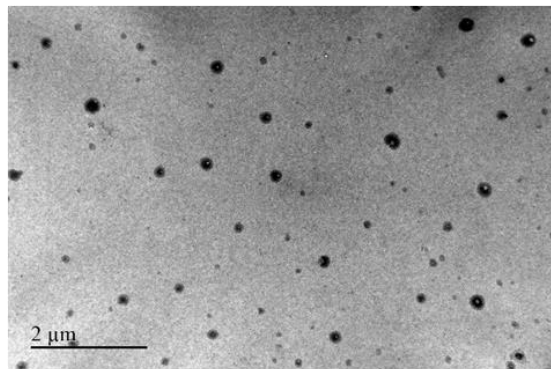
**(e) S(-)  
T(+)  
P(+)**



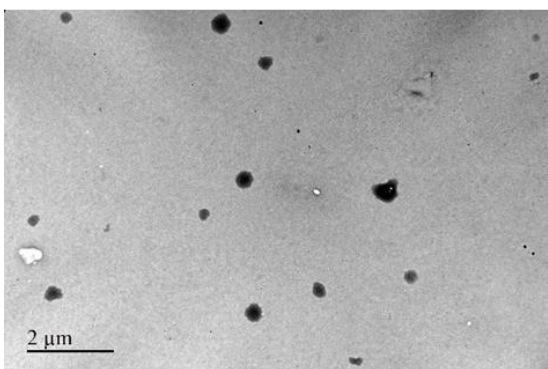
**(b) S(+)  
T(-)  
P(+)**



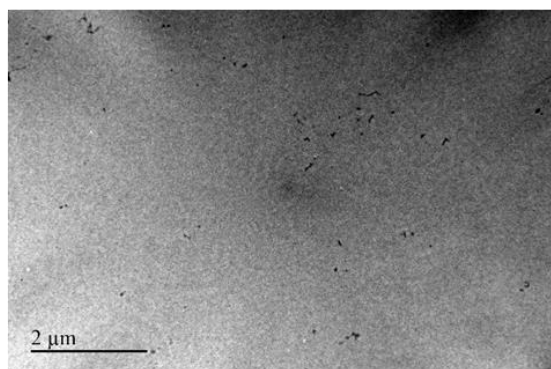
**(f) S(-)  
T(-)  
P(+)**



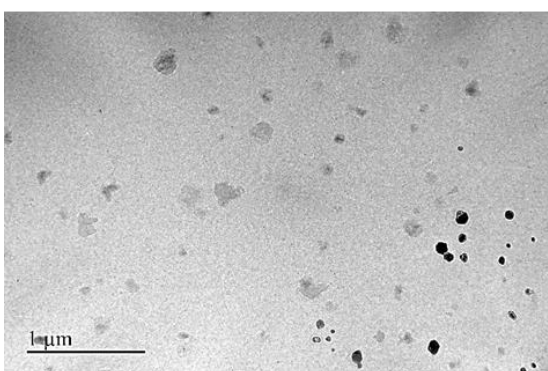
**(c) S(+)  
T(+)  
P(-)**



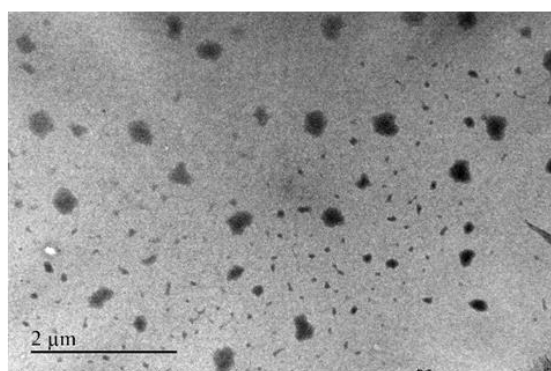
**(g) S(+)  
T(+)  
P(+)  
/ pH = 5.5**



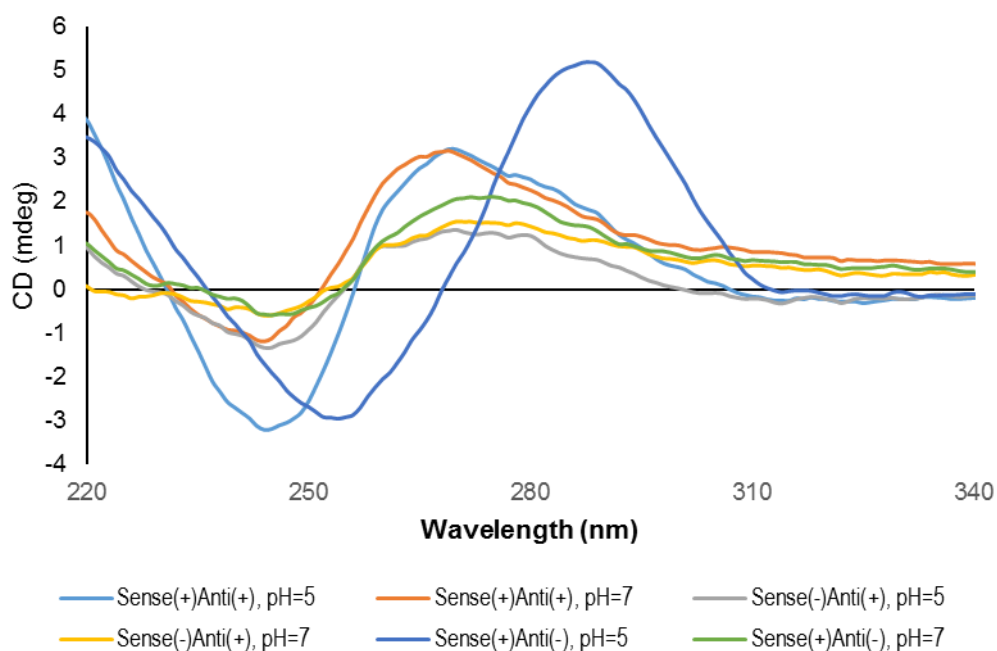
