Supporting Information

A Nanogel Based Oral Gene Delivery System Targeting SUMOylation Machinery to Combat Gut Inflammation

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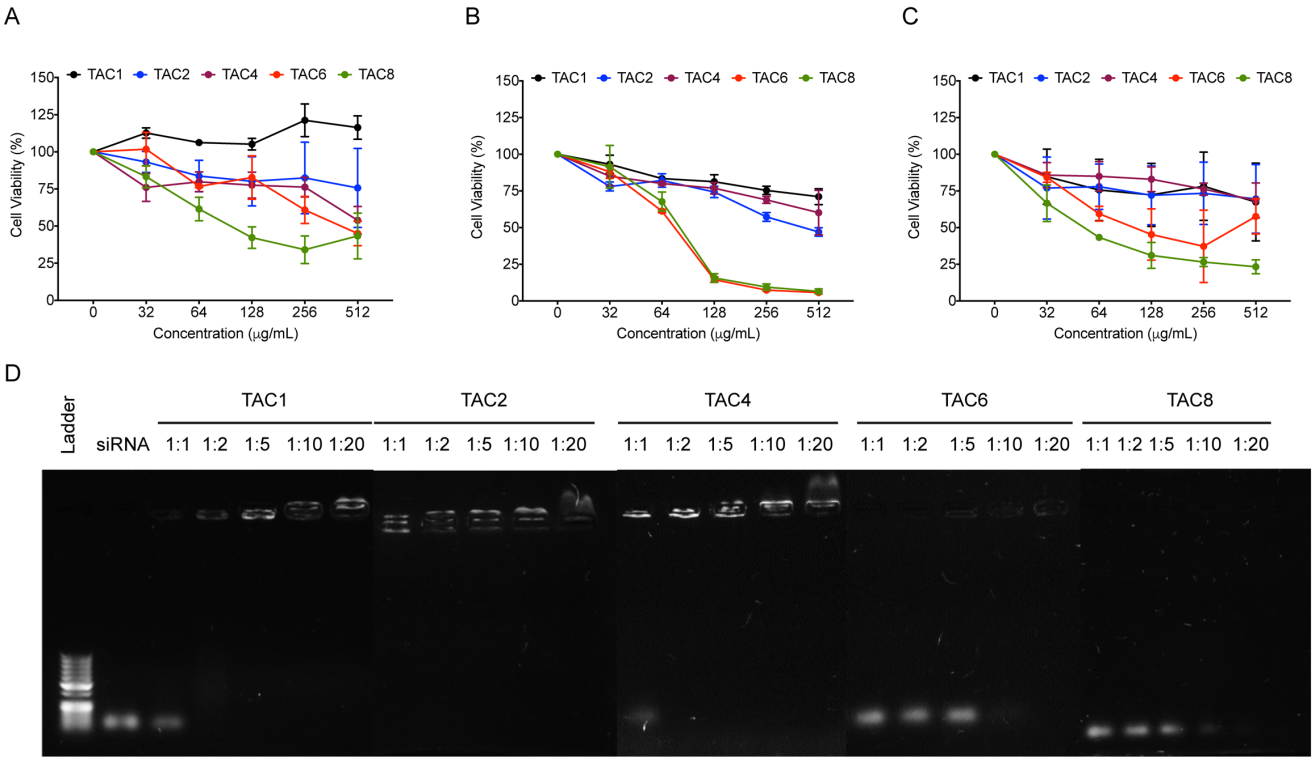


Figure S1. A-C) Cell viability (%) of HEK293 (A), LLC (B) and THP1 (C) cells on treatment with different concentrations of **TAC1-TAC8** using MTT assay. (D) Gel electrophoresis images of siRNA mixed with different polymers **TAC1-TAC8** at different (w/w) ratios.

