

ORAL PRESENTATION

Open Access

0895. Identification and validation of a miRNA as a diagnostic biomarker of diffuse alveolar damage in an animal model of acute lung injury and adult respiratory distress syndrome in mechanically ventilated patients

P Cardinal-Fernández^{1,2}, A Ferruelo^{1,2}, N Rego³, Y Rojas^{1,2}, A Ballén-Barragán^{1,2}, R Granados^{1,4}, C Jaramillo², E Lopez-Hernández⁵, L Martínez-Caro^{1,2}, N Nin^{6,7}, R Herrero^{1,2}, MA de la Cal^{1,2}, A Esteban^{1,2}, JA Lorente^{1,2,8*}

From ESICM LIVES 2014

Barcelona, Spain. 27 September - 1 October 2014

Objective

To discover a miRNA with diagnostic characteristics for diffuse alveolar damage (DAD) in an animal of acute lung injury (ALI) and in patients with the ARDS.

Methods

Male rats (325-372 gr) underwent mechanical ventilation for 2.5 h with $V_T=9$ ml/kg + PEEP=5 cm H₂O (low V_T , LV, n=10); or $V_T=25$ ml/kg + PEEP=0 cm H₂O (high V_T , HV, n=19) (11 of 19 developed DAD at histological examination). Whole miRNA expression (RNA-seq-Single Read, 72 cycles, Illumina GalIx) was analyzed in lung parenchyma. miRNA expression in LV vs. HV and in HV-DAD vs. HV-no-DAD was compared. We used a data mining strategy to prioritize the most relevant miRNA within the miRNAs differentially expressed. Prioritized miRNAs were validated in (1) serum from the same group of rats (RT-PCR); (2) human lung tissue (preserved at -80° after sampling) from autopsies of patients with ARDS (RT-PCR and *in situ* hybridization) (n=20); (3) human serum from mechanically ventilated patients obtained during the first 24 hours of ICU admission (n=66, 14 nonsurvivors). A p value < 0.05 was considered statistically significant. Results are median (IQR), and odds ratio (OR [95% confidence interval]). RT-PCR results were expressed $\times 10^{-4}$. Categorical

and continuous variables were compared with χ^2 and Mann-Whitney, respectively. Predictive multivariate logistic analysis was used to identify independent risk factors. The area under ROC curve (AUROC, mean \pm SEM) was used to assess the discriminatory capacity. Multiple-comparison was adjusted by FDR. The local Ethics Committee approved this study.

Results

19 miRNAs were differentially expressed **in rat lungs** between the 3 groups, one of them (herein named miRNA A) containing the information to classify animals in the 3 groups (97% correct classification in the original dataset, and 86% in 5 fold cross-validation analysis). **In rat serum**, miRNA A expression differed in the 3 groups (p=0.045) (AUROC for the presence of DAD 0.76 [0.521-1.000], p=0.036 for the difference with the line of identity). miRNA expression **in human serum** was associated with mortality. Variables in multivariate analyses for the prediction of mortality were: SAPS II score (OR 1.05 [1.01-1.10], p=0.02), and miRNA A expression (OR 1.06 [1.01-1.12; p=0.04] (AUROC for the logistic model 0.84 [0.73-0.96]; for SAPSII 0.76 [0.60-0.92] and for miRNA A 0.76 [0.63-0.89]). miRNA A was more expressed **in lung tissue** from 39 patients with the diagnosis of ARDS than in patients without ARDS (p< 0.01). In **human lung parenchyma** miRNA A was detected (RT-PCR), localized in alveolar type II cells, macrophages and interstitium (*in situ* hybridization).

¹Centro de Investigación Biomédica En Red de Enfermedades Respiratorias (CIBERES), Getafe, Spain

Full list of author information is available at the end of the article

Conclusions

We have identified one miRNA associated with DAD in an animal model of ALI, that is expressed in human lung tissue, and whose expression in human serum correlates with mortality and with the diagnosis of ARDS.

Grant acknowledgment

FIS 12/02898, FIS 11/02791, FIS 12/02451, European Network (7th FP) ITN 264864.

Authors' details

¹Centro de Investigación Biomédica En Red de Enfermedades Respiratorias (CIBERES), Getafe, Spain. ²Hospital Universitario de Getafe, Intensive Care Service and Burn Unit, Getafe, Spain. ³Institut Pasteur de Montevideo, Unidad de Bioinformática, Montevideo, Uruguay. ⁴Hospital Universitario de Getafe, Pathology Department, Getafe, Spain. ⁵Hospital Universitario de Getafe, Getafe, Spain. ⁶Hospital de Torrejón, Intensive Care Service, Madrid, Spain. ⁷Hospital Español, Intensive Care Service, Montevideo, Uruguay. ⁸Universidad Europea de Madrid, Madrid, Spain.

Published: 26 September 2014

doi:10.1186/2197-425X-2-S1-O21

Cite this article as: Cardinal-Fernández *et al.*: 0895. Identification and validation of a miRNA as a diagnostic biomarker of diffuse alveolar damage in an animal model of acute lung injury and adult respiratory distress syndrome in mechanically ventilated patients. *Intensive Care Medicine Experimental* 2014 **2**(Suppl 1):O21.

Submit your manuscript to a SpringerOpen[®] journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Immediate publication on acceptance
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► springeropen.com
