

Antiplatelet activity of staphylococcus aureus lipoteichoic acid is mediated through a cyclic AMP pathway

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Abstract

In this study, Gram-positive *Staphylococcus aureus* ence Ltd. All rights reserved. lipoteichoic acid (LTA) dose dependently (0.1–1.0 mg/mL) and time dependently (10–60 min) inhib- Key Words: Gram-positive bacteria; LTA; Platelet aggregated platelet aggregation in human platelets stimu- gation; Cyclic AMP; Protein kinase C lated by agonists (i.e., thrombin and collagen). LTA also dose dependently inhibited intracellular Traditionally recognized as a consequence of Ca²⁺ mobilization in human platelets stimulated Gram-negative bacteraemia, septic shock by collagen. In addition, LTA (0.5 and 1.0 mg/mL) can also be caused by Gram-positive organdose dependently increased the formation of cyclic isms, fungi, and probably viruses and parasites. Al- AMP but not cyclic GMP in platelets. LTA (0.5 though relatively rare in the 1970s, the incidence of and 1.0 mg/mL) did not significantly increase the Gram-positive septic shock has increased markedly production of nitrate within a 10-min incubation over the past 15 years [1]. On the basis of this period. Rapid phosphorylation of a platelet protein evidence, it seems reasonable to conclude that beof Mr 47,000, a marker of protein kinase C activa- tween one-third and one-half of all cases of sepsis tion, was triggered by PDBu (0.03 mM). This phos- are currently caused by Gram-positive organisms, phorylation was dose dependently inhibited by and that the incidence of Gram-positive sepsis LTA (0.5 and 1.0 mg/mL) within a 10-min incuba- should continue to rise for at least the next few tion period. Furthermore, LTA (0.5 and 1.0 mg/ years [1]. mL) also inhibited platelet aggregation induced by Septic shock can be defined as sepsis with hypo- PDBu (0.03 mM) in human platelets. tension, resulting in impaired tissue perfusion de- These results indicate that the antiplatelet activ- spite adequate fluid resuscitation. Sepsis is believed ity of LTA may be involved in the increase of cyclic to result from complex mechanisms involving acti- AMP, leading to inhibition of intracellular Ca²⁺ vation of a number of cells, most notably monomobilization and protein kinase C activity. There- cytes, T cells, neutrophils, and platelets. The result fore, LTA-mediated alteration of platelet function may contribute to bleeding

diathesis in septicemic and endotoxemic patients. . 2000 Elsevier SciIn
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