Interferon-dependant mechanisms of antiviral resistance of the human lung vascular endothelium infected with rhinovirus HRV16 – relevance in asthma exacerbations

Mateusz Gawrysiak[1], Michał Szymański[1], Mateusz Kobierecki[1], Adrian Gajewski[1], Robert Szewczyk[1], Izabela Gulbas[1], Aleksandra Likońska[1], Sylwia Michlewska[2], Marek L. Kowalski[1], Maciej Chałubiński[1]

[1]*Department of Immunology and Allergy,Medical University of Lodz, Poland*
[2]*Laboratory of Microscopic Imaging and SpecializedBiological Techniques, University of Lodz, Poland*

Introduction

Human rhinovirus (HRV) can causeasthma exacerbations. We have shown that HRV16 may infect human lung vascular endothelium *via* ICAM-1 entry receptor.

Aim

To assess the effect of HRV16 on interferon-dependant mechanisms of antiviral resistance of the human lung endothelium.

Material end methods

Human primary lung microvascular endothelial cells (HMVEC-L) were incubated with HRV16 (MOI 3.0) for 3 h, washed and cultured for 72 h. Virus copy number, interferon, cytokine, TLR3, TLR7, MDA5 and RIG-I mRNA expression was assessedby real time PCR, while protein levels by BioPlex. OAS-1and PKR expression were assessed in real time PCR, flow cytometry and confocal microscope. OAS-1 and PKR gene silencing was performed by siRNA transfection.

Results

In HMVEC-L, viral copy number reachedpeak at 5 h upon incubation with HRV16, than decreased.This was associated with up-regulation of TLR3, TLR7, MDA5 and RIG-I – sensors of viral RNA ($p < 0.05$). The decrease of viral load observed after 5 h was accompanied by up-regulation of OAS-1 and PKR mRNA expression and increase at protein level ($p < 0.05$) – enzymes leading to virus degradation and inhibiting its replication. HRV16induced the release of cytokines responsible for the antiviral

immune mechanisms ($p < 0.05$) and NK cell recruitment (RANTES, IP-10, MIP-1β, $p < 0.05$). After OAS-1 and PKR silencing, higher viral copy numbers were observed in comparison to HMVEC-Ls without transfection of siRNA.

Conclusions

HRV16 may activate intracellular in- terferon-dependent mechanisms of antiviral resistance in HMVEC-L. This enlightens the lung endothelium as a potent orchestrator of antiviral immune response in rhinoviral asthma exacerbations.

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