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CFTR, *P. aeruginosa* and apoptosis in respiratory epithelium

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Keywords

Apoptosis, CFTR, *Pseudomonas aeruginosa*, respiratory epithelium

Context

Stimulation of NF-?B translocation and transcription of interleukin (IL)-8 are used by epithelial cells to recruit polymorphonuclear neutrophils to eliminate bacteria, and can also induce apoptosis, degeneration and cell replacement at mucosal sites in response to a pathogen. There is evidence for an effect of mutant cystic fibrosis transmembrane conductance receptor (CFTR) on the epithelial induction of both proinflammatory and apoptotic pathways. The aims of this study were to look at the effect of wild type (PAO1) and avirulent mutants of Pseudomonas aeruginosa on induction of apoptosis in airway epithelial cells in the presence or absence of functional CFTR.

Significant findings

Human nasal polyp or bronchial epithelial cells with intact tight junctions did not undergo apoptotic transformation upon exposure to PAO1, whereas an immortalized human tracheal epithelial cell line lacking tight junctions or a human bronchial epithelial cell line with disrupted tight junctions underwent significant apoptotic transformation after exposure to PAO1. Comparison of normal and CFTR mutant cell lines demonstrated neither significant differences in induction of apoptosis following exposure to PAO1, nor differences in the degree of apoptosis seen in the lungs of normal and *CFTR*$^{-/-}$ mice in response to a chronic PAO1 agar bead challenge. PAO1 virulence factors associated with invasion (pili, full length lipopolysaccharide, or functional type III secretion) were necessary for the induction of apoptosis in the tracheal epithelial cell line lacking tight junctions. The authors concluded that intact tight junctions and stimulation of NF-?B (pro-inflammatory and anti-apoptotic) by PAO1 provide resistance to apoptosis in airway epithelial cells, that sloughing is an unlikely common response to infection, and that CFTR mutations do not appear to modulate apoptotic responses.

Comments

This paper demonstrates that apoptosis does not follow *P. aeruginosa* challenge to respiratory epithelium unless fully virulent bacteria and damage affecting tight junction integrity are present. Other studies have suggested that in normal lungs, *P. aeruginosa* binds to intact CFTR, stimulating uptake of the bacteria and subsequent shedding of the epithelial cell as an anti-infective mechanism. This work implies that shedding may not be the primary defensive response to *P. aeruginosa* infection of airway epithelium, unlike other mucosal surfaces. The conclusions are, necessarily, relevant for the cell lines and mouse strains evaluated and do not preclude the possibility that the pulmonary epithelium has an apoptotic response to a bacterial challenge, whereas the factors identified here are inherently present in the host.

Methods

Tissue culture, confocal microscopy, chronic infection model, TUNEL assay

Additional information

References

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