

Supporting Information for

Multi-stage assembled *Lactobacillus reuteri*-capsule patch for persistent anti-infection

Chen Zhou^{a b c}, Yuxiang Wang^{a b}, Ming Yang^c, Hao Guo^{a b}, Xiang Ren^d, Gongbing Liu^d, Hailong Wang^d, Wei Wei^c, Yujiang Fan^{a b}, Hongning Wang^{c*}, Yong Sun^{a b c*}

a. National Engineering Research Center for Biomaterials, Sichuan University, 29 Wangjiang Road, Chengdu, Sichuan, 610064, PR China

b. College of Biomedical Engineering, Sichuan University, 29 Wangjiang Road, Chengdu, Sichuan, 610064, PR China

c. Animal Disease Prevention and Green Development Key Laboratory of Sichuan Province, College of Life Sciences, Sichuan University, 29 Wangjiang Road, Chengdu, Sichuan, 610064, PR China

d. Varnotech Biopharm (Chengdu) Ltd, Building 6, No. 670 Haifa Road, Chengdu Medical Zone, Chengdu, Sichuan, 610064, PR China

e. Department of Emergency, West China Hospital, Sichuan University, Chengdu, Sichuan, 610064, PR China

* Corresponding authors at: Biomaterials Building, Sichuan University, Chengdu, 610064, China.

E-mail addresses:

whongning@163.com (Hongning Wang); sunyong8702@scu.edu.cn (Yong Sun)

Results and discussion

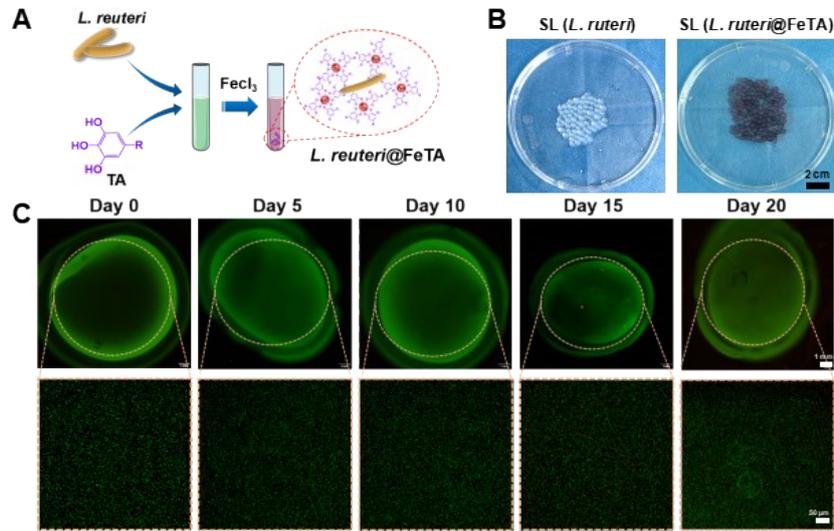


Fig. S1. (A) The synthesis schematic of *L. reuteri*@FeTA. (B) Representative images of SL capsule with *L. reuteri* and *L. reuteri*@FeTA, respectively. (C) CLSM images of *L. reuteri* living/dead strain in SL capsule.

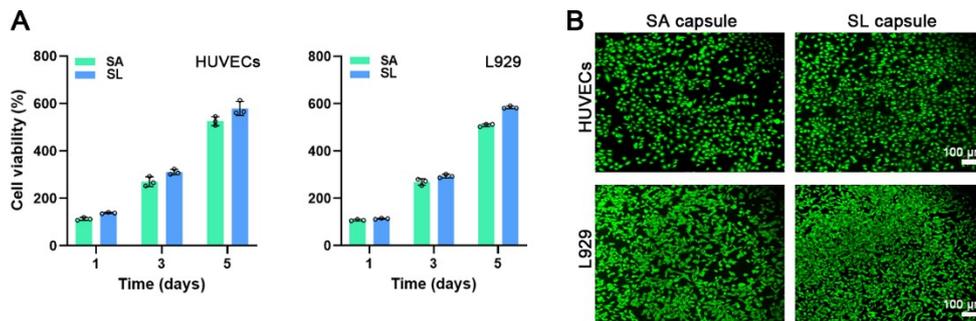


Fig. S2. The viability (A) and microscopic images (B) of Live/Dead stains HUVECs and L929 cells incubated by SA and SL capsule after 5 days.

