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Response to Letter to the Editor - Letter in Response to 13-01510 (Xia)

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Keywords

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We appreciate the interest in our paper (1) providing data demonstrating lung injury is not present in mice after sepsis induced by cecal ligation and puncture (CLP). Our study was designed to determine if there was lung injury in mice that would die after CLP compared to those who would survive. Two control groups were included: a positive control of mice with lung injury induced by bacterial pneumonia and a negative control group of mice receiving only normal saline. Our manuscript did not focus on the differences in lung injury in septic mice compared to normal mice. Unfortunately Li, Lou, and Xia have misinterpreted our results (2). The data specifically shows that there is no lung injury after CLP, but there is lung injury in mice with bacterial pneumonia. The figure legends compared the positive control, bacterial pneumonia, to the negative control, normal saline. While the septic mice show some respiratory physiology changes, tidal volume was maintained and, importantly, no hypoxemia developed indicating no loss of lung function due to injury following CLP. There was also a concern that antibiotics were altering the development of lung injury. It should be pointed out that all the mice that underwent CLP received antibiotic therapy so this would not account for the differences. As highlighted in the Discussion section, organ injury happens in septic patients even if they receive antibiotic treatment and an animal model of disease should take into account what already is common practice in the clinical scenario. The Ebong study published in 1999 (3) was also done by our laboratory and was listed as reference #27. The fluid resuscitation protocol was identical in both papers. There was one significant difference between the two models, the original Ebong paper used the inbred mouse strain BALB/c while the 2013 paper used outbred mice. The focus of the 2013 Critical Care Medicine paper was not to compare sepsis models, but rather to determine if there was lung injury in CLP mice who are predicted to die compared to those mice who are predicted to live. We have used the outbred mouse model for several publications (4–6). There was also a concern that lung injury developed in the last 24 hours prior to death. In the editorial that accompanied the publication several reasons were provided why it is unlikely

that significant pulmonary injury would develop in the late stages of peritonitis (7), reasons with which we agree. We also stated that mice were monitored for the first five days, and no hypoxia was present during the 48 to 72 hour time interval. Due to space constraints, these data were not shown. Since hypoxia did not develop in the CLP mice who would die at any time prior to their death, it would be appropriate to conclude that lung injury never develops after CLP in mice. We hope that this information clarifies the issues.

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