The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022)
01–30 NOVEMBER 2022 | ONLINE

Larger Particle Size Resulted in Longer Lung Retention Time of Inhaled Solid Lipid Nanoparticles

Chaired by DR. ALFREDO BERZAL-HERRANZ;
Co-Chaired by PROF. DR. MARIA EMÍLIA SOUSA

pharmaceuticals MDPI

Zhengwei Huang [1,*], Jiajun Chen [1], Chuanbin Wu [1], Xin Pan [2]

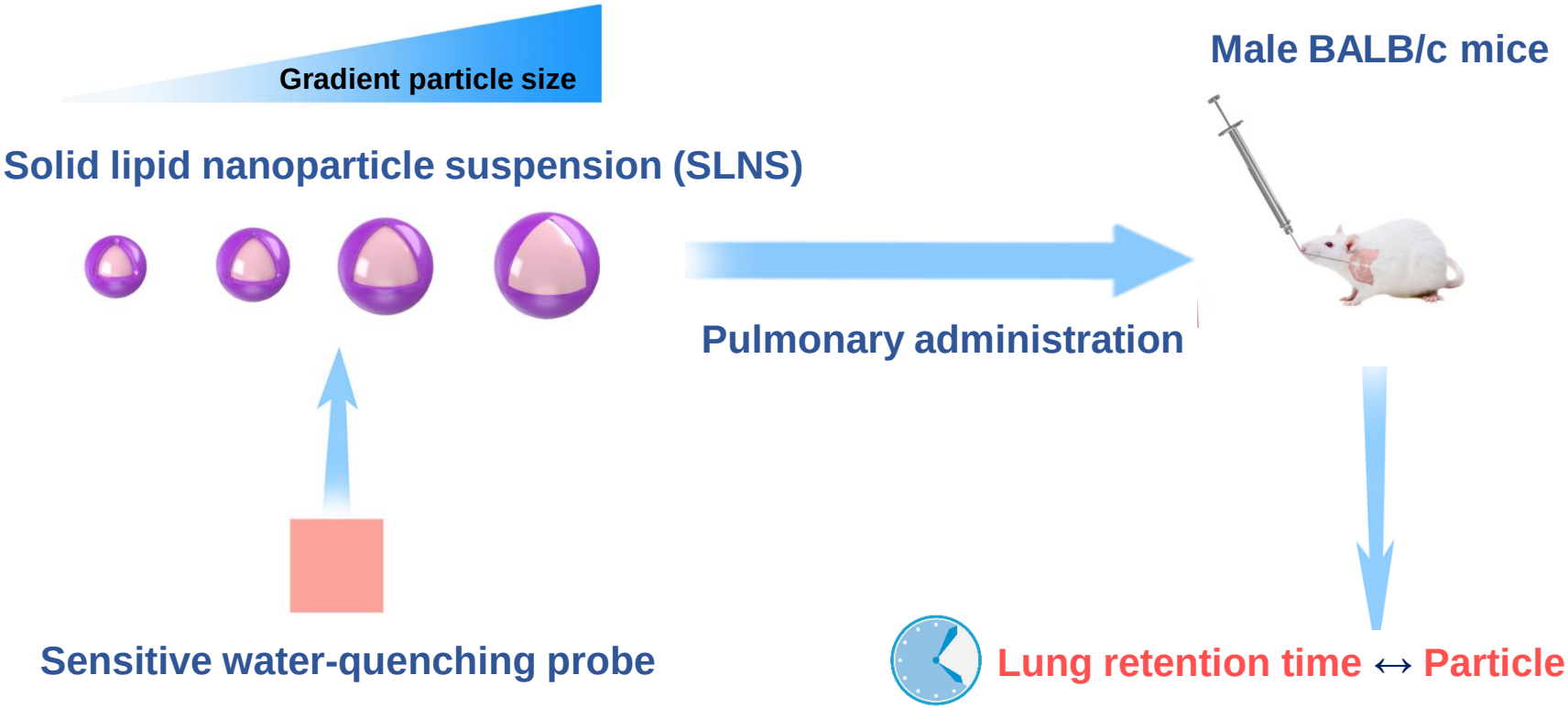
[1] College of Pharmacy, Jinan University, Guangzhou 511443, Guangdong, P. R. China;
[2] School of Pharmaceutical Sciences, Sun Yat-Sen University, Guangzhou 510006, Guangdong, P. R. China.