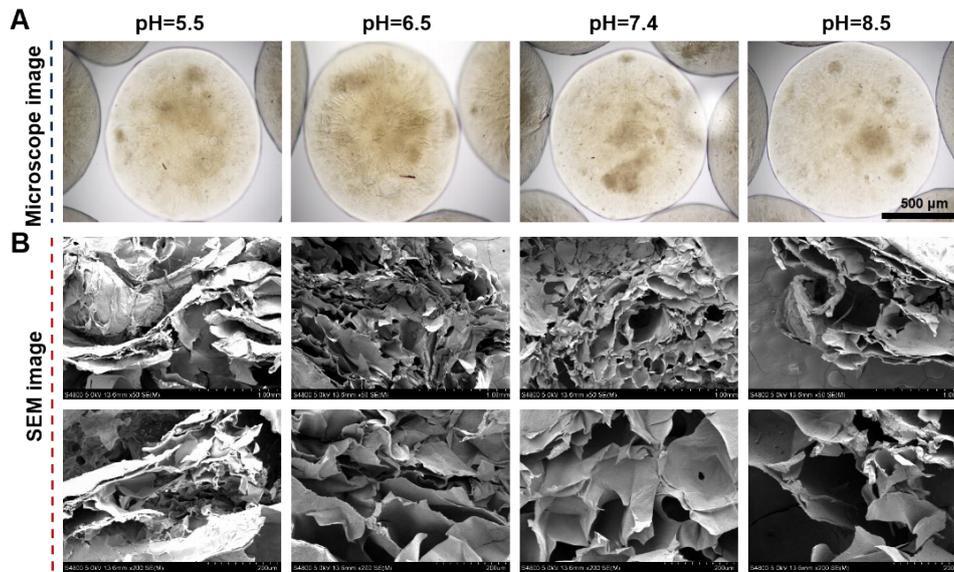


Fig. S3. (A) Representative images of SL capsule in different pH value at microscopy. (B) Representative SEM images of SL capsule in different pH value.

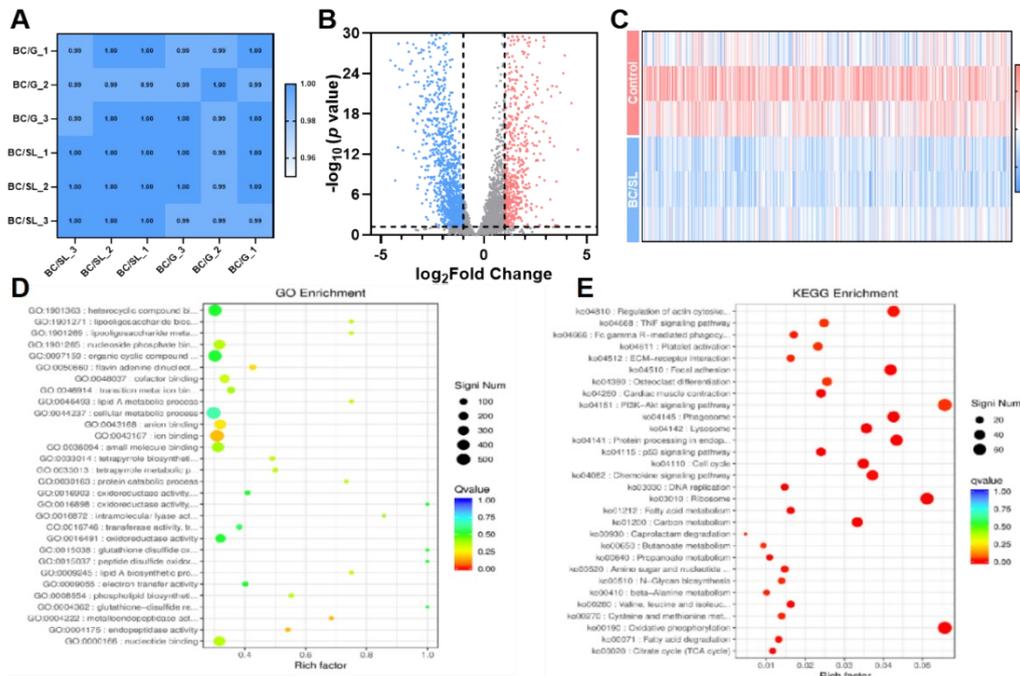


Fig. S4. Transcriptomic analysis in bacteria (*P. aeruginosa*) of BC/SL vs. control. (A) Heatmap of Pearson correlation. (B) Volcano plot of differentially expressed genes. (C) Heatmap analysis of differentially expressed genes. The enrichment of (D) GO terms and (E) KEGG pathways.

