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infection by Gram-negative bacteria. However, despite the overuse of these antibiotics, resistance in these pathogens is increasing. Development of the bacterial cell envelope in Gram-negative bacteria is being studied as a means to inhibit or kill the bacteria. Gram-negative bacterial cell envelopes are important by providing a barrier that can repel peptide and low molecular weight antibiotics as well as maintaining the morphology of the bacterium. However, one of the key components of the cell envelope is lipopolysaccharide (LPS), a glycolipid consisting of lipid A and polysaccharide core. In the absence of complete bacterial cell envelope, the LPS can be lethal to the bacteria. In this study, we present the chimera between the LPS and polymyxin B (LPS-PMB) and demonstrate that it is a bactericidal compound against Gram-negative bacteria. LPS-PMB kills Gram-negative bacteria in a time and dose-dependent manner via induction of outer membrane permeability and reactive oxygen species (ROS) production. In addition, LPS-PMB shows long-lasting bactericidal activity in vivo in a murine pneumonia model, and it can penetrate human lung epithelial cells. These characteristics of LPS-PMB make it a potential candidate for the development of new antibacterial drugs. Acknowledgements The authors thank Dr. I. M. Maurer (University of Alabama at Birmingham, Alabama) for providing PA531 and PA1502 and the USDA-ARS WPGSC for clone C4-4. This work was supported by the National Institute of Allergy and Infectious Diseases and National Institute of General Medical Sciences (NIAID/NIGMS) under contract no. N01-AI-30094 (PI: Doo-Hyung Kim) and P20GM103481-13. Figures Fig. 1. Bactericidal activity of the chimera LPS-PMB against Gram-negative bacteria. (a) Time-dependent bactericidal activity of LPS-PMB against Gram-negative bacteria, A. baumannii, E. coli, K. pneumonia 595f342e71

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