Supplementary information

Polysaccharide depolymerase potentiates antibiotic efficacy against *Acinetobacter baumannii* pneumonia via low-serum-dependent mechanisms

Honglan Wang [1], Ping Zeng [1], Pengfei Zhang [1], Zhong Zuo [1], Yannan Liu [2], Jiang Xia [3], Jenny Ka Wing Lam [4], Hak-Kim Chan [5], Sharon Shui Yee Leung [1]*

[1] School of Pharmacy, the Chinese University of Hong Kong, Hong Kong SAR, China

[2] Emergency Medicine Clinical Research Center, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, 100020, China

[3] Department of Chemistry, the Chinese University of Hong Kong, Hong Kong SAR, China

[4] Department of Pharmaceutics, UCL School of Pharmacy, University College London, 29-39 Brunswick Square, WC1N 1AX, UK

[5] Sydney Pharmacy School, University of Sydney, Sydney, NSW 2006, Australia

* Corresponding author. E-mail address: sharon.leung@cuhk.edu.hk (S.S.Y. Leung).

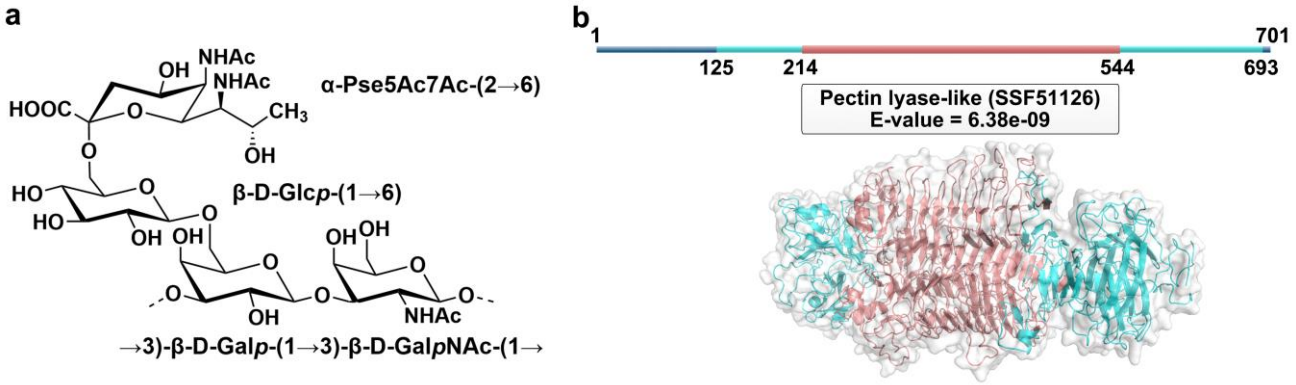

Figure S1. Structural and functional analysis of the depolymerization activity of Dpo71 against MDR-AB2 bacterial capsule. (a) The unit structure of K2 capsular polysaccharide of AB bacteria. (b) Bioinformatic analysis of the structure and domain of the putative tail fiber Dpo71 (UniProtKB accession number: K4P093).

