Supporting information

All human studies were performed in compliance with ethical protocols approved by Jagiellonian University Institutional Bioethics Committee. All participants provided their written informed consent to participate in these studies as recommended by the ethical board. Normal human keratinocytes were isolated from skin of healthy donors as previously described (14). Keratinocytes were cultured until confluency in KGM-Gold medium (Lonza) to generate passage 1-3 cells. Cells were then differentiated in CnT-Prime 3D Barrier Medium (CELLnTEC) for 3 days followed by the treatment with p4.

Fig. S1. Little effect of P4 on human keratinocyte viability.

Human primary keratinocytes derived from the skin of healthy females $(47\pm7 \text{ years old})$ (14) were cultured until confluency in KGM-Gold medium followed by differentiation in CnT-Prime 3D medium for 3 days. Cells were then treated with the indicated doses of p4 or vehicle (-) in PBS for 2h. (A) Cell viability was determined using MTT assay or (B) LDH assay. Reduction of the tetrazolium dye MTT to formazan by the p4-treated cells is shown as a % of vehicle-treated cells (A). LDH activity present in conditioned media is shown as a % of TritonX-treated cells (B). Each data point for a given condition represents an independent donor, and the horizontal line indicates the mean value in each group. n=4, ** p< 0.005 by one-way ANOVA with post-hoc Dunnett's test.

Fig. S2. TEM images of p4-treated S. aureus demonstrate massive cell wall lesions.

S. *aureus* strain 8325-4 was incubated with vehicle (PBS) or 100 μ M of the indicated peptides for 2h. Cells were imaged by TEM. Scale bars - 200 nm. Data are from one experiment and are representative of at least three experiments.