**(d) S(+)  
T(-)  
P(-)**



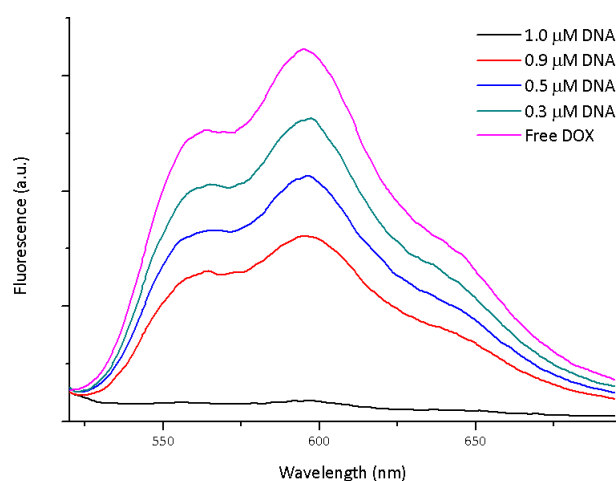
**(h) S(+)  
T(+)  
P(-)  
/ pH = 5.5**



**Supplementary Figure 7** TEM image of various PRNCs

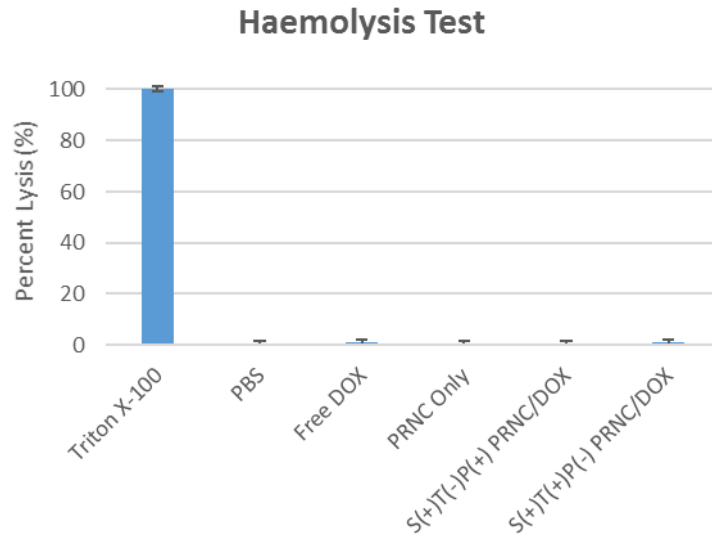


**Supplementary Figure 8** CD spectra of i-motif DNA at different pH. Characteristic peak around 240 nm indicates the formation of i-motif structure in Sense(+) Anti(+) condition.

