Journal of Respiratory Medicine

Mini Review Open Access

Larger Air Spaces Instead of Small ones Resulting Reduced Surface Area of the Lungs

Himender M*

Department of Microbiology, University of Hong Kong, Hong Kong

Abstract

Histone deacetylases include four classes of enzymes that catalyze the removal of acetyl functional groups from the lysine residues of both histone and non-histone proteins. Histone deacetylases is one of the class I Histone deacetylases and has been encoded by its gene in humans. Since Histone deacetylases has been overexpressed in a variety of human cancers, it has been employed as one of the attractive therapeutic anticancer targets based on structural features of this protein and inhibitory activity and selectivity of targeting drugs.

Keywords: Deacetylases; Inhibitory activity; Targeting drugs; Gene in humans; Anticancer targets; COPD;

Introduction

Additionally, an increase in the enzyme activity is linked to a number of lung diseases such as asthma and COPD Histone deacetylases inhibitors are applied for treatment of asthma through decreasing infiltration of inflammatory cells and content of cytokines in lungs. It has been reported that increased influx of macrophages in lungs has been recognized as the pathogenesis of allergic asthma, whereas the macrophages are polarized into two phenotypes of M1 (classically activated macrophages) and M2 (alternatively activated macrophages) in inflammatory responses to pathogens. M1 and M2 macrophages are distinguished by the differential expression of molecules such as nitric oxide and arginase. However, Histone deacetylases -related macrophage polarization in asthma is still largely unknown [1]. Gal-3 as a member of the beta-galactoside-binding protein family plays an important role in cell-cell adhesion, cell-matrix interactions and inflammation. This protein also involves the pathogenesis of asthma. PCI-34051 is a potent and specific Histone deacetylases inhibitor with > 200-fold selectivity over other class I Histone deacetylases. Given many studies in which the inhibitor displays a therapeutic benefit in diseased conditions, it is necessary to decipher the role of the PCI-targeted enzyme in allergic lung inflammation and to gain the understanding of the relatively extensive events associated with its inhibition at cellular and molecular levels [2]. This would be important to broaden a potential therapeutic window in identifying and developing novel inhibitors for the treatment of asthma. This study was to investigate the effects of Histone deacetylases inhibitor PCI-34051 on OVA-exposed lungs and IL-4 treated macrophages. Our results indicate that there is interaction between Histone deacetylases and Gal-3 proteins, which influences macrophage-2 polarization in the events of AHR and allergic airway inflammation.

Discussion

Specific pathogen-free, female BALB/c mice weighting about 20 g were purchased from the Center for Experimental Animals at China Medical University. Those animals were housed at animal facility of our hospital for the duration of the experiments [3]. All procedures were reviewed and approved by the Institutional Animal Care and Use Committee of The First Affiliated Hospital of China Medical University. Forty-eight mice were randomly divided into four groups of twelve animals for each. The protocol for making animal model is modified according to previous studies. Mice were sensitized with intra-peritoneal injection of an equivalent volume of 0.9% saline or ovalbumin complexed with 2 mg Al 3 in 0.2 ml NS on days 0, 7 and 14. On day 21, mice started to receive aerosol inhalation of NS or OVA at a flow rate of 3 ml/min for 30 min by an ultrasonic nebulizer. This procedure was carried out once a day for seven consecutive days. Some of mice inhaled budesonide for 30 min or received IP injection of PCI-34051 once a day prior to the challenge. The animals in the control were only exposed to NS for the same time period. Measurements in this study were performed 24 h after the final aerosol [3]. The left lungs of three mice in each group were fixed with 4% paraformaldehyde for hematoxylin and eosin and Periodic Acid-Schiff (PAS) staining. The right lungs of the same mice were fixed by vascular perfusion with formaldehyde fixative solution. After that, the lungs were embedded in paraffin and frozen at − 80 °C for the assay of immunocytochemistry and immunofluorescence. The left and right lungs from another three mice in each group were harvested and the frozen samples were stored at − 80 °C for protein and mRNA analysis. Measurement of airway responsiveness Six mice from each group were used to evaluate pulmonary resistance in vitro [4]. Airway responses to inhaled acetyl-β-metha-choline were measured non-invasively in conscious, unrestrained mice using barometric whole-body plethysmography. Airway responsiveness was expressed in enhanced pause, which is a measure of bronchoconstriction. Briefly, mice were placed in a whole-body chamber, and basal readings for airway responsiveness were obtained and then averaged for 3 min. Subsequently, the animals were aerosolized with increasing concentrations of metha-choline. The readings for the Penh value were taken after each nebulization. The degree of airway resistance was expressed as an increase in the value relative to the baseline. Cell counts in bronchio-alveolar lavage fluid and serum IL- 4 level Lung after measuring Penh was lavaged by instillation and withdrawal of 1.0 ml of NS through a Li et al. tracheal cannula, and an equal volume of BALF was collected from each mouse. The BALF sample was centrifuged at 4 °C and total cells were counted using a hemo-cytometer under a microscope. Two hundred microliter of a cell suspension from each sample was applied to a glass