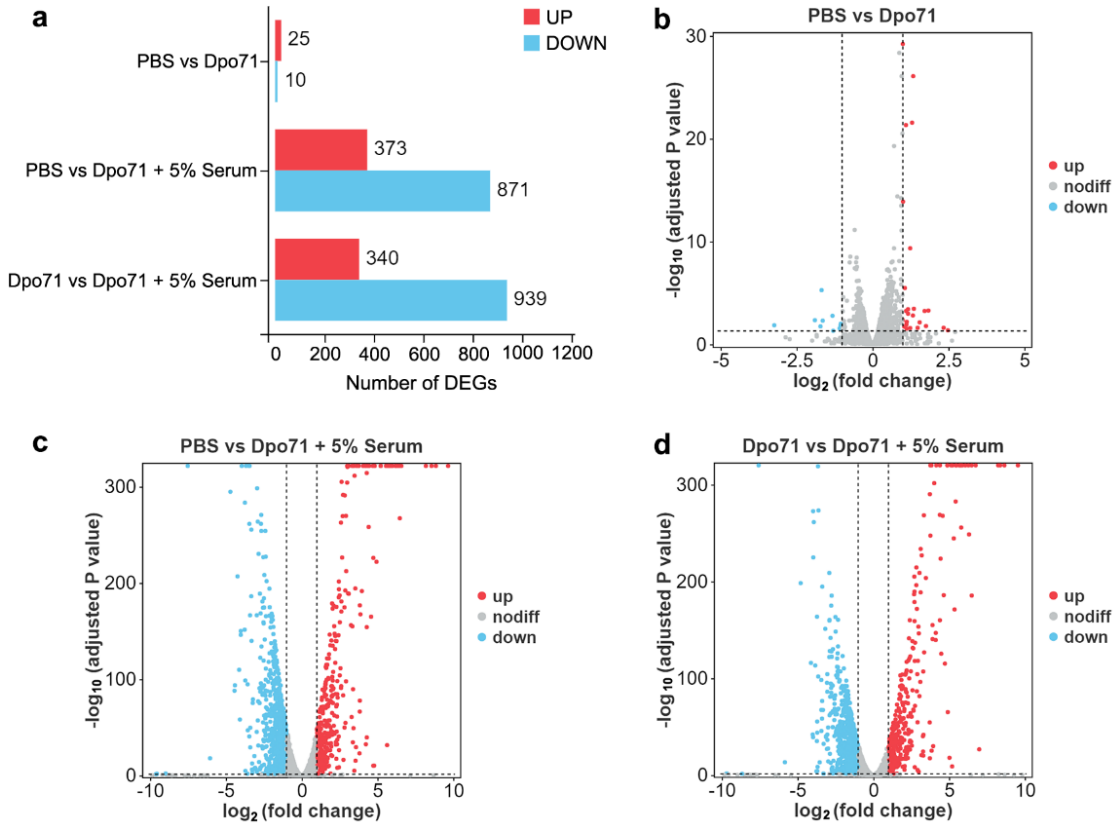

Figure S2. Basic analysis of differentially expressed genes (DEGs) in bacteria treated with PBS, Dpo71, and Dpo71 + 5% serum. (a) Column plot of DEGs among the three groups. (b) Volcano plot of DEGs in bacteria treated with PBS and Dpo71. (c) Volcano plot of DEGs in bacteria treated with PBS and Dpo71 + 5% serum. (d) Volcano plot of DEGs in bacteria treated with Dpo71 and Dpo71 + 5% serum.