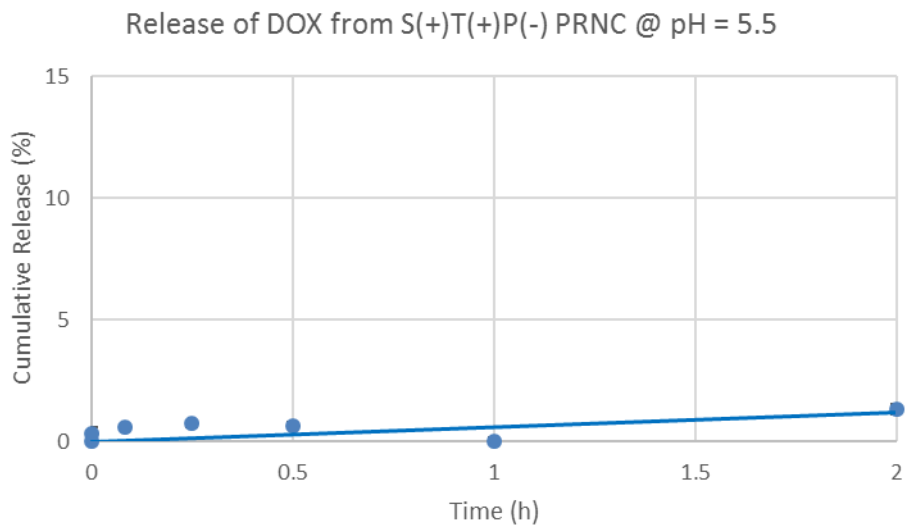


**Supplementary Figure 9** Drug loading properties of PRNC. Fluorescent spectrum shows quenching of DOX fluorescence upon intercalation within dsDNA. Maximum 5 DOX molecule is loaded in single *i-motif* dsDNA.