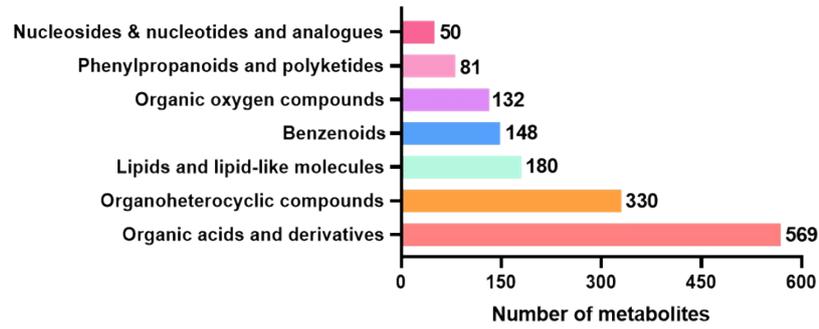


Fig. S5. The metabolite analysis of BC/SL.

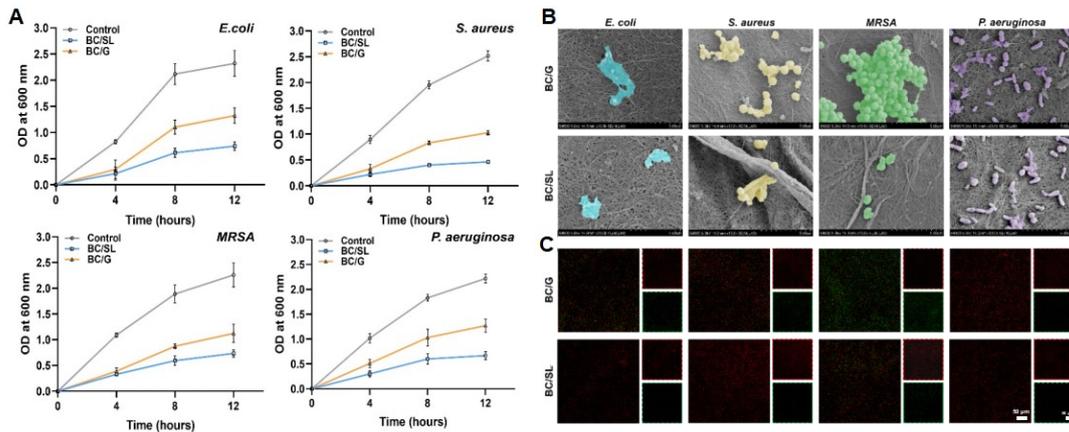


Fig. S6. The growth curve of bacteria (A), representative SEM images (B), and CLSM images (C) of bacteria living/dead strain under sample influence, at 1st cycle of bacterial supplementation.

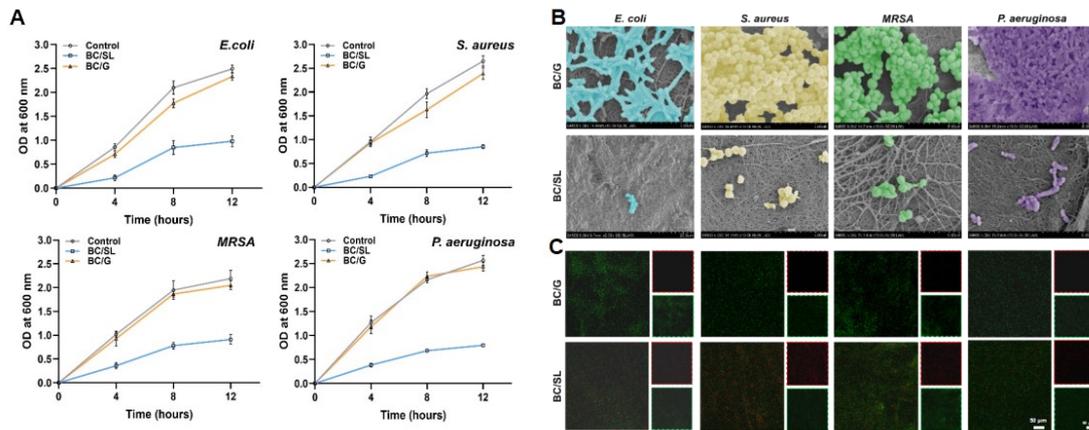


Fig. S7. The growth curve of bacteria (A), representative SEM images (B), and CLSM images (C) of bacteria living/dead strain under sample influence, at 2nd cycle of bacterial supplementation.

