

Figure S1. DHE and DAPI staining of RAW264.7 cells. (a) DAPI staining; (b) DHE staining. 10, 20 and 40 are representative of 10, 20, 40  $\mu$ g/mL Nisin A. Scale bar is representative of 200  $\mu$ m



Figure S2. DCFH-DA and DAPI staining of RAW264.7 cells. (a) DAPI staining; (b) DCFH-DA staining. 10, 20 and 40 are representative of 10, 20, 40  $\mu$ g/mL Nisin A. Scale bar is representative of 200  $\mu$ m



Figure S3. Morphology of RAW264.7 cells treated by Nisin A with different concentrations. 10, 20 and 40 are representative of 10, 20, 40  $\mu$ g/mL Nisin A. Scale bar is representative of 200  $\mu$ m

## **Supporting Materials**



Figure S4. Oxidative phosphorylation metabolites alterations induced by Nisin A



Figure S5. ROS-related metabolites induced by Nisin A



Figure S6. Inflammatory related metabolites alterations induced by Nisin A



Figure S7. Nisin A-induced differential metabolites about sphingolipid signaling pathway





by Nisin A



Figure S9. Differential expressed metabolites about protein digestion and absorption pathway induced by Nisin A



Figure S10. Differential metabolites about purine metabolism induced by Nisin A



Figure S11. (a-b) Mean levels of metabolites of different groups, including model group (LPS alone) and treated group (LPS + nisin A). Bar diagrams show means  $\pm$  SD with every dot representing an individual (n=3). p < 0.05 was set as the threshold for significance by one-way ANOVA followed by post hoc comparisons using Duncan's multiple range test. Different letters are representative of significant difference.



Figure S12. (a-b) The levels of nisin A in the murine stomach and intestine 0.5 h and 3 h after oral administration, determined by ELISA analysis. Bar diagrams show means  $\pm$  SD with every dot representing an individual (n=3). p < 0.05 was set as the threshold for significance by one-way ANOVA followed by post hoc comparisons using Duncan's multiple range test. Different letters are representative of significant difference.



Figure S13. (a) The levels of nisin A in murine serum 0.5 h and 3 h after oral administration, determined by ELISA analysis. Bar diagrams show means  $\pm$  SD with every dot representing an individual (n=3). p < 0.05 was set as the threshold for significance by one-way ANOVA followed by post hoc comparisons using Duncan's multiple range test. Different letters are representative of significant difference.