Supporting Information

Local Intratracheal Delivery of Perfluorocarbon Nanoparticles to Lung Cancer Demonstrated with Magnetic Resonance Multimodal Imaging

Lina Wu^{a,#}, Xiaofei Wen^{a,#}, Xiance Wang^a, Chunan Wang^a, Xilin Sun^a,

Kai Wang^a, Huiying Zhang^b, Todd Williams^b, Allen J. Stacy^b,

JunjieChen^b, Anne H. Schmieder^b, Gregory M. Lanza^b, Baozhong Shen^{a,*}

^a 1.Molecular Imaging Research Center (MIRC), Harbin Medical University, Harbin, Heilongjiang, China 2.TOF-PET/CT/MR center, The Fourth Hospital of Harbin Medical University, Harbin, Heilongjiang, China.

^b Department of Medicine, Division of Cardiology, Washington University School of Medicine, 4320 Forest Park Avenue, Saint Louis, MO 63108, USA

The authors contributed equally to this work.

^{*}Corresponding author: E-mail: <u>shenbzh@vip.sina.com</u>



Figure S1. Physicochemical characterization of M-PFC NPs. (A) The particle morphology from TEM image; (B) Fluorescence spectrum after excitation at 535 nm; (C) Stability studyin pure water and 0.9% saline solution at 37° C



Figure S2. Comparison of the oxygen dissolvement and release power between water

and PFC emulsion. (A) oxygen dissolvement content with different interval of O_2 at 25 $\ \ C$ (B) Oxygen release test at 25 $\ \ C$ after stop the airflow. (the green triangle in A is a value waited for around 15 min after stopping the O_2 ventilation, for the reading had exceeded the instrument detection limit at the point)



Figure S3. Comparison of cell apoptosis before and after the treatment of multifunctional PFCs with different concentrations (A) BEAS-2B cells (B) lung cancer H520 cells (scale bars=50 µm).



Figure S4. Cell cycle analyses of BEAS-2B cells (A) one representative image of control groups; (B) in the presence of 9 mM M-PFC NPs for 24 hr; (C) Percentages of cells in each phase of the cell cycle. Data represent mean \pm SD, n=3 ***P < 0.001 (One-way ANOVA analysis of variance).

Test	Control(No	PFC treated			
	treatment)	24h I.V.	24h I.T.	7d I.V.	7d I.T.
BUN(mmol/L)	9.3±2.1	7.2±0.5	6.6±2.2	11.40±0.4	9.3±0.1
CREA(µmol/L)	19.8±4.0	22.5±1.6	19.1±1.5	21.9±3.5	19.8±1.0
TP (g/L)	49.0±2.3	59.0±1.6	54.1±4.5	48.3±3.7	49.0±4.8
ALB (g/L)	28.6±2.4	33.4±3.2	31.8±2.4	26.7±2.9	28.6±0.4
GLO (U/L)	20.4±0.6	25.6±2.2	22.3±2.8	21.6±0.9	20.4±6.5
A/G	1.4±0.1	1.3±0.2	1.4±0.2	1.2±0.1	1.4±0.3
AST(U/L)	207.3±20.4	154.7±21.1	177.7±45.6	185.0±78.7	207.3 ± 104.7
ALT(U/L)	56.5±60.3	61.0±4.0	46.7±14.8	57.7±8.6	56.5±13.4
LDH(U/L)	2619.7±1561.1	2575.3±62.2	1654.3±1216.7	2599.0±246.4	2619.7 ±698.6

Table S1. Clinical pathologic detection on liver and renal function following IV or IT administration

Table S2. Clinical pathologic detection on electrolytes and hematology following IV or IT administration

Test	Control(No treatment)	PFC treated				
		24h I.V.	24h I.T.	7d I.V.	7d I.T.	
K(mmol/L)	5.8±0.2	5.2±0.3	5.4±0.4	6.1±1.0	5.8±1.4	
Na(mmol/L)	151.2±1.7	153.3±0.8	151.7±2.4	151.7±2.6	151.2±1.2	
Cl(mmol/L)	110.3±1.3	111.6±0.8	107.5±4.6	114.4±2.8	110.3±4.0	
WBC*	6.0±2.2	2.8±0.8	8.7±5.9	3.8±0.3	8.2±2.2	
LYMPH%	87.7±4.8	70.1±9.6	77.1±2.8	86.3±6.6	76.0±3.3	
RBC*	9.3±1.2	9.9±0.7	8.5±0.8	8.9±1.0	9.8±1.2	
HGB*	140.5±15.5	149.5±8.5	129.5±12.5	131.0±12.1	147.5±16.5	
HCT*	44.9±5.1	48.0±2.1	40.8±2.8	43.0±4.0	46.0±4.2	
MCV	46.0±3.3	48.8±1.9	48.0±1.3	48.4±1.6	46.9±1.3	
МСН	14.5±1.0	14.8±0.4	14.8±0.4	14.9±0.3	15.1±0.2	
МСНС	315.0±3.0	312.0±4.0	315.5±10.5	308.5±4.5	320.0±7.0	
RDW-CV	19.9±2.4	19.0±1.0	18.6±0.4	20.5±1.8	18.1±0.6	
PLT	460.0±221.3	663.5±165.0	641.5±31.5	313.5±254.5	698.0±40.1	
PDW	6.6±0.1	7.6±0.3	7.8±0.8	7.4±0.3	7.3±0.7	



Figure S5. Representative images of *in vivo* ¹H-MRI after I.T. and I.V. delivery of M-PFC NPs. (A,B) R_1 color mapped MR images; T_1 -weighted MR images of the same ROI of tumor; (C,D) R_1 color mapped MR images; T_1 -weighted MR images of the same ROI of muscle; (E,F,G,H) R_1 color mapped MR images; T_1 -weighted MR images of the same ROI of tumor and muscle, respectively.



Figure S6. Fluorescence microscopy images of tumor slices from the rabbits handled by different treatments (A) Intratracheal delivery; (B) Intravenous injection (scale bars= $100 \ \mu m$).