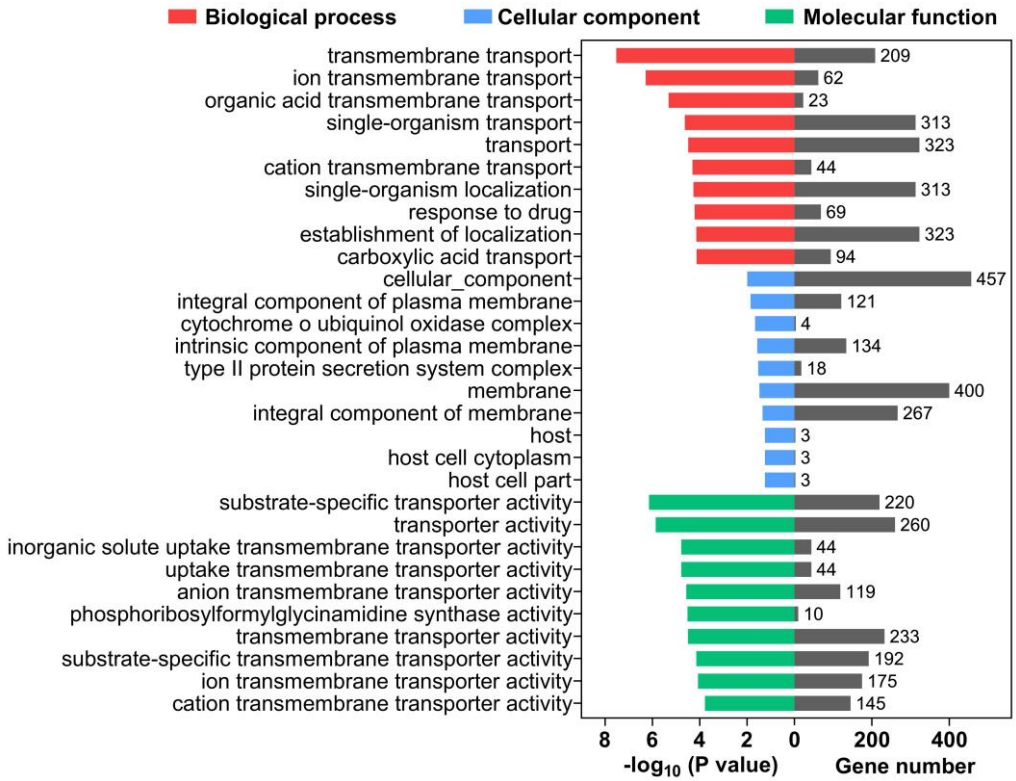

Figure S3. Gene Ontology (GO) enrichment analysis of DEGs in bacteria treated with Dpo71 and Dpo71 + 5% serum.

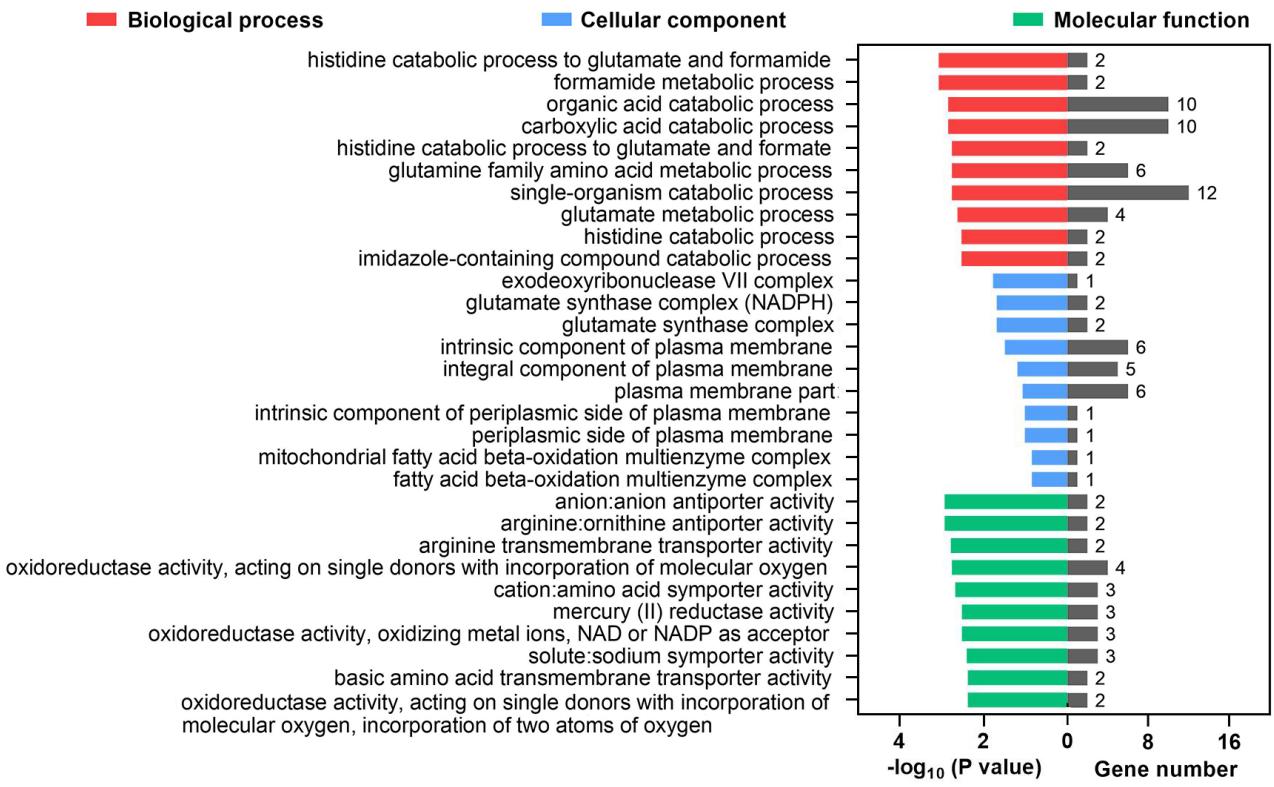

Figure S4. Gene Ontology (GO) enrichment analysis of DEGs in bacteria treated with PBS and Dpo71.

