JOURNAL CLUB

Reduced pH in the airways alters bacterial killing in CFTR^{-/-} porcine lungs

Molecular defects in the cystic fibrosis (CF) transmembrane conductance regulator (CFTR) gene are well understood. Despite this, how defects in the CFTR lead to CF is not clear. This paper addresses the mechanism of impaired bacterial killing in a CF model of disease developed in pigs (CFTR^{-/-}), which mirrors human disease.

Viability of bacteria within the airways of newborn pigs was assessed using bacteria bound to gold grids. In 6-hour-old pigs, there was a significant reduction in killing of bacteria when grids were applied to the tracheal surface of CFTR^{-/-} pigs compared with wild-type pigs. This finding was reproduced in cultured epithelial cells suggesting that the defect was not due to dysfunctional innate immune cells.

Airway Surface Liquid (ASL) was harvested from the CFTR^{-/-} and wildtype pigs and the ability of ASL to modulate bacterial killing in epithelial cultures was assessed. There was no difference in the ability of ASL to kill bacteria and no difference in levels of known antimicrobials within ASL. However, a reduction of pH levels to that seen within CFTR^{-/-} ASL in vivo decreased bacterial killing. Moreover, correcting the ASL pH to normal levels corrected this deficit.

This paper demonstrates that an early reduction of pH of ASL in CFTR^{-/-} pigs may alter early bacterial killing within the airways. It is unclear whether treating this would have an effect on lung inflammation. Modulation of abnormal ASL pH improves killing and therefore this finding may have wider implications for treating respiratory diseases where ASL pH is altered.

► Pezzulo AA, Tang XX, Hoegger MJ, *et al.* Reduced airway surface pH impairs bacterial killing in the porcine cystic fibrosis lung. *Nature* 2012;487:109–13.

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