* Corresponding author: huangzhengw@jnu.edu.cn

暨南大學 JINAN UNIVERSITY
中山大學 SUN YAT-SEN UNIVERSITY

Larger Particle Size Resulted in Longer Lung Retention Time of Inhaled Solid Lipid Nanopartices

Graphical Abstract

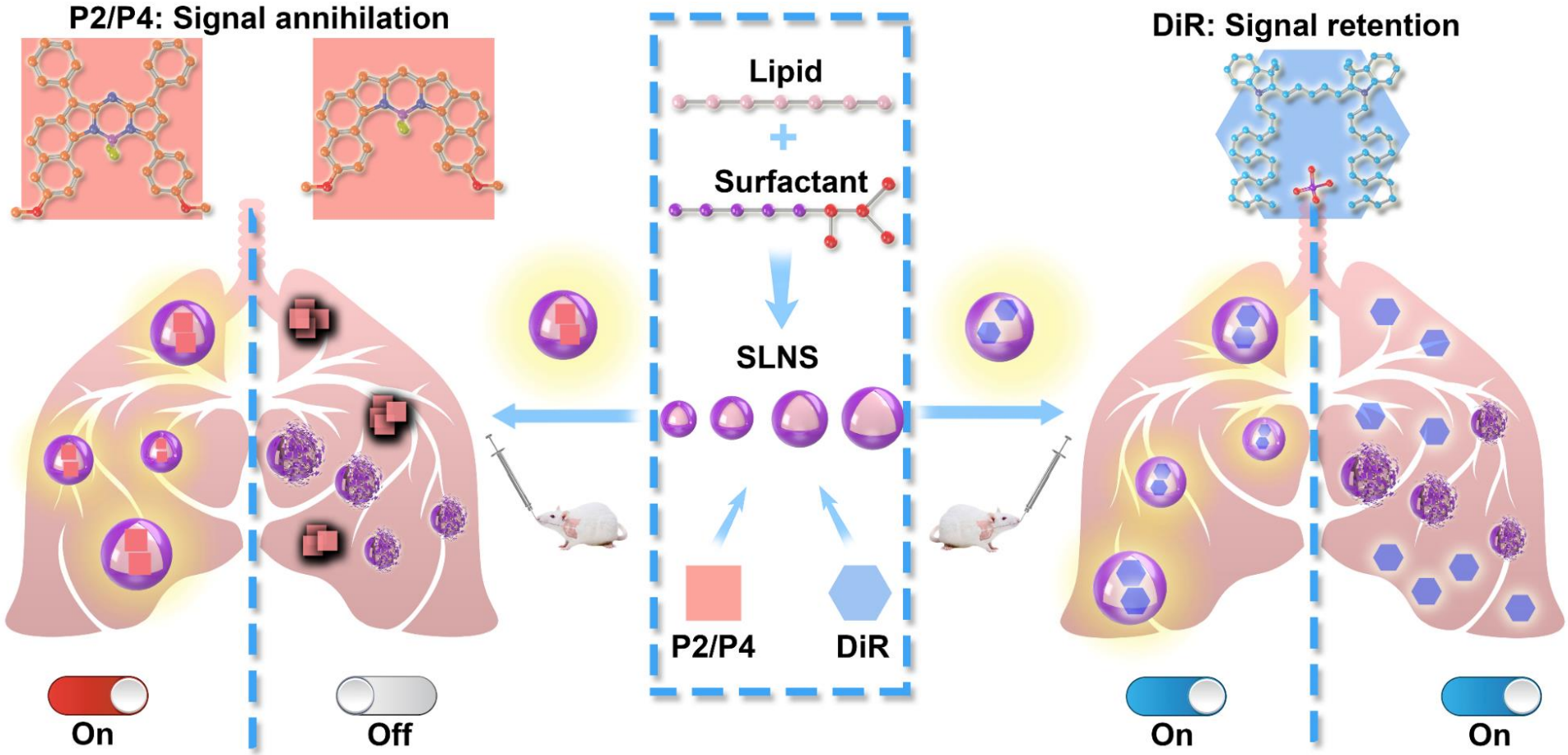


Abstract:

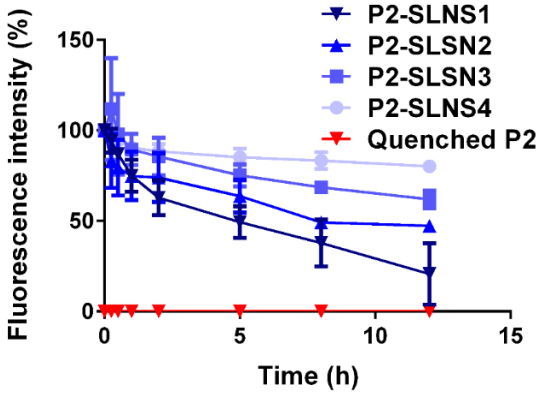
Particle size-lung retention time correlation is a vital guiding principle in developing pulmonary nanoparticle drug delivery systems (PNDDS). Fluorescence probes with accurate water-quenching attributes, which are emissive under PNDDS encapsulation while quenched after release in physiological environments, reflex fluorescence signals of intact PNDDS and thus unambigously clarify the lung retention profile of PNDDS. Herein, water-quenching probe P2 was used to investigate the particle size-lung retention time correlation. P2-loaded PNDD, viz. solid lipid nanoparticles (SLN) with different sizes, were prepared by high-pressure homogenization, encoded as P2-SLN1~P2-SLN4. Particle sizes of P2-SLN1~P2-SLN4 were measured, and then endotracheally aerosolized to male BALB/c mice (22-26 g), and P2 fluorescence signals were detected by living imaging. Half-life ($T_{1/2}$) and mean retention time ($MRT_{0\rightarrow\infty}$) were computed by WinNonlin to describe lung retention time. $T_{1/2}$ or $MRT_{0\rightarrow\infty}$ was plotted versus particle size, and linear regression was performed. P2-SLN1~P2-SLN4 possessed average sizes of circa 120, 240, 360 and 480 nm respectively with good size distribution homogeneity. After inhalation, P2 fluorescence intensity continuously decreased in the pulmonary region. Noticeably, $T_{1/2}$ or $MRT_{0\rightarrow\infty}$ were positively correlated to particle size, with great model-fitness (R^2>0.99, p<0.05). Therefore, larger particle size (within the range of 120-480 nm) caused longer retention time. A positive particle size-lung retention time correlation in SLN was demonstrated. For the development of PNDDS, appropriately increase the particle size would enhance lung retention, *vice versa*.

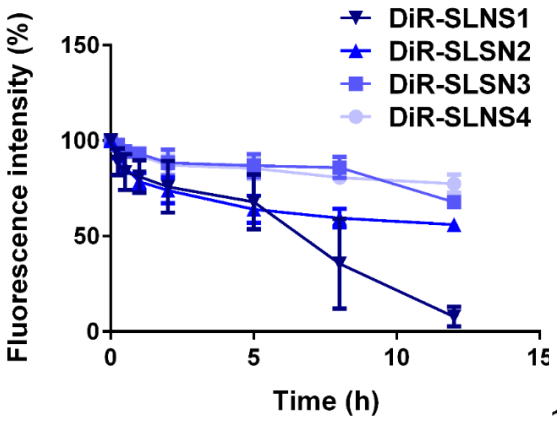
Keywords: Particle size; Lung retention time; Solid lipid nanoparticles; Pulmonary delivery