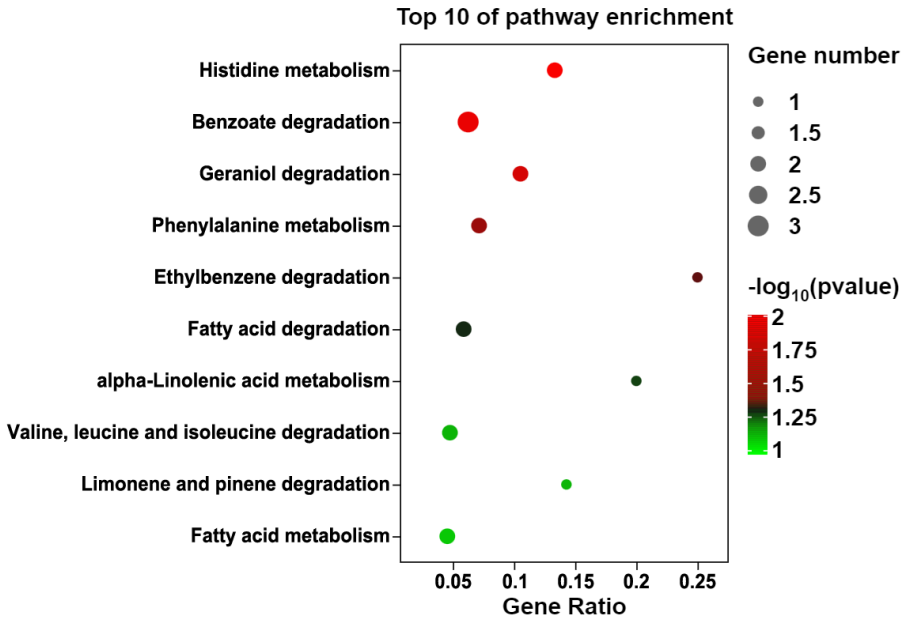

Figure S5. Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis of DEGs in bacteria treated with PBS, and Dpo71. The top 10 enriched pathways were shown.