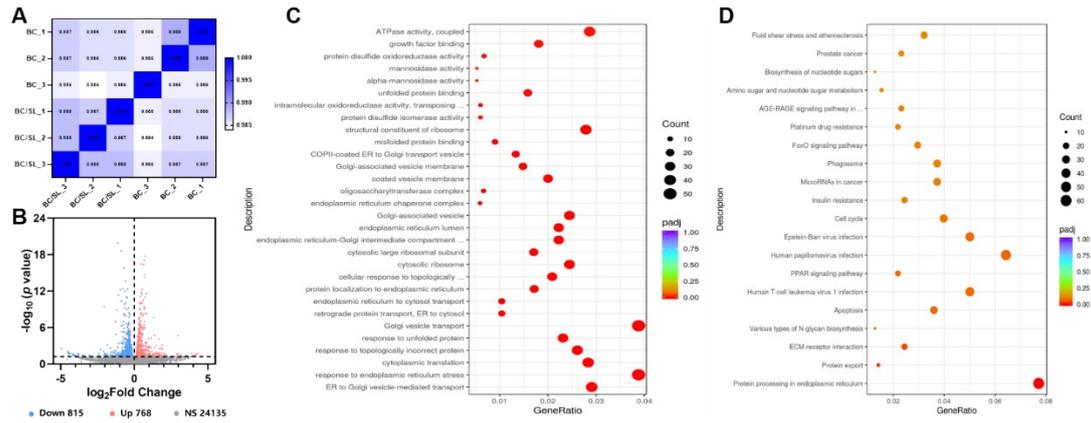


Fig. S8. Transcriptomic analysis in cell (L929) of BC/SL vs. BC/G. (A) Heatmap of Pearson correlation. (B) Volcano plot of differentially expressed genes. (C) Heatmap analysis of differentially expressed genes. The enrichment of (D) GO terms and (E) KEGG pathways.

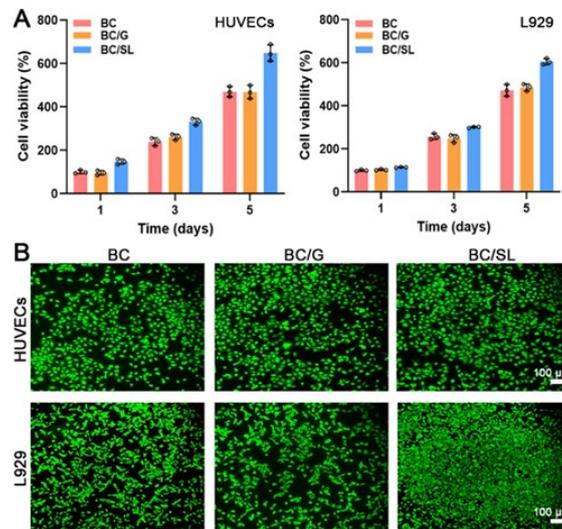


Fig. S9. The viability (A) and microscopic images (B) of Live/Dead stains HUVECs and L929 cells incubated by BC, BC/G, and BC/SL after 5 days.