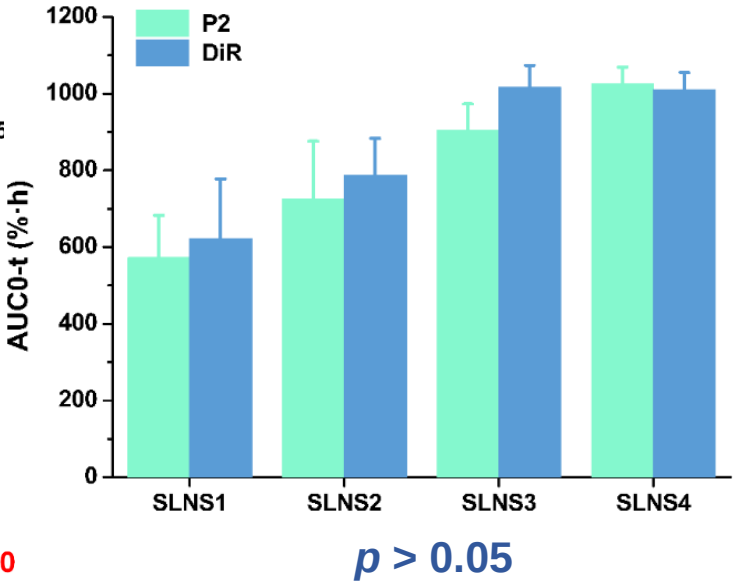
Introduction

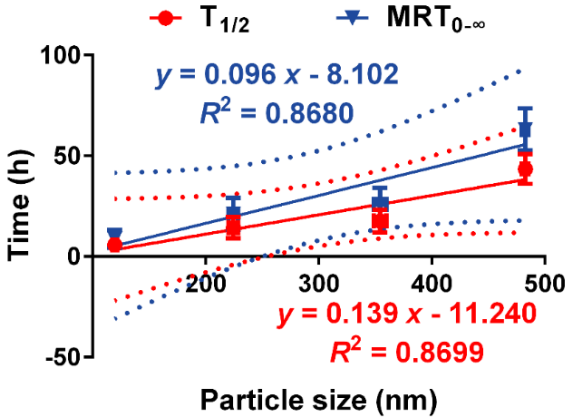


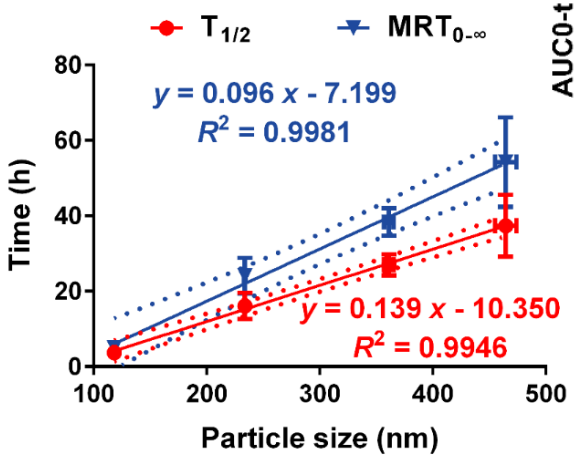
Results and discussion



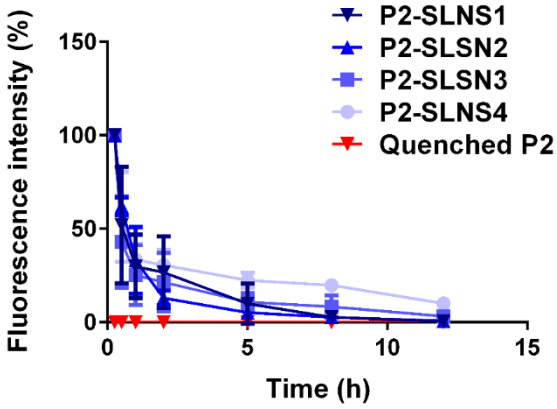


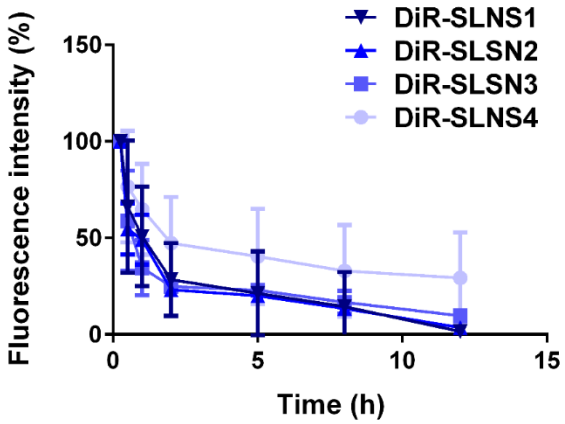


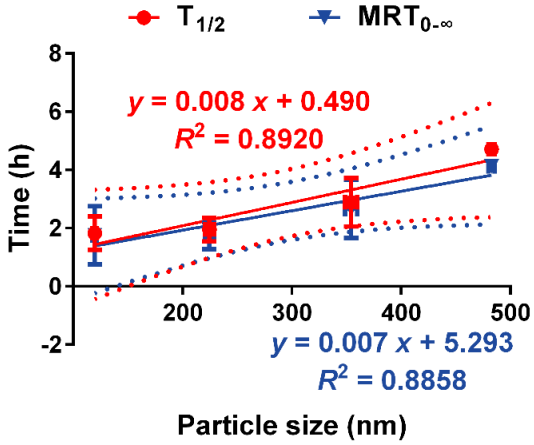


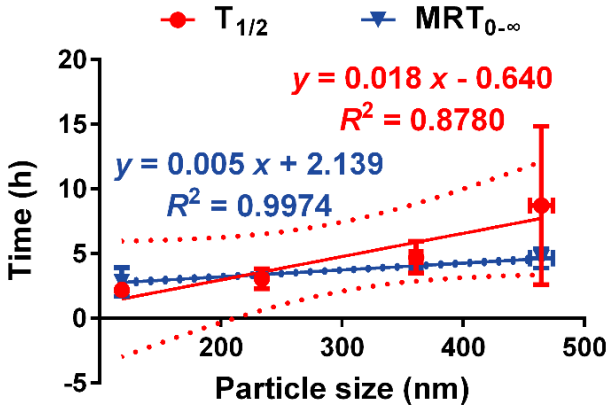


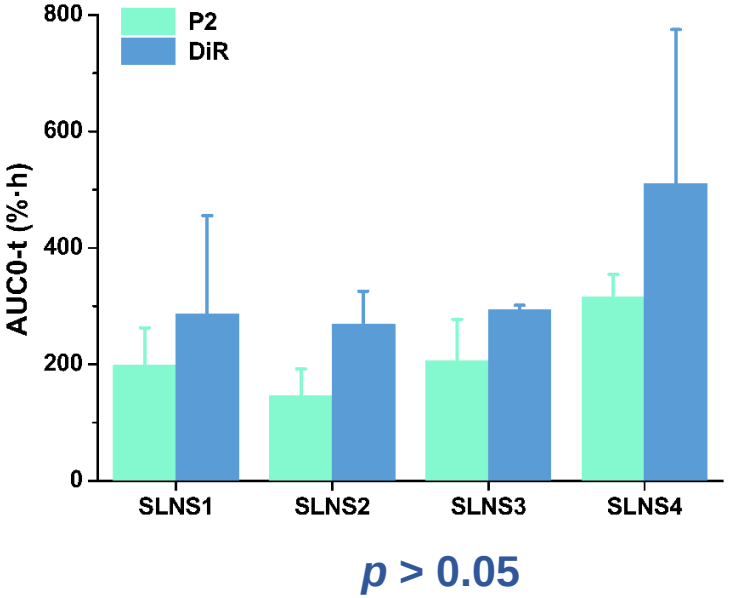