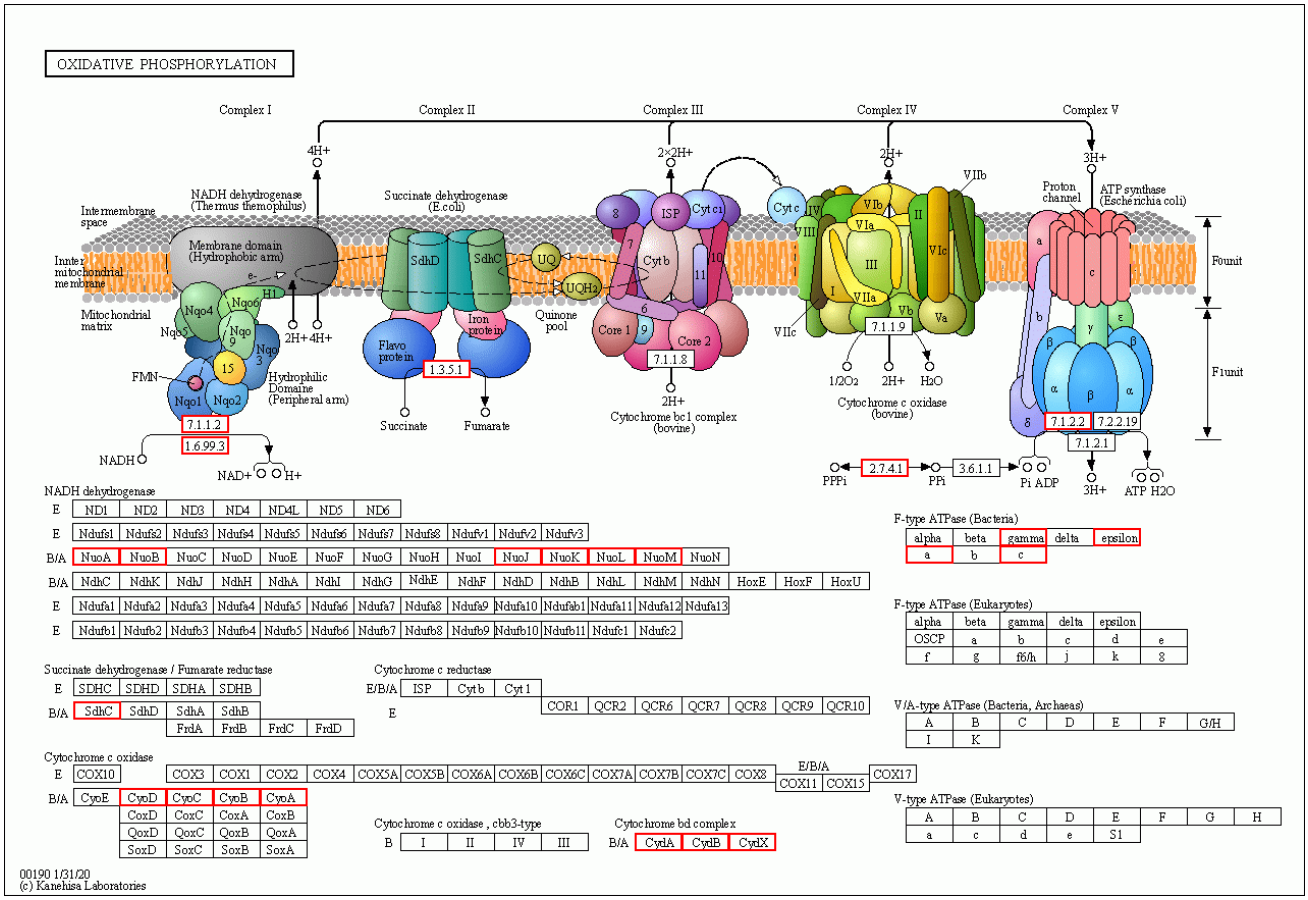

Figure S6. OXPHOS-related DEGs (marked in red box) in bacteria treated with Dpo71 and Dpo71 + 5% serum.

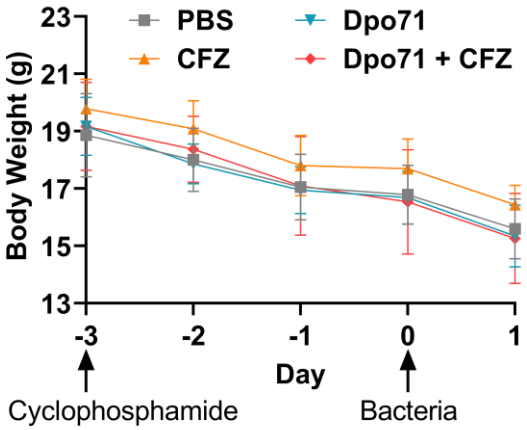

Figure S7. Body weight change of BALB/c mice pneumonia models during the overall course of *in vivo* study.

