Electronic Supplementary Material

General synthesis of silica-based yolk/shell hybrid nanomaterials and *in vivo* tumor vasculature targeting

Feng Chen[1], Shreya Goel[2], Sixiang Shi[2], Todd E. Barnhart[3], Xiaoli Lan[4] (✉), and Weibo Cai[1,2,3,5] (✉)

[1] *Department of Radiology, University of Wisconsin-Madison, WI 53705, USA*

[2] *Materials Science Program, University of Wisconsin-Madison, WI 53705, USA*

[3] *Department of Medical Physics, University of Wisconsin-Madison, WI 53705, USA*

[4] *Department of Nuclear Medicine, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China*

[5] *University of Wisconsin Carbone Cancer Center, Madison, WI 53705, USA*
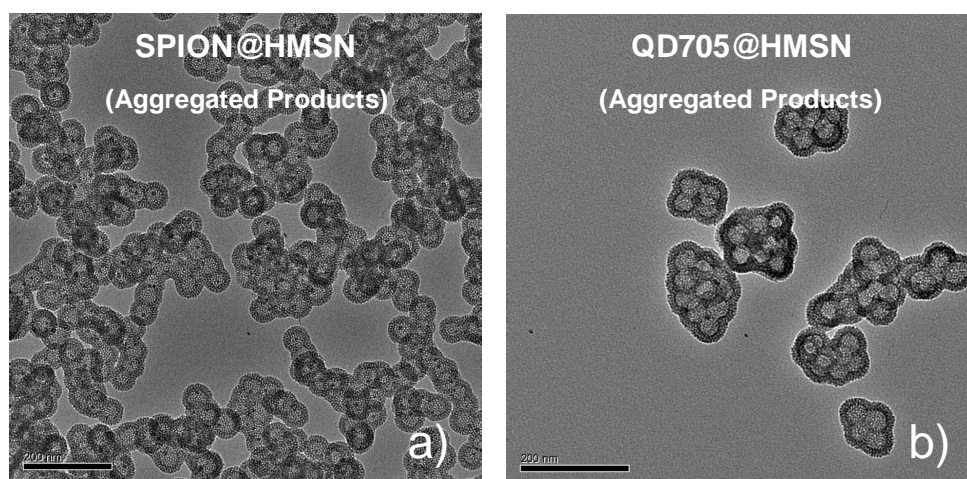
SUPPLEMENTARY FIGURES

Figure S1 TEM images of (a) SPION@HMSN and (b) QD705@HMSN with severe nanoparticle aggregations.

Address correspondence to Xiaoli Lan, LXL730724@hotmail.com; Weibo Cai, wcai@uwhealth.org

SUPPLEMENTARY TABLES

Table S1 [89]Zr-labeling yields of UCNP@HMSN at 75 °C in solutions with different pH values

	0.5 h	1 h	3 h	9 h	22 h
75 °C, pH 8	65.3 %	74.9 %	84.2 %	87.4 %	90.4 %
75 °C, pH 2	1.2 %	1.3 %	1.8 %	1.4 %	0.6 %

Table S2 [89]Zr-labeling yields of UCNP@HMSN at 37 °C in solutions with pH 8

	2 h	4 h	6 h	22 h
37°C, pH 8	42.1 %	58.8 %	71.1 %	82.4 %

Table S3 Region-of-interest (ROI) quantitative analysis of PET images from targeted group mice injected with UCNP@[89Zr]HMSN-PEG$_{5k}$-TRC105 (n=3).

Targeted (n=3)	Liver		Blood		Tumor		Muscle	
	Ave.	Std.	Ave.	Std.	Ave.	Std.	Ave.	Std.
0.5 h	20.73	0.70	22.60	3.72	2.43	0.31	0.88	0.28
6 h	26.30	2.52	9.10	4.28	10.03	0.90	0.60	0.20
24 h	29.83	3.39	1.77	0.49	9.63	0.60	0.53	0.09
48 h	32.30	4.85	0.84	0.10	9.50	0.92	0.52	0.08

Table S4 ROI quantitative analysis of PET images from non-targeted group mice injected with UCNP@[89Zr]HMSN-PEG$_{5k}$ (n=3).

Non-targeted (n=3)	Liver		Blood		Tumor		Muscle	
	Ave.	Std.	Ave.	Std.	Ave.	Std.	Ave.	Std.
0.5 h	26.60	2.69	30.50	1.56	2.15	0.35	0.74	0.18
6 h	46.70	1.27	5.40	1.13	4.15	1.20	0.37	0.10
24 h	57.70	1.70	0.86	0.01	4.70	1.98	0.23	0.01
48 h	54.95	2.76	0.39	0.07	4.30	1.56	0.32	0.12

Table S5 ROI quantitative analysis of PET images from blocking group mice injected with UCNP@[89Zr]HMSN-PEG$_{5k}$-TRC105 and 1 mg of free TRC105 antibody (n=3).

Blocking (n=3)	Liver		Blood		Tumor		Muscle	
	Ave.	Std.	Ave.	Std.	Ave.	Std.	Ave.	Std.
0.5 h	27.67	3.23	28.80	1.81	1.90	0.10	0.84	0.12
6 h	40.13	5.15	10.60	2.34	4.27	0.74	0.56	0.14
24 h	48.93	5.06	1.14	0.20	4.60	0.85	0.53	0.24
48 h	46.93	3.63	0.72	0.14	3.90	0.70	0.42	0.17

Table S6 *Ex vivo* biodistribution data of ^{89}Zr-radiolabeled yolk/shell nanoparticles at 48 h post-injection (n=3). The radioactivity in organs was measured using a gamma-counter and presented as %ID/g (mean ± std.). Targeted group: UCNP@[^{89}Zr]HMSN-PEG$_{5k}$-TRC105; Non-targeted group: UCNP@[^{89}Zr]HMSN-PEG$_{5k}$; Blocking group: UCNP@[^{89}Zr]HMSN-PEG$_{5k}$-TRC105 with 1 mg of unlabeled TRC105 (each mouse).

	Targeted (n=3) Non		targeted (n=3) Blocking (n=3)		Targeted (n=3) Non	
	Ave.	Std.	Ave.	Std.	Ave.	Std.
Blood	0.43	0.08	0.39	0.21	0.45	0.26
Skin	1.67	0.25	0.57	0.25	0.46	0.13
Muscle	0.25	0.14	0.33	0.22	0.30	0.03
Bone	3.10	1.20	3.43	0.27	1.42	1.60
Heart	0.69	0.28	0.36	0.03	0.47	0.14
Lung	0.65	0.72	0.70	0.48	0.63	0.27
Liver	30.12	1.85	38.37	3.53	33.05	0.31
Kidney	2.13	0.61	1.43	0.16	2.28	0.57
Spleen	21.00	0.68	25.03	4.17	24.98	4.29
Pancreas	0.62	0.12	0.25	0.04	0.25	0.07
Stomach	0.78	0.23	0.39	0.11	0.68	0.42
Intestine	1.59	0.92	1.82	1.41	1.48	0.89
Tumor	5.37	0.19	2.41	0.24	2.30	0.45
Tail	1.74	0.22	2.32	0.94	1.41	0.82
Brain	0.14	0.10	0.06	0.06	0.07	0.01