Intensive Care Medicine Experimental
a SpringerOpen Journal

POSTER PRESENTATION Open Access

0987. FAS activation alters tight junction proteins in pulmonary alveolar epithelial cells

R Herrero[1,2*], F Puig[2,3], R Guillamat[2,3], L Prados[4], Y Rojas[1], A Artigas[2,3], A Esteban[1,2], JA Lorente[1,2,5]

From ESICM LIVES 2014
Barcelona, Spain. 27 September - 1 October 2014

Introduction

Active soluble Fas ligand (sFasL) accumulates in lung fluid of patients with acute respiratory distress syndrome (ARDS), and causes apoptosis and inflammation in lung epithelial cells [1]. Alveolar epithelial damage induced by Fas receptor activation results in protein-rich lung edema [2]. Dysfunction of the tight junction proteins may contribute to the formation of lung edema.

Objectives

Determine whether sFasL increases protein permeability of the alveolar epithelium by mechanisms involving disruption of the tight junction proteins in ARDS.

Methods

Primary human pulmonary alveolar epithelial cells were cultured in permeable transwell chambers. After reaching maximal confluency, the cells were incubated for 0.5, 1, 2 or 4 h with medium with or without human recombinant sFasL (rh-sFasL). Protein permeability of the cell monolayer was measured by using fluorescein-labeled albumin (FITC-Albumin). C56BL/6 wild-type mice and *lpr* (Fas deficient) mice were treated with an intratracheal dose of rh-sFasL (25 ng/g b.w.) or PBS, and the lungs were studied 16 h later. We performed immunofluorescence double staining for the detection of tight junction proteins (ZO-1 and Occludin) and apoptosis (Terminal Transferase dUTP Nick End Labeling assay).

Results

In vitro, human sFasL increased protein permeability of the alveolar epithelial cell monolayer (medium only: 17.17 ± 2.4% vs rh-sFasL: 28.0 ± 3.6%, means ± SD, $p < 0.05$, t-test), altered the distribution of the tight junction proteins ZO-1 and Occludin, and induced apoptosis. In vivo, intratracheal instillation of rh-sFasL, which increases pulmonary protein permeability in wild-type but not in *lpr* mice, altered the distribution of ZO-1 and Occludin, and induced apoptosis in cells of the alveolar walls only in wild-type but not in *lpr* mice.

Conclusions

Activation of the Fas/FasL system increased protein permeability of the pulmonary alveolar epithelium *in vitro* and *in vivo*. This increased permeability was associated with disruption of tight junctions and apoptosis. These results provide a mechanism that could be targeted for the prevention of lung edema in ARDS.

Grant acknowledgment
FIS 12/02451, FIS 12/02898, FIS 11/02791.

Authors' details
[1]Hospital Universitario de Getafe, Servicio de Cuidados Intensivos, Getafe, Spain. [2]CIBERES (CIBER Enfermedades Respiratorias), ISC III, Madrid, Spain. [3]Corporació Sanitária i Universitária Parc Taulí-UAB, Area de Cuidados Críticos, Sabadell, Spain. [4]Hospital Universitario de Getafe, Laboratorio de Análisis Clínicos, Getafe, Spain. [5]Universidad Europea de Madrid, Madrid, Spain.

Published: 26 September 2014

References

1. Matute-Bello G, *et al*: **Soluble Fas ligand induces epithelial cell apoptosis in humans with acute lung injury (ARDS).** *J Immunol* 1999, **163(4)**:2217-25.
2. Herrero R, *et al*: **The biological activity of FasL in human and mouse lungs is determined by the structure of its stalk region.** *J Clin Invest* 2011, **121(3)**:1174-90.

doi:10.1186/2197-425X-2-S1-P72
Cite this article as: Herrero *et al.*: 0987. FAS activation alters tight junction proteins in pulmonary alveolar epithelial cells. *Intensive Care Medicine Experimental* 2014 **2**(Suppl 1):P72.

[1]Hospital Universitario de Getafe, Servicio de Cuidados Intensivos, Getafe, Spain
Full list of author information is available at the end of the article