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Lung alert

Role for Major Vault Protein in the innate immunity of respiratory epithelium

Major Vault Protein (MVP) is thought to be important for innate immunity and is found in antigen-presenting cells and epithelia throughout the respiratory system. This study investigated the role of MVP in human respiratory epithelium, particularly in response to infection with *Pseudomonas aeruginosa*.

As *P aeruginosa* initiates an innate immune response by forming lipid rafts on contact with lung epithelial cells, the authors analysed proteins recruited to lipid rafts and compared them with lipid rafts from uninfected cells. Using mass spectrometry, MVP was shown to be present in high concentrations within rafts. Immunofluorescence staining of *P aeruginosa* infected cells confirmed co-localisation of bacteria with MVP.

MVP recruitment into lipid rafts by wild type-CF transmembrane conductance regulator (WT-CFTR) gene-expressing cells was compared with cells expressing the ΔF508-CFTR gene. Cells expressing ΔF508-CFTR formed only 30% of the amount of MVP produced by WT-CFTR cells in the first 15 min of infection, although overall MVP expression was similar for both. Experimentally truncating the lipopolysaccharide outer core of *P aeruginosa* impaired CFTR binding and eliminated MVP formation entirely. Lungs harvested from MVP knockout mice infected with *P aeruginosa* showed 55% less epithelial internalisation of the bacteria with a subsequent 3.5-fold increase in bacterial burden and increased mortality rate.

This paper supports a role for MVP in the innate immune response. Lack of MVP may increase susceptibility to infection. This work suggests that CFTR binding of bacterial lipopolysaccharide promotes the recruitment of MVP into lipid rafts which, in turn, enhances the epithelial internalisation of *P aeruginosa*. The means by which MVP achieves has yet to be revealed and further studies are needed.

► Kowalski MP, Dubouix-Bourandy A, Bajmoczi M, *et al*. Host resistance to lung infection mediated by major vault protein in epithelial cells. *Science* 2007;**317**:130–2

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