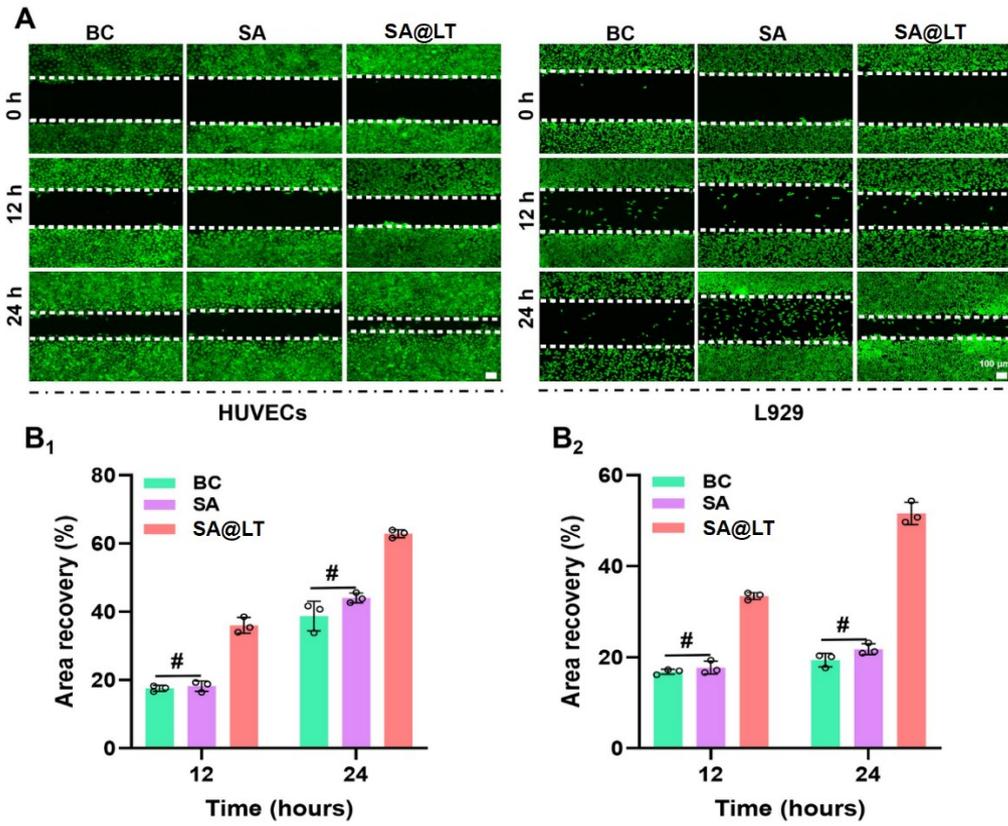


Fig. S10. The migration of L929 cells and HUVECs in a scratch assay (A) with statistics of the area recovery rate (B) incubated by BC, BC/G, and BC/SL.

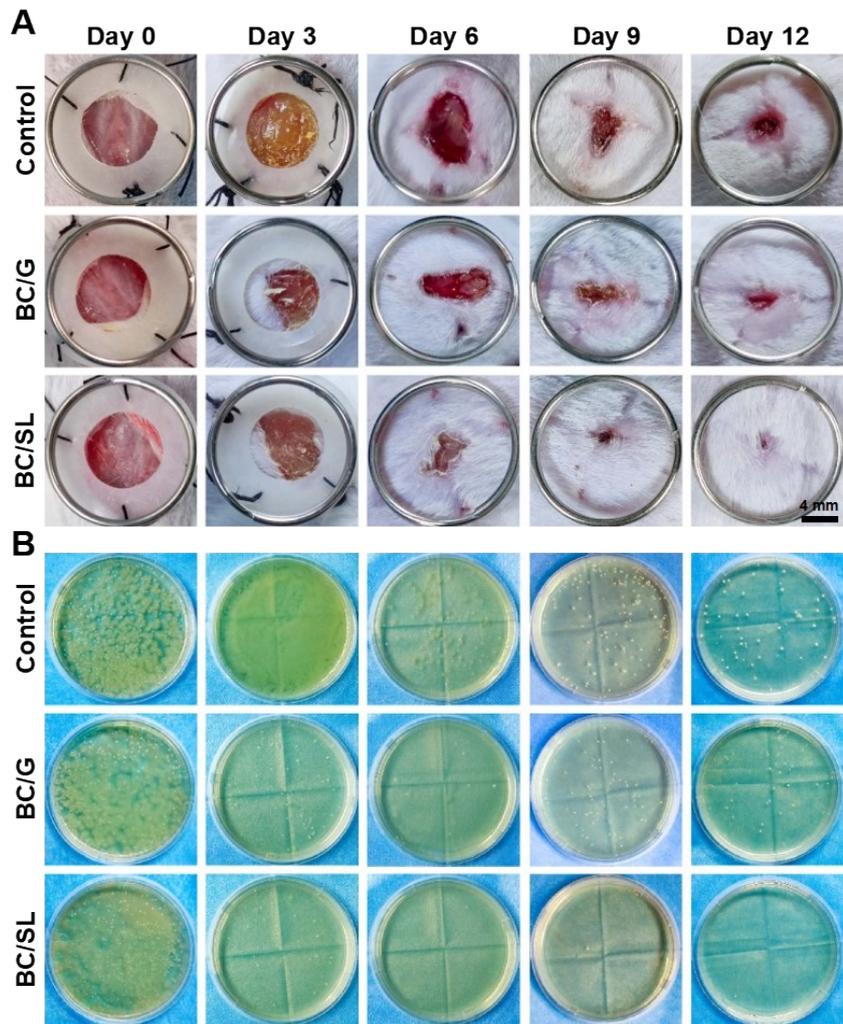


Fig. S11. Representative image of wounds (A) and survival bacteria clones (B) at a predetermined time. The wound site without additional bacteria.