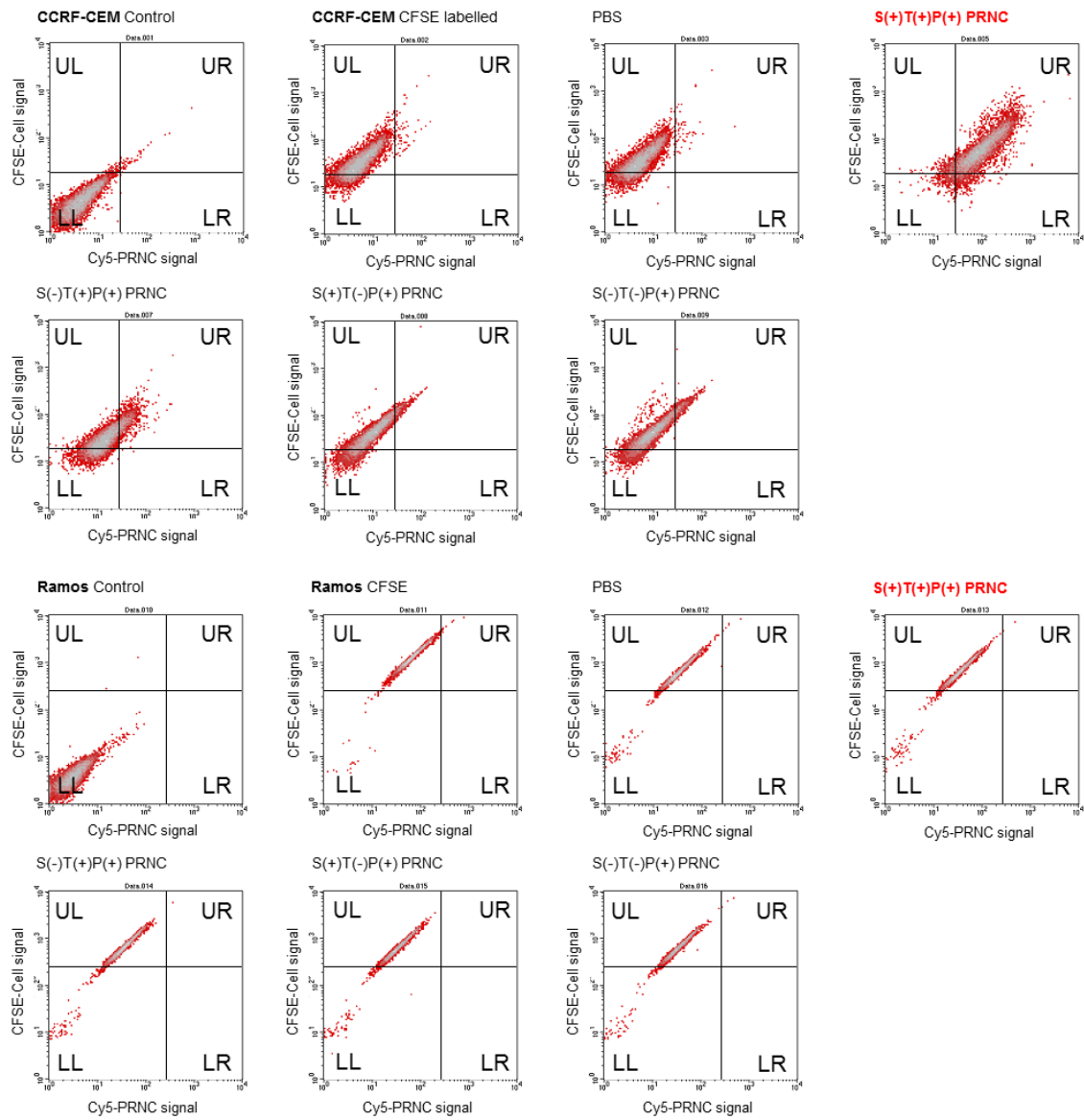




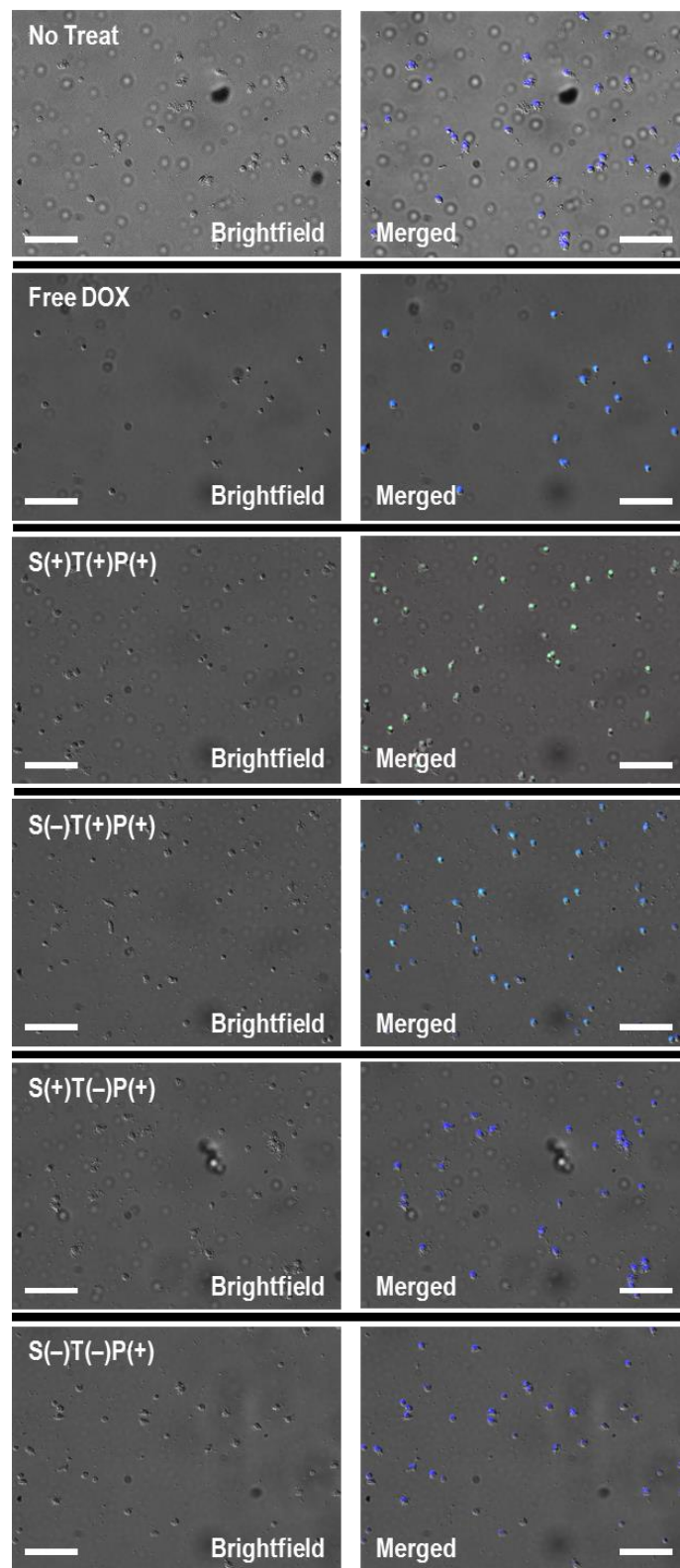
**Supplementary Figure 10** Haemolysis test of PRNC and control groups. No significant lysis of red blood cell is observed in DOX loaded PRNCs.