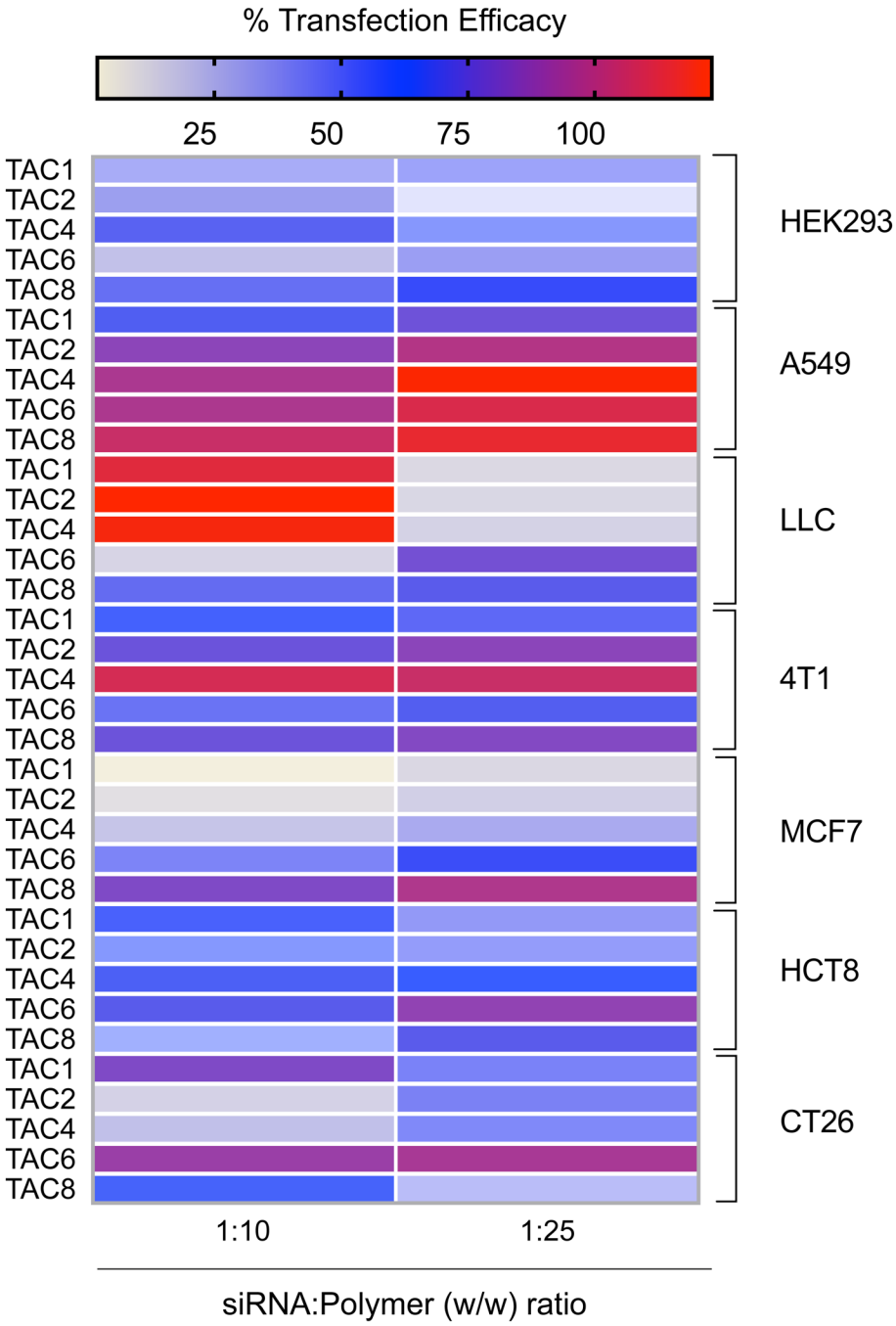
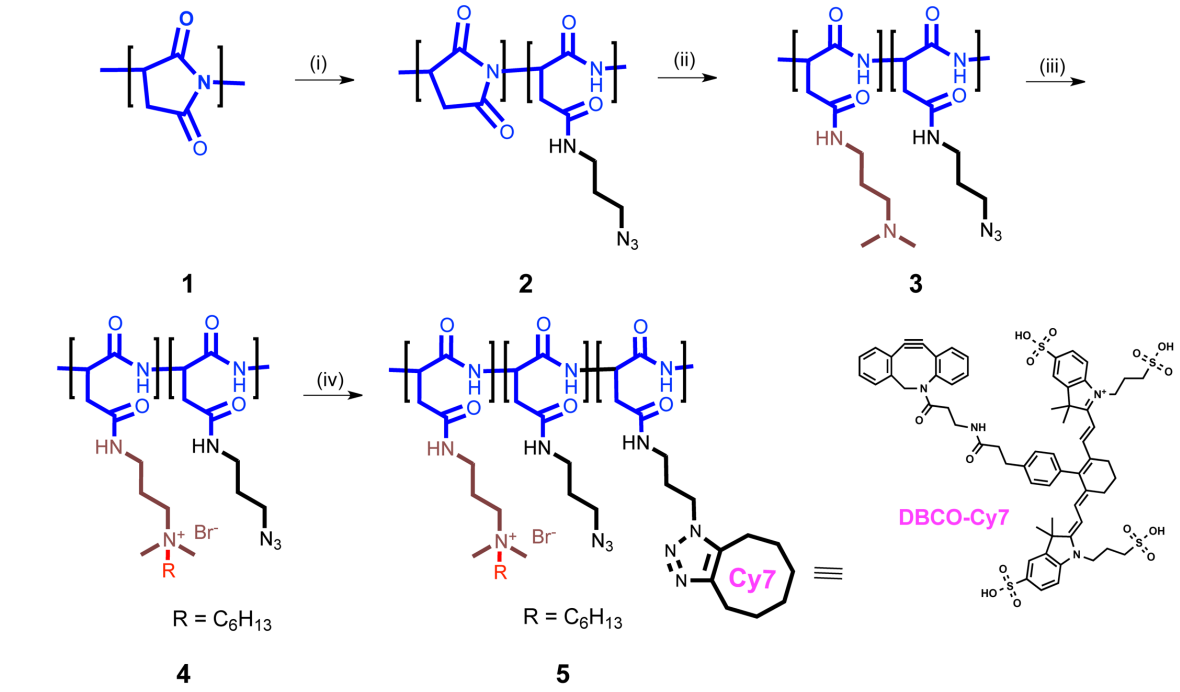