Results and discussion



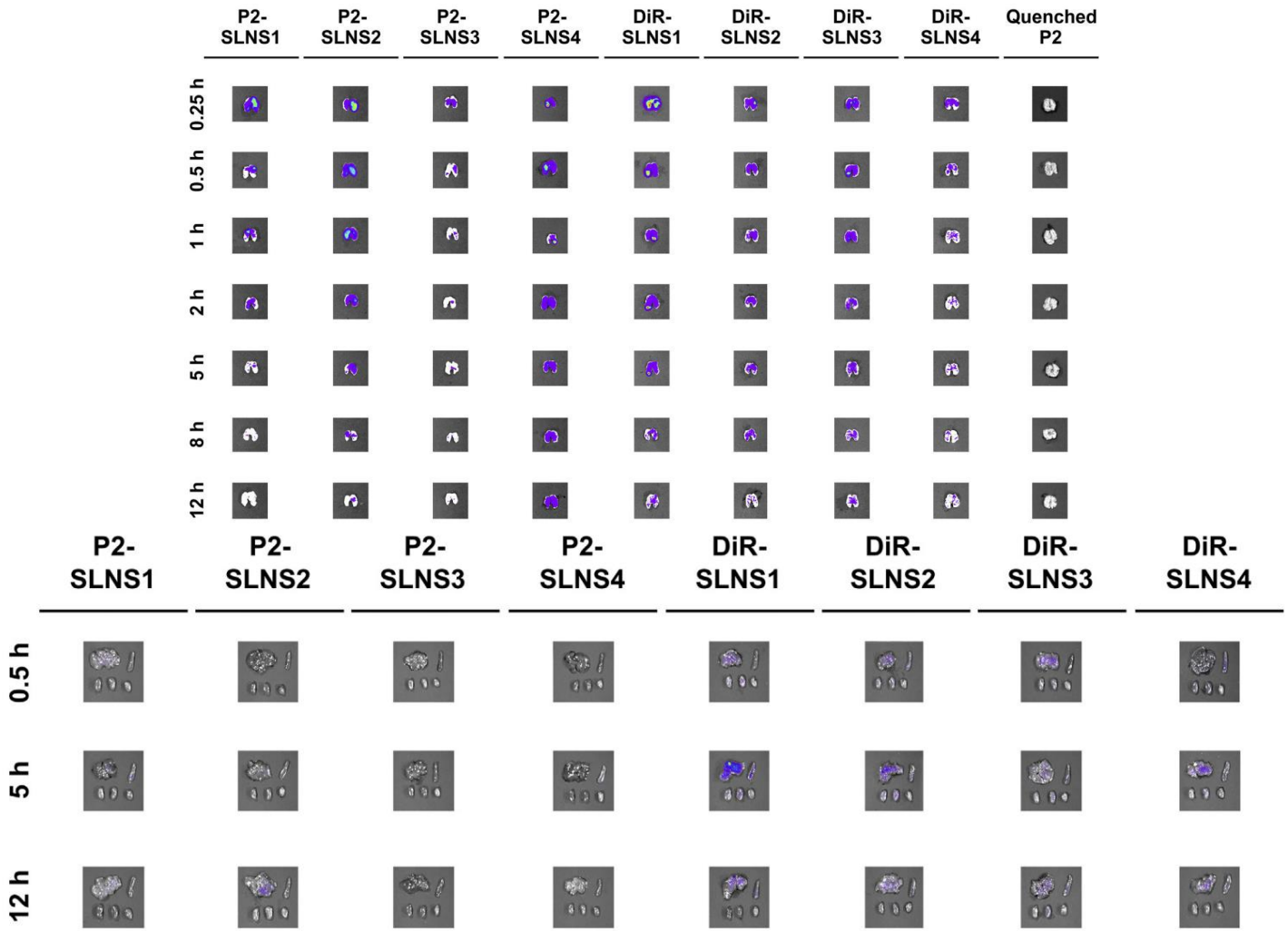








Results and discussion



Conclusions

- P2 can be applied to detect the integrity and explore the lung retention time of the SLNS systems.
- There is a positive correlation between the particle size and the lung retention of the SLNS systems.
- The SLNS systems mainly stayed intact in the pulmonary region, while they decomposed in other organs.
- The reticuloendothelial system (RES) was the main accumulation site and the liver showed the highest accumulation.

Acknowledgments

暨南大學 JINAN UNIVERSITY

中山大學 SUN YAT-SEN UNIVERSITY

A.Prof.
Zhengwei Huang

Mr.
Jiajun Chen

Prof.
Chuanbin Wu

A.Prof.
Xin Pan

NSFC
National Natural Science Foundation of China