

## Supplementary Information

### TPGS-based and S-thanatin functionalized nanorods for overcoming drug resistance in *Klebsiella pneumonia*

Xiaojuan Wang<sup>1</sup>, Xiaoling Xu<sup>2</sup>, Shaojun Zhang<sup>1</sup>, Na Chen<sup>1</sup>, Yunfeng Sun<sup>2</sup>, Kuifen Ma<sup>1</sup>, Dongsheng Hong<sup>1</sup>, Lu Li<sup>1</sup>, Yongzhong Du<sup>2\*</sup>, Xiaoyang Lu<sup>1\*</sup>, Saiping Jiang<sup>1\*</sup>

<sup>1</sup> Department of Clinical Pharmacy, The First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China

<sup>2</sup> Institute of Pharmaceutics, College of Pharmaceutical Sciences, Zhejiang University, 866 Yu-Hang-Tang Road, Hangzhou, 310058, China

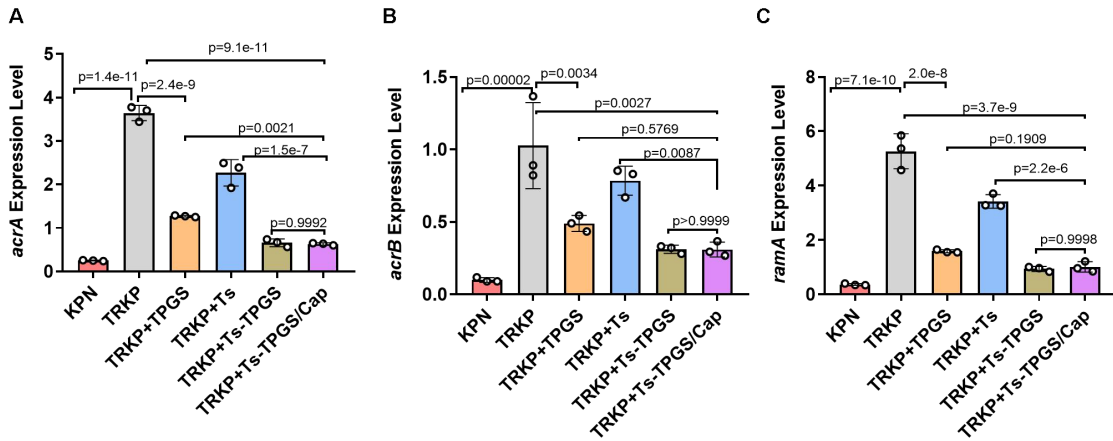
#### Correspondence:

Saiping Jiang, [E-mail: j5145@zju.edu.cn](mailto:j5145@zju.edu.cn)

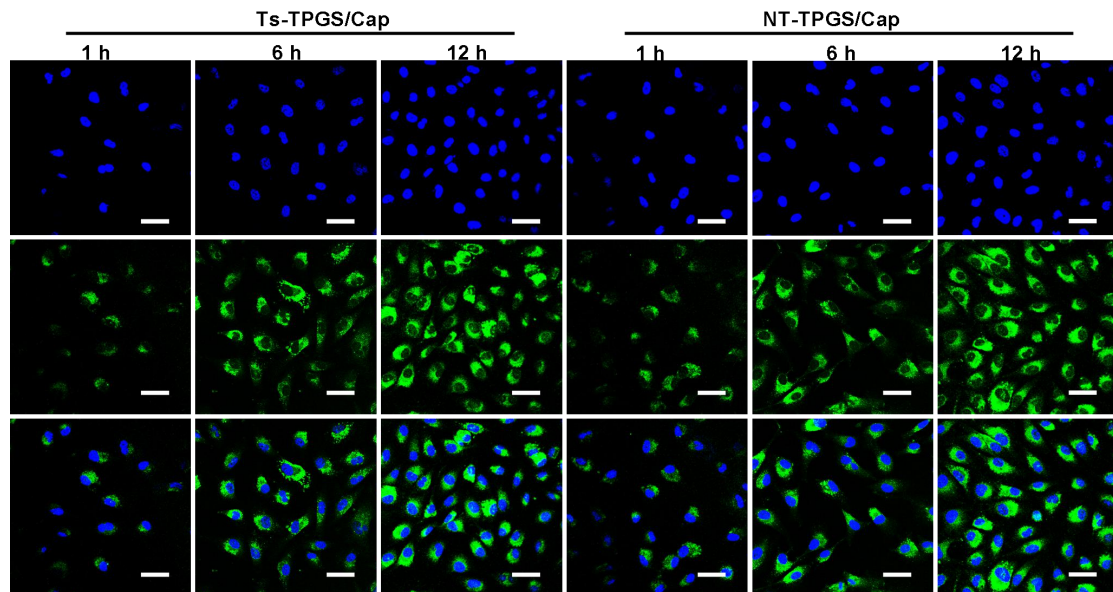
Xiaoyang Lu, [E-mail: luxiaoyang@zju.edu.cn](mailto:luxiaoyang@zju.edu.cn)

Yongzhong Du, [E-mail: duyongzhong@zju.edu.cn](mailto:duyongzhong@zju.edu.cn)

