CFTR IS REQUIRED FOR CELLULAR ENTRY AND INTERNALIZATION OF CHLAMYDIA TRACHOMATIS IN FALLOPIAN TUBE AND OTHER EPITHELIAL CELLS
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Background Chlamydia trachomatis is an obligate intracellular Gram-negative pathogen affecting over 600 million people worldwide with 92 million new cases occurring globally each year. C. trachomatis enter the cells and replicate to infect different tissues/organs, giving rise to a spectrum of pathological conditions; however, the exact mechanism or receptor(s) for their entry is not well understood.

Materials & methods We used direct immunofluorescence assay, epithelial cell invasion and bacterial uptake inhibition assays, real-time reverse transcriptase chain reaction and cell culture methods. Western blot analysis, co-localization and immunoprecipitation, short circuit current measurement and election microscopy were also used. Results Here we report that cystic fibrosis transmembrane conductance regulator (CFTR), an apical epithelial anion channel, is required for cellular entry and internalization of C. trachomatis. Human epithelial cell lines expressing functional CFTR internalized more C. trachomatis than the cells expressing mutant Δ508 CFTR. The in vitro cellular uptake of C. trachomatis can be blocked by CFTR inhibitors or antibody, and the in vivo cellular uptake of C. trachomatis in CFTR mutant (CFTR−/−) mice was significantly less compared with that in the wild-type. Direct interaction between CFTR and C. trachomatis lipopolysaccharide (LPS) is demonstrated by their immune-co-localization and co-immunoprecipitation. Despite an increase in CFTR expression observed upon C. trachomatis LPS challenge, a reduction in its ion channel activity is observed, consistent with the notion that CFTR functions as a receptor for cellular entry and internalization of C. trachomatis, with compromised ion-channel function.

Conclusion These findings, demonstrate that CFTR functions as a cell-surface receptor for epithelial cell entry, and internalization of C. trachomatis, and targeting CFTR may lead to the development of new treatment strategies to curtail the spread of chlamydial infections and reduce its devastating effects including infertility.

KEYWORDS: CFTR, Chlamydia trachomatis, fallopian tube epithelial cells, infertility, receptor