**Supplementary Figure 11** Release of DOX from non-pH responsive control groups in acidic condition



**Supplementary Figure 12** Flow cytometry analysis results of CCRF-CEM transplanted mice treated with series of PRNCs



**Supplementary Figure 13** Additional images of *in vivo* cytotoxicity evaluation. Brightfield and merged images of the microscopic samples identical to **Figure 5**. (Scale bar = 100  $\mu\text{m}$ )

## 2. Supplementary Tables

**Supplementary Table 1** Sequences of DNAs used in this experiment

Name	Sequence
DNA <sub>i</sub>	5' - AAA ACC CTA ACC CTA ACC CTA ACC C - 3'
cDNA <sub>i</sub>	5' - AAA AGC GTT AGC GTT AGG GTT AGG G - 3'
DNA <sub>a</sub>	5' - TTT TTA TCT AAC TGC TGC GCC GCC GGG AAA ATA CTG TAC GGT TAG A - 3'
sc_DNA <sub>i</sub>	5' - AAA ACG ATT CAC GGC TGT ACG ACA T - 3'
sc_cDNA <sub>i</sub>	5' - AAA AAT GTC GTA CAG CCG TGA ATC G - 3'
sc_DNA <sub>a</sub>	5' - TTT TAA ATG CGT CTT AGC AAT TAC GGA CAG TAG CAT CAC TTT AGT T - 3'

**Supplementary Table 2** Types of PRNCs used in this experiment

Name	Details
S(+) <i>T</i> (+)P(+)	Sliding (+) / Targeting (+) / <i>i-motif</i> (+)
S(+) <i>T</i> (-)P(+)	Sliding (+) / Targeting (-) / <i>i-motif</i> (+)
S(-) <i>T</i> (+)P(+)	Sliding (-) / Targeting (+) / <i>i-motif</i> (+)
S(-) <i>T</i> (-)P(+)	Sliding (-) / Targeting (-) / <i>i-motif</i> (+)
S(+) <i>T</i> (+)P(-)	Sliding (+) / Targeting (+) / <i>i-motif</i> (-)
S(+) <i>T</i> (-)P(-)	Sliding (+) / Targeting (-) / <i>i-motif</i> (-)

**Supplementary Table 3** IC50 values of various DOX loaded PRNCs towards CCRF-CEM and Ramos cells

Sample	IC50 value ( $\mu\text{M DOX}$ )	
	CCRF-CEM	Ramos
Free DOX	0.45	1.8
S(+) <i>T</i> (+)P(+)	0.4	2.4
S(+) <i>T</i> (-)P(+)	0.57	6.7
S(+) <i>T</i> (+)P(-)	0.75	N/A
S(+) <i>T</i> (-)P(-)	1.5	N/A
S(-) <i>T</i> (+)P(+)	1.25	N/A
S(-) <i>T</i> (-)P(+)	1.25	N/A

**Supplementary Table 4** ROI fluorescence mean intensity calculation of microscopic images

Sample	DAPI	AnnexinV	PI	DAPI to AV	DAPI to PI
PBS	6352.89	496.9	802.98	8%	14%
DOX	11962.05	4276.95	340.96	36%	6%
S(+) <i>T</i> (+)P(+)	5607.61	6872.27	6938.39	123%	124%
S(-) <i>T</i> (+)P(+)	5911.65	2893.5	650.45	49%	12%
S(+) <i>T</i> (-)P(+)	10266.87	478.61	290.89	5%	5%
S(-) <i>T</i> (-)P(+)	3680.74	576.46	472.95	16%	8%