<b>Content</b>	<b>Page</b>
<b>Supplementary Fig. 1</b> The inhibitory effect of TPGS on efflux pumps.	<b>S3</b>
<b>Supplementary Fig. 2</b> Fluorescence images of EA.hy926 cells after incubation with NT-TPGS/Cap and Ts-TPGS/Cap nanorods.	<b>S4</b>
<b>Supplementary Fig. 3</b> The quantitative analysis of bacterial counts in the BALF of KPN-infected and TRKP-infected pneumonia mice	<b>S5</b>
<b>Supplementary Table 1.</b> FIC indices against KPN and TRKP.	<b>S6</b>
<b>Supplementary Table 2.</b> Primer sequences for efflux pump genes	<b>S6</b>

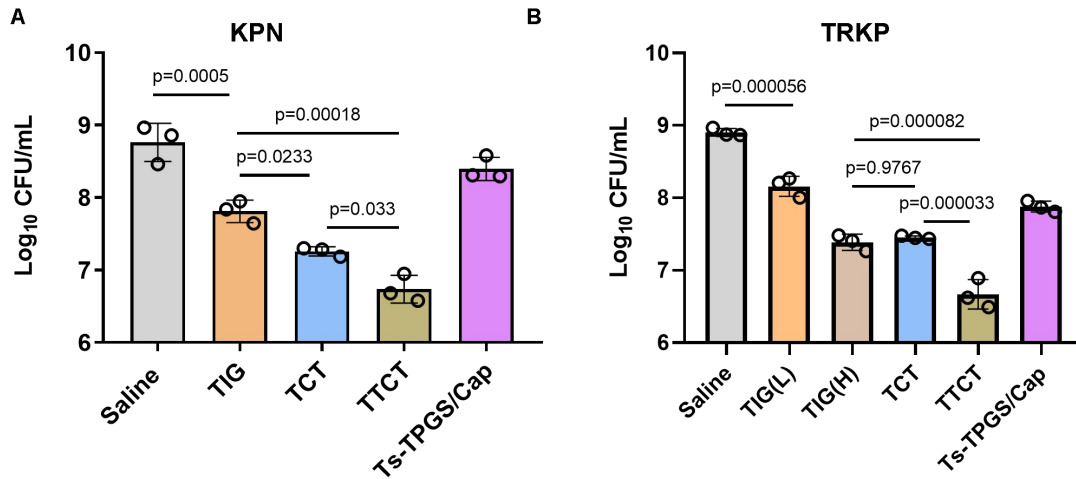


**Supplementary Fig.1** The inhibitory effect of TPGS on efflux pumps. The expression levels of (A) *acrA*, (B) *acrB* and (C) *ramA* of TPGS, Ts, Ts-TPGS and Ts-TPGS/Cap nanorods treated TRKP by RT-PCR method. KPN and TRKP without any treatment were used as control. Ts: S-thanatin peptide; TPGS: tocopheryl polyethylene glycol succinate; Ts-TPGS/Cap: Ts-TPGS functionalized calcium phosphate nanorods; KPN: *Klebsiella pneumonia*; TRKP: tigecycline-resistant *Klebsiella pneumonia*. Data are presented as the mean  $\pm$  SD (n=3 independent experiments). One-way analysis of variance (ANOVA) with post hoc Tukey tests were performed in A, B and C.



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**Supplementary Fig.2** Fluorescence images of EA.hy926 cells after incubation with NT-TPGS/Cap and Ts-TPGS/Cap nanorods. The cells were labeled with DAPI (blue), and the green fluorescence signal indicated the nanorods. Scale bar = 50  $\mu\text{m}$ . Ts-TPGS/Cap: Ts-TPGS functionalized calcium phosphate nanorods; NT-TPGS/Cap: non-targeting peptide-TPGS functionalized calcium phosphate nanorods. The experiments were repeated independently for three times with similar results.



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13 **Supplementary Fig.3** The quantitative analysis of bacterial counts in the BALF of  
 14 KPN-infected (A) and TRKP-infected pneumonia mice after 48 h receiving various  
 15 treatments. TIG: free tigecycline; TIG(L): low dose of tigecycline (15 mg/kg); TIG  
 16 (H): high dose of tigecycline (45 mg/kg); TCT: tigecycline loaded TPGS/Cap  
 17 nanorods; TTCT: tigecycline-loaded Ts-TPGS/Cap nanorods; KPN: *Klebsiella*  
 18 *pneumonia*; TRKP: tigecycline-resistant *Klebsiella pneumonia*; BALF:  
 19 bronchoalveolar lavage fluid. Data are presented as the mean  $\pm$  SD (n = 3 mice).  
 20 One-way analysis of variance (ANOVA) with post hoc Tukey tests were performed  
 21 in A and B.

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**Supplementary Table 1. FIC indices against KPN and TRKP**

Microorganisms	Combination	MIC (ug/mL)		FICI	Interpretation
		Individual	Combined		
TRKP	TIG	4	1	0.375	synergistic
	Ts	16	2		
KPN	TIG	1	0.5	0.75	additive
	Ts	16	4		

**Supplementary Table 2. Primer sequences for efflux pump genes**

Primer name	Primer Sequence
<i>acrA</i> -F	ATGTGACGATAAACCGGCTC
<i>acrA</i> -R	CTGGCAGTTCGGTGGTTATT
<i>acrB</i> -F	CGATAACCTGATGTACATGTCC
<i>acrB</i> -R	CCGACAACCATCAGGAAGCT
<i>ramA</i> -F	GCATCAACCGCTGCGTATT
<i>ramA</i> -R	GGGTAAAGGTCTGTTGCGAAT
<i>16s-rRNA</i> -F	CAGCTCGTGTCGTGAGATGT
<i>16s-rRNA</i> -R	CGTAAGGGCCATGATGACTT