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# Lung & Respiratory Care

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## Guozheng Wang

### Extracellular histone-induced acute lung injury

A lthough intra-nuclear histones play essential roles in DNA packaging and gene regulation, released histones following extensive cell or organ damage are toxic to pathogens but also to host hematopoietic, endothelial and epithelial cells. Cellular toxicity mainly results from direct membrane binding and resultant calcium influx with our work showing that this can directly trigger neutrophil MPO release and NETosis. In patients with severe trauma and sepsis, we found that high circulating histone levels correlated significantly to the incidence of acute lung injury (ALI) as well as markers of endothelial damage and coagulation activation. Using histone-infusion mouse models we showed that ALI with oedema, neutrophil congestion, NETs and thrombus formation impairs pulmonary microcirculation as indicated by pressure increase and even enlargement of right ventricle in extreme conditions. Since the lungs are the predominant sites of neutrophil margination and alveolar neutrophil infiltration is the hallmark of ALI, histone-induced neutrophil congestion, MPO release and NETs formation may provide an explanation as to why lungs are more susceptible to histone toxicity than other organs and new targets for managing ALI.

#### Biography

Guozheng Wang MBChB, MD, Ph.D, has both medical and biological backgrounds. After 12 years practice of internal medicine in Southeast University of China, full time biomedical research in UK Universities (including Cambridge, Oxford and Liverpool) has been performed for over 20 years. Current focus is on the pathophysiology, diagnosis, and therapy development of sepsis and other critical illnesses.

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