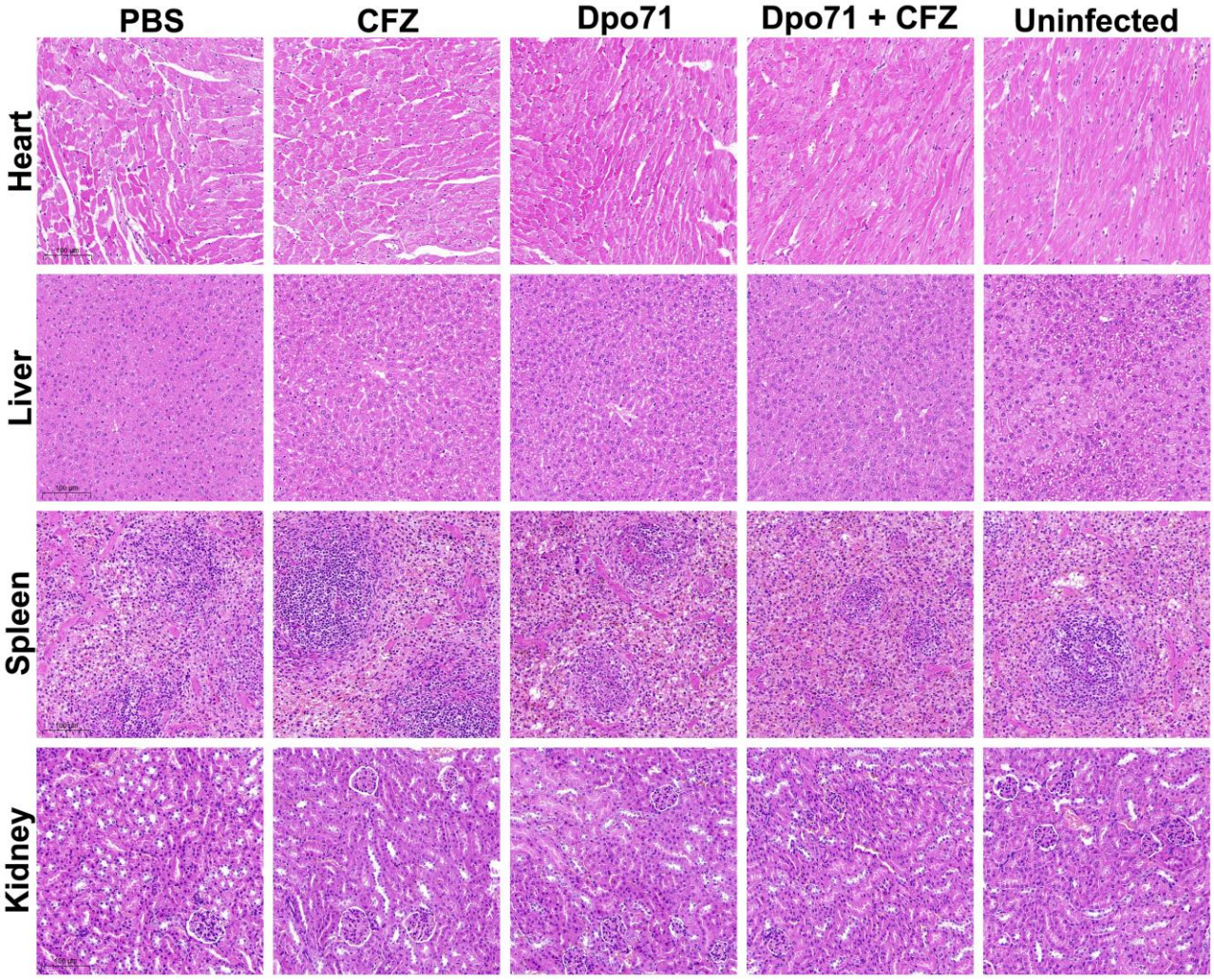

Figure S8. Histopathological examination of major organs (Heart, Liver, Spleen, and Kidney) after various treatments. The scale bar is 100 μm.

Table S1. MIC values of Dpo71, six antibiotics, and their combinations with 10 μg/mL Dpo71 in the absence or presence of 5% serum

Agents	MIC (μg/mL)			
	no serum	+ 5% serum	no serum + 10 μg/mL Dpo71	+ 5% serum + 10 μg/mL Dpo71
Dpo71	ND	≥ 40	-	-
Colistin (CST)	≥ 2	≥ 2	≥ 2	≥ 0.5
Meropenem (MEM)	≥ 8	≥ 8	≥ 8	≥ 2
Ceftazidime (CFZ)	≥ 64	≥ 64	≥ 64	≥ 2
Ciprofloxacin (CIP)	≥ 64	≥ 64	≥ 64	≥ 2
Amikacin (AMK)	≥ 1024	≥ 1024	≥ 1024	≥ 2
Gentamicin (GEN)	≥ 1024	≥ 1024	≥ 1024	≥ 8