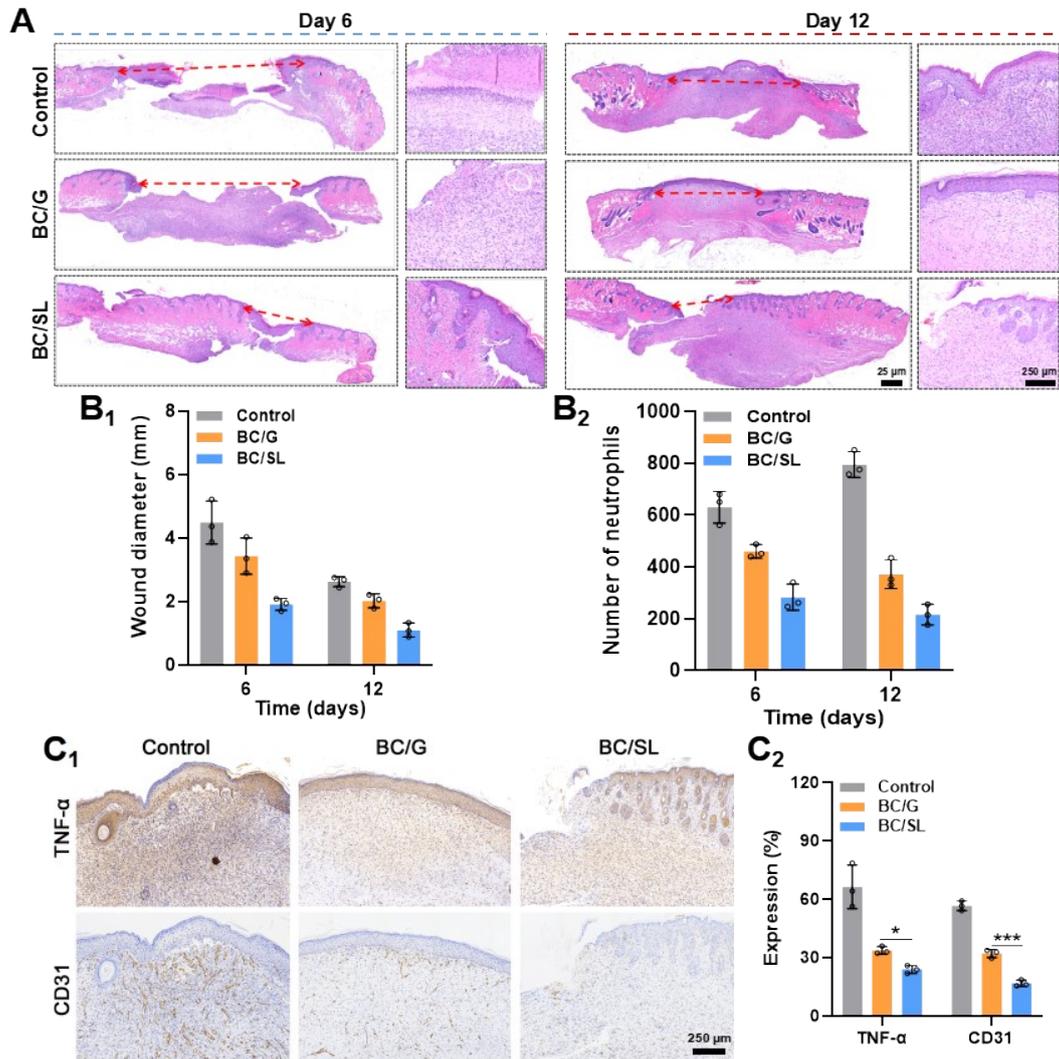


Fig. S12. (A) Images of H&E stained wound tissue 6 days and 12 days. (B1) The statistics of wound diameter, (B2) number of new hair follicles. The immunohistochemistry of TNF- α and CD-31 in wound tissue at 12 days with the expression statistics. The wound site without additional bacteria.