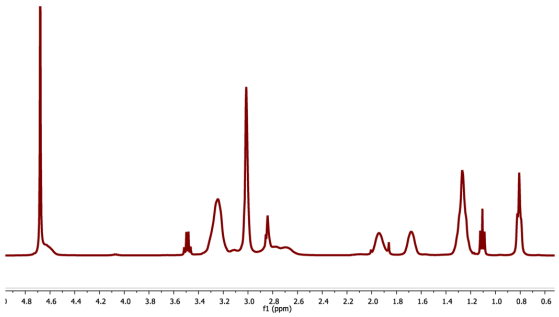
Figure S2. Heat map showing % transfection efficiency with respect to Lipofectamine 2000 of **TAC1-TAC8** based polyplexes at different siRNA to polymer (w/w) ratios in different mammalian cell types.

A



Reagents and reaction conditions: (i) 3-Azido-1-propanamine, DMF, 25˚C, 12h; (ii) 3-(Dimethylamino)-1-propylamine, DMF, 25˚C, 12h; (iii) *n*-Hexylbromide (R-Br), MeOH, 25˚C, 8h; (iv) DBCO-Cy7, DMF:H_2O (1:1), 25˚C, 12h.

B



C

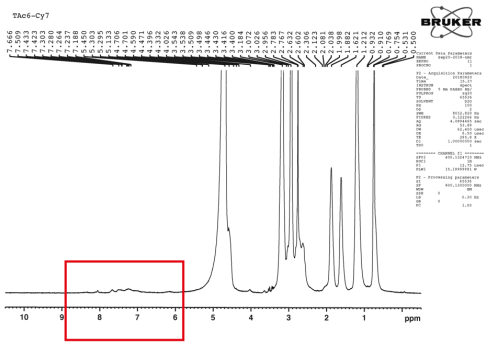


Figure S3. A) Synthesis of NIR (Cy7)-derived **TAC6** polymer where azide-derived **TAC6** polymer was reacted with DBCO-Cy7 by click chemistry. B-C) Characterization spectra of TAC6-Azide (compound **4**) and TAC6-NIR probe (compound **5**) showing the appearance of aromatic peaks. Final quantification of Cy7 conjugation was done by fluorescence.