***Corresponding author:** Himender Makker, Department of Microbiology, University of Hong Kong, Hong Kong, E-mail: makker.h@hotmail.com

Received: 18-Apr-2023, Manuscript No. JRM-23-91922; **Editor assigned:** 21-Apr-2023, PreQC No. JRM-23-91922(PQ); **Reviewed:** 05-May-2023, QC No. JRM-23-91922; **Revised:** 11-May-2023, Manuscript No. JRM-23-91922(R); **Published:** 18-May-2023, DOI: 10.4172/jrm.1000160

Citation: Himender M (2023) Larger Air Spaces Instead of Small ones Resulting Reduced Surface Area of the Lungs. J Respir Med 5: 160.

slide using a cytospin and then the slide was stained with Wright-Giemsa for the differential cell counts. The serum was obtained after blood clot is removed by centrifuging for ELISA. Antibody for the murine IL-4 was purchased from Pharmingen and the IL-4 level was determined using Infinite 200 PRO according to the manufacturer's direction. Histo-pathologic examination Lungs were surgically removed and were inflated in 4% paraformaldehyde for 24 h. Lungs of mice were embedded in paraffin and cut into a 4-μm section which was stained with H&E or PAS solution for evaluating inflammatory conditions and the presence of mucus production in the lungs. The stained specimens were visually observed under a light microscope at a magnification of 40 and photographed to compare morphological changes [5]. Cell culture The RAW264.7 murine macrophage-like cell line was used for investigation of mechanism of action of PCI based on the fact that alveolar macrophages can polarize into many different phenotypes in allergic asthma. The cells purchased from The Cell Bank of Type Culture Collection of Chinese Academy of Sciences and cultured in Dulbecco's Modified Eagle's Medium supplemented with 10% foetal bovine serum and 1% penicillin/streptomycin sulfate. Cells were grown in 6-well plates to 90% confluence and then stimulated with 20 ng/ml recombinant mouse IL-4 for 24 h since the cytokine induces macrophage activation. Some cells were treated with HDAC8 inhibitor for 30 min prior to stimulation with IL-4 or NS as a control. To provide visual details about macrophage phenotypes and protein abundance in lung tissues and the cells, IHC and IF procedures were used according to the manufacturer's protocol. Briefly, the slices of lung samples were mounted on slides and dehydrated using alcohol washes. The sections were incubated with primary antibodies of CD68 at 1:100, CD86 at 0.5 μg/ml and CD163 at 1:500 overnight at 4 °C [6]. On the following day the sections were incubated with a HRP-conjugated secondary antibody at 1:5000 for 1 h at 37 °C. Reaction with a 3,3′-Diaminobenzidine on the sections can produce a brown product at the site of the target antigen. Slides were washed three times with phosphate-buffered saline and observed using a light microscope at × 400 magnification. To investigate co-distribution of HDAC8 and Cal-3 in the tissues and the cells, we used rabbit and rat primary antibodies at 1:100 to detect two distinct antigens on the same samples. Double staining IF was processed with simultaneous incubation of two sets of the antibodies [7]. Briefly, the sample section was washed twice in TBST after fixing with acetone and then blocked with 1% BSA for 30 min at a room temperature. Afterwards, the section placed in a humidified box was co-incubated with the mixture of two primary antibodies in PBS containing 1% BSA and stayed overnight at 4 0 C. After washing three times with TBST, the section was incubated with the mixtures of a goat-anti-rabbit and a goat-anti-rat IgG secondary antibodies at 1:400 at RT for 1 h in dark. Color responses were raised in different species with two different fluoro-chromes (TRITC-conjugated against rabbit and FITC-conjugated against rat). The section was stained with DAPI for 10 min and was mounted on a glass slide, and cover slipped with anti-fading medium [8]. Areas of interest on the stained tissue were visualized using a confocal microscope and photographed using a Digital Sight DSFi1 camera and the NIS-Elements software package. Lung tissues were collected and the lysate was prepared using a rapidly oscillating masher in modified RIPA buffer. Macrophages were lysed in the buffer supplemented with protease inhibitors and homogenized. Supernatants from lungs and cells were obtained with centrifuge for 20 min at 4 °C, respectively [9]. Protein concentrations of the supernatants were determined by the BCA method. The supernatants were stored at −70°C until use [10]. Briefly, aliquots of lung tissue and cell lysates were loaded onto a 10% SDS polyacrylamide gel. In histo-pathological examination, representative images of lung sections showed more severe infiltration of peri-bronchial inflammatory cells and a large amount of mucus secretion in the OVA-exposed lungs than the NS-treated lungs. Treatment with BUD and PCI-34051 resulted in significant reduction in the cell infiltration and mucus accumulation in the challenged lungs.