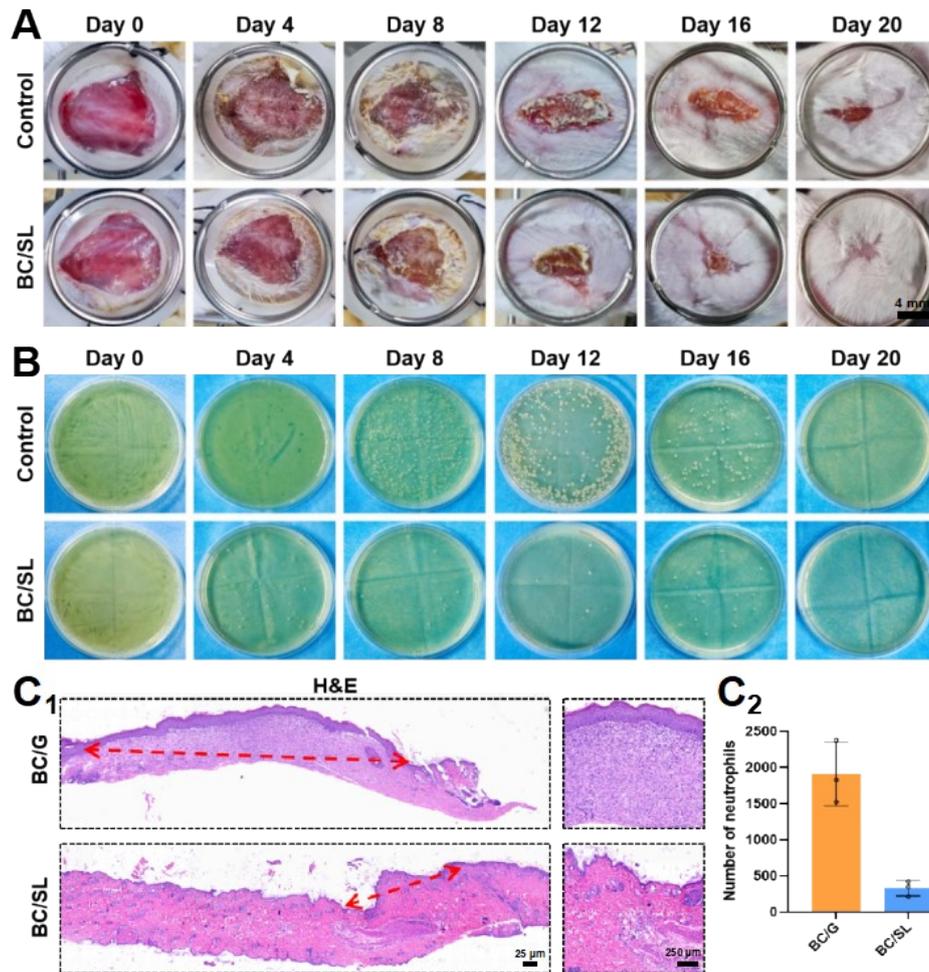


Fig. S13. Representative image of wounds (A) and survival bacteria clones (B) at a predetermined time. (C) Images of H&E stained wound tissue at days. The wound site was infected by *P. aeruginosa* in large area.

Tab. S1. Primer sequence used in q-PCR analysis (human).

Gene name	Forward primer	Reverse primer
<i>GAPDH</i>	TTCCACCCATGGCAAATTCC	GACTCCACGACGTACTIONCAGC
<i>COL8A</i>	TGACACCTGAGGTCAAGCAC	ATCTTGACCAGGCTAGCAG
<i>HMOX1</i>	TTGATGGGGTGAAACCTCCG	TGTCTGCCGTTGTAGAGCAG
<i>CCN1</i>	CTTTTCAACCCTCTGCACGC	AGGACGCACTTCACAGATCC
<i>CCN4</i>	CTCTAACGTCAATGCCCGGT	CCTGCGAGAGTGAAGTTCGT
<i>SOD2</i>	GTGGGAGTCCAAGGTTTCAGG	TAGTAAGCGTGCTCCCACAC
<i>FGFR</i>	ACCAAACCAAACCCTGTAGC	CCTCCAATTCGGTGGTCAGG
<i>KLF</i>	CCGTCCTATGCCGCTACAAT	TCGCAGAAGTGGATACGTCG
<i>CSF2</i>	TCAAAGAAGCCCTGAACCTCC	GGTGAAATTGCCCCGTAGAC