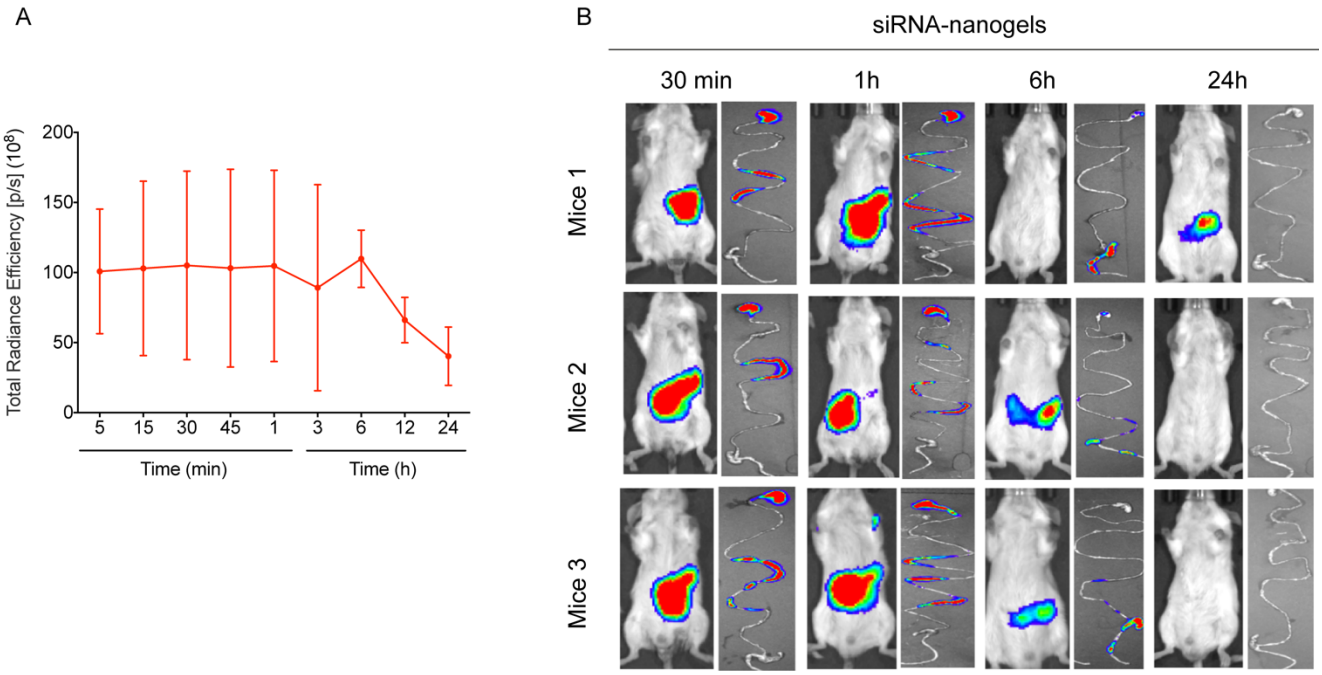


Figure S4. A) Quantification of bioluminescence of three mice from colon region at different time points on oral feeding of NIR-**TAC6**-derived siRNA-nanogels. B) Bioluminescent images of whole mice body and excised GIT at different times after oral feeding of NIR-**TAC6**-derived siRNA-nanogels.

Table S1. Sequences of the primers used in the study.

Human Genes		
	Forward Primer (5’ to 3’)	Reverse Primer (5’ to 3’)
GAPDH	CCCTTCATTGACCTCAACTA	CCAAAGTTGTCATGGATGAC
PIAS1	TGCCTTGACACCAAAC	GCTTTGGTTCCACACCG
Mouse Genes		
	Forward Primer (5’ to 3’)	Reverse Primer (5’ to 3’)
B2M	TTCTGGTGCTTGTCTCACTGA	CAGTATGTTCGGCTTCCCATTC
IL8	CACCTCAAGAACATCCAGAGCT	CAAGCAGAACTGAACTACCATCG
PIAS1	AAGCATGCTCTGACAGTGG	TGGCTCTCTGCAGTTACACC
TNF-α	CATCTTCTCAAAATTCGAGTGACAA	TGGGAGTAGACAAGGTACAACCC
IFN-γ	TCTTGGCTTTGCAGCTCTTC	TGTTGCTGATGGCCTGATTG
IL-1β	CAGGATGAGGACATGAGCACC	CTCTGCAGACTCAAACTCCAC
IL-10	TGCACTACCAAAGCCACAAG	TCAGTAAGAGCAGGCAGCAT
IL-22	ACCTTTCCTGACCAAACTCA	AGCTTCTTCTCGCTCAGACG