Abstract

Objective

High mobility group box-1 (HMGB1) has been reported to be involved in influenza A virus-induced acute respiratory distress syndrome (ARDS). We studied the efficacy of an anti-HMGB1 mAb using an in vitro model of TNF-α stimulation or influenza A virus infection in human pulmonary microvascular endothelial cells (HMVECs).

Methods

Vascular permeability of HMVECs was quantified using the Boyden chamber assay under tumor necrosis factor-α (TNF-α) stimulation or influenza A virus infection in the presence of anti-HMGB1 mAb or control mAb. The intracellular localization of HMGB1 was assessed by immunostaining. Extracellular cytokine concentrations and intracellular viral mRNA expression were quantified by the enzyme-linked immunosorbent assay and quantitative reverse transcription PCR, respectively.

Results

Vascular permeability was increased by TNF-α stimulation or influenza A infection; HMVECs became elongated and the intercellular gaps were extended. Anti-HMGB1 mAb suppressed both the increase in permeability and the cell morphology changes. Translocation of HMGB1 to the cytoplasm was observed in the non-infected cells.

Although anti-HMGB1 mAb did not suppress viral replication, it did suppress cytokine production in HMVECs.

Conclusion

Anti-HMGB1 mAb might be an effective therapy for severe influenza ARDS.

Keywords: Influenza, Acute respiratory distress syndrome, High mobility group box 1, Human pulmonary microvascular endothelial cell, Cytokine, Tumor necrosis factor-α