Comment on "Changes and Regulation of the C5a Receptor on Neutrophils during Septic Shock in Humans"

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We read the recent paper by Unnewher and colleagues (1) with interest. This paper adds to the growing literature on the role of C5a in human critical illness. The finding of reduced neutrophil CD88 expression in human sepsis was first identified by Furebring and colleagues in 2002 (2). This finding was confirmed in a study of patients with hospital-acquired sepsis (3), in which we demonstrated a correlation between CD88 expression and neutrophil phagocytic function. This was further developed in a longitudinal cohort study demonstrating reduced neutrophil CD88 predicted subsequent diagnosis of nosocomial infection (4). Interestingly, we found that low CD88 was not specific to patients presenting to the intensive care unit (ICU) with sepsis, and patients with sterile insults showed similar reductions in expression. This tallied with previous findings from Huber-Lang’s team demonstrating reduced neutrophil CD88 expression in humans following major trauma (5). This apparently maladaptive response to infective and sterile insults may help explain why secondary infections remain so prevalent in the ICU.

The association between low neutrophil CD88 and mortality from septic shock is supported by our recent analysis of a range of markers of immune cell dysfunction in critical illness (6). Low neutrophil CD88 was the strongest predictor of subsequent nosocomial infection and a significant predictor of death from infective insults but, interestingly, not of death from sterile insults.

The crucial next step in the field of complement-mediated immune dysfunction will be effective therapies, either targeting the complement pathway itself or down-stream mediators of dysfunction (4).

Andrew Conway Morris,* Thomas S. Wilkinson,† Timothy S. Walsh,* and A. John Simpson‡

*Centre for Inflammation Research, University of Edinburgh, Edinburgh, Midlothian EH16 4TJ, United Kingdom; †Institute of Life Science, Infection and Microbiology, Swansea University, Swansea, Glamorgan SA2 8PP, United Kingdom; and ‡Institute of Cellular Medicine, University of Newcastle, Newcastle-upon-Tyne, Tyne and Wear NE2 4HH, United Kingdom

Address correspondence and reprint requests to Andrew Conway Morris, Centre for Inflammation Research, Queen’s Medical Research Institute, 47 Little France Crescent, University of Edinburgh, Edinburgh, Midlothian EH16 4TJ, U.K. E-mail address: mozza@doctors.org.uk

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