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Journal club

Role of kinase suppressor of Ras-1 in *Pseudomonas aeruginosa* infections

Respiratory infection with *Pseudomonas aeruginosa* can have serious implications, particularly on a background of immunodeficiency, cystic fibrosis and mechanical ventilation. In this study, by conducting a series of experiments on mice, the authors identified the key role of the kinase suppressor of Ras-1 (Ksr1), an enzymatic protein, in the innate host response to *P aeruginosa* infection.

Ksr1 deficiency impairs the bactericidal activity of alveolar macrophages and, as a consequence, Ksr1-deficient mice were found to die of sepsis from failed clearance of *P aeruginosa*. The bactericidal activity of alveolar macrophages and neutrophils is mediated by the formation and release of nitric oxide (NO) and peroxynitrite, which is triggered by Ksr1. This occurs through a previously unidentified pathway where Ksr1 functions as a unique scaffold and mediates the interaction between inducible NO synthase (iNOS) and heat shock protein 90, thereby activating iNOS and releasing NO, which kills the bacteria.

The authors concluded that this study identifies a unique role of Ksr1 in bacterial infection and they have shown a link between Ksr1 and the regulation of bacterial pneumonia and sepsis.

► **Zhang Y**, Li X, Carpinteiro A, *et al*. Kinase suppressor of Ras-1 protects against pulmonary *Pseudomonas aeruginosa* infections. *Nat Med* 2003;**17**:341—6.

Syed Huq

Correspondence to Dr Syed Huq, ST5 Respiratory Medicine, Liverpool Heart and Chest Hospital, Liverpool, UK; syedhuq@nhs.net

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