

## JIC Award 2011

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The Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases established the “JIC Award” to commend high-quality papers published in the *Journal of Infection and Chemotherapy*. In each volume of the Journal, one article is selected on the vote of the JIC Award Selection Committee. For volume 17, 2011, the following article was selected.

### Degradation of interleukin 8 by the serine protease MucD of *Pseudomonas aeruginosa*

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#### Abstract

We investigated the influence of the type III effector, ExoS, on the host epithelial cell response to *Pseudomonas aeruginosa* infection, and we found that disruption of the *exoS* gene caused a significant increase in the amount of interleukin-8 (IL-8) in the culture medium of Caco-2 cells. We show that IL-8 was degraded in the culture medium following infection of the cells with the wild-type (PAO1), but not the *exoS* knock-out (the  $\Delta$ *exoS*) strain. Purified ExoS protein itself did not degrade IL-8. We next show that IL-8 degradation by PAO1 was inhibited by the addition of serine protease inhibitors. These results



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strongly suggest that a bacterial serine protease that degrades IL-8 is expressed and secreted into the culture medium of Caco-2 cells infected with PAO1, and that the expression of this protein is repressed in cells infected with the  $\Delta$ *exoS* strain. The PAO1 genome encodes 28 different protease genes, including two serine proteases: *PA3535* and *mucD*. *PA3535* and *mucD* gene knock-outs were constructed ( $\Delta$ *mucD* and  $\Delta$ *PA3535*), and  $\Delta$ *mucD* but not  $\Delta$ *PA3535* showed reduced IL-8 degradation. To understand the significance of IL-8 degradation, we next evaluated neutrophil infiltration in lungs excised from mice intranasally infected with the *P. aeruginosa* strains. Increased neutrophil infiltration was observed in PAO1-infected mice, but not in  $\Delta$ *exoS*- or  $\Delta$ *mucD*-infected mice. Taken together, our results suggest that *P. aeruginosa* escapes from phagocytic killing due to IL-8 degradation following the secretion of the MucD serine protease, whose expression appears to be influenced by ExoS.