Conclusion

In centri-lobular emphysema ventilatory disturbances were caused not only by the centriacinar dilated spaces delaying gas diffusion, but also by scattered bronchiolar stenosis situated at the termination of the conducting air passages. The stenosis seemed the more important cause. It was shown statistically that chronic arterial pulmonary hypertension and right ventricular hypertrophy were mainly the result of functional disturbances, especially hypoxia and abnormalities of VA/Q produced by the two structural changes situated at the end of the small airways.

Acknowledgement

None

Conflict of Interest

None

References

1. Gergianaki I, Bortoluzzi A, Bertsias G (2018) Update on the epidemiology, risk factors, and disease outcomes of systemic lupus erythematosus. Best Pract Res Clin Rheumatol EU 32:188-205.
2. Cunningham AA, Daszak P, Wood JLN (2017) One Health, emerging infectious diseases and wildlife: two decades of progress? Phil Trans UK 372:1-8.
3. Sue LJ (2004) Zoonotic poxvirus infections in humans. Curr Opin Infect Dis MN 17:81-90.
4. Pisarski K (2019) The global burden of disease of zoonotic parasitic diseases: top 5 contenders for priority consideration. Trop Med Infect Dis EU 4:1-44.
5. Kahn LH (2006) Confronting zoonoses, linking human and veterinary medicine. Emerg Infect Dis US 12:556-561.
6. Slifko TR, Smith HV, Rose JB (2000) Emerging parasite zoonosis associated with water and food. Int J Parasitol EU 30:1379-1393.
7. Bidaisee S, Macpherson CNL (2014) Zoonoses and one health: a review of the literature. J Parasitol 2014:1-8.
8. Cooper GS, Parks CG (2004) Occupational and environmental exposures as risk factors for systemic lupus erythematosus. Curr Rheumatol Rep EU 6:367-374.
9. Parks CG, Santos ASE, Barbhaiya M, Costenbader KH (2017) Understanding the role of environmental factors in the development of systemic lupus erythematosus. Best Pract Res Clin Rheumatol EU 31:306-320.
10. M Barbhaiya, KH Costenbader (2016) Environmental exposures and the development of systemic lupus erythematosus. Curr Opin Rheumatol US 28:497-505.