Inflammatory stimuli down-regulate AQP3 expression and AQP5 function in airway epithelial cells

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Abnormal water metabolism, such as edema and increased viscosity of airway surface fluid, is related to the phathophysiology of inflammatory lung diseases. Several aquaporins (AQPs) are expressed in the lung tissue. Among them, AQP3 and AQP5 are expressed in bronchial and alveolar epithelial cells, respectively, and mediate water movement across the epithelia. Despite of the importance of these AQPs, the effects of inflammatory stimuli on their expression and function have not been understood. In this study, therefore, we first examined the effect of pro-inflammatory cytokines on AQP3 expression in A549 lung epithelial cells. IL-1β significantly decreased the amount of AQP3, assessed by western blots. This decrease in AQP3 was consistent with the decrease in AQP3 mRNA and its promoter activity, suggesting IL-1β inhibits transcription of AQP3 gene. On the other hand, plasma membrane water permeability in MLE-12 cell, which expresses AQP5, was considerably decreased by the treatment of NO donors. This decrease in water permeability by NO was insensitive to guanylate cyclase inhibitor. In addition, NO donors increased the amount of S-nitrosylated AQP5, and the effects of NO donors were abolished in *Xenopus* oocytes expressing AQP5 cysteine mutants, suggesting that NO decreased water permeability by S-nitrosylation of AQP5. Taken together, these data suggest that water movement across the airway epithelial cells may be down-regulated in inflammatory conditions, by decreasing expression of AQP3 and NO-induced S-nitrosylation of AQP5. These down-regulations may be important to the abnormal water metabolism in inflammatory lung diseases.