High-volume ventilation induces pentraxin 3 expression in multiple acute lung injury models in rats

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Okutani D, Han B, Mura M, Waddell TK, Keshavjee S, Liu M. High-volume ventilation induces pentraxin 3 expression in multiple acute lung injury models in rats. Am J Physiol Lung Cell Mol Physiol 292: L144–L153, 2007. First published August 25, 2006; doi:10.1152/ajplung.00002.2006.—Pentraxin 3 (PTX3) is an acute-phase protein, which can be produced by a variety of tissue cells at the site of infection or inflammation. It plays an important role in innate immunity in the lung and in mediating acute lung injury. The aim of this study was to determine the effect of mechanical ventilation on PTX3 expression in multiple lung injury models. Male Sprague-Dawley rats were challenged with intravenous injection of lipopolysaccharide (LPS) or hemorrhage followed by resuscitation (HS). The animals were then subjected to either relatively higher (12 ml/kg) or lower (6 ml/kg, positive end-expiratory pressure of 5 cmH2O) volume ventilation for 4 h. High-volume ventilation significantly enhanced PTX3 expression in the lung, either alone or in combination with LPS or hemorrhage. A significant increase of PTX3 immunohistochemistry staining in the lung was seen in all injury groups. The PTX3 expression was highly correlated with the severity of lung injury determined by blood gas, lung elastance, and wet-to-dry ratio. To determine the effects of HS, LPS, or injurious ventilation (25 ml/kg) alone on PTX3 expression, another group of rats was studied. Injurious ventilation significantly damaged the lung and increased PTX3 expression. A local expression of PTX3 induced by high-volume ventilation, either alone or in combination with other pathological conditions, suggests that it may be an important mediator in ventilator-induced lung injury. Pentraxin; inflammation; ventilator-induced lung injury; sepsis; hemorrhagic shock

Pentraxin 3 (PTX3) is one of the upregulated genes in human acute lung injury models in rats.

PTX3, the first identified long pentraxin, is a member of pentraxin superfamily characterized by cyclic multimeric structure, sharing a COOH-terminal domain with classic pentraxins, such as C-reactive protein and serum amyloid P. While the source of classic pentraxins is the liver, PTX3 is produced by a variety of tissue cells, such as endothelial cells (9), fibroblasts (35), chondrocytes and synoviocytes (39), adipose tissue cells (2), and cells of the monocyte/macrophage lineage (23, 57), upon exposure to inflammation signals, such as IL-1β, TNF-α, and lipopolysaccharide (LPS) (4, 23, 57). The expression of PTX3 in multiple types of tissue cells may imply a mechanism for a local amplification of innate resistance at the site of infection and inflammation (40). Moreover, the circulating PTX3 levels are very low in normal human subjects, but are rapidly elevated in patients with severe inflammations (21, 39, 43). Clinically, the elevated PTX3 levels might be a sensitive marker for an early diagnosis and prognosis for patients with severe illness, such as acute myocardial infarction (34, 48).

It has been reported that PTX3-deficient mice are more susceptible to invasive pulmonary aspergillosis (21), suggesting that PTX3 has a nonredundant role in antifungal innate immune response in the lung. However, the role of PTX3 in mediating ALI is less clear. Using PTX3 knock-in mice carrying multiple copies of PTX3 gene under the control of its own promoter, it has been shown that endotoxin induced PTX3 overexpression in these animals, which improved survival (12). In contrast, when these transgenic mice were exposed to intestinal ischemia-reperfusion injury, overexpression of PTX3 increased mortality and worsened the local and systemic inflammatory responses, with increased vascular permeability, hemorrhage, neutrophil accumulation, and tissue concentrations of proinflammatory cytokines/chemokines (53). Results from these transgenic animal studies indicate that PTX3, as many other proinflammatory mediators, may play an important role in host defense in the lung; its overexpression could also be detrimental in inflammatory responses, depending upon the types of challenge and local/systemic condition. Moreover, the effects of mechanical ventilation on PTX3 expression are

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unknown. Thus, characterizing the PTX3 expression from wild-type animals under a variety of pathological condition will help understand its regulatory mechanisms in vivo and reveal its role in ALI.

We hypothesized that PTX3 production is a highly regulated process depending on the initial insults, which can be further affected by the mechanical ventilation regimen. This hypothesis was tested in multiple lung injury models in rats, where animals were subjected to intravenous injection of LPS or hemorrhage, followed by resuscitation. The animals were then randomized to receive either low- or high-volume ventilation; both regimens are clinically used. Here we show that high-volume ventilation could initiate PTX3 expression in the lung and enhance PTX3 production induced by LPS or HS. Moreover, significant correlations have been observed between PTX3 expression and the severity of lung injury.

MATERIALS AND METHODS

Animals. Experiments were performed with male Sprague-Dawley rats weighing 300–350 g (Charles River, Montreal, Quebec, Canada). All animals received care in compliance with the Principles of Laboratory Animal Care formulated by the National Society for Medical Research, the Guide for the Care and Use of Laboratory Animals (National Institutes of Health publication no. 85–23, revised 1985), and the Guide to the Care and Use of Experimental Animals formulated by the Canadian Council on Animal Care. The experimental protocol was approved by the Institutional Animal Care and Use Committee.

Rat models of hemorrhagic and sepsis. The rat HS model used in our experiments has been described previously (1, 16). Rats were anesthetized with 80 mg/kg of ketamine hydrochloride (Ketaset; Ayerst Veterinary Laboratories, Guelph, Ontario, Canada) and 8 mg/kg of xylazine (Rompun; Bayer, Toronto, Ontario, Canada) administered intraperitoneally. A tracheostomy was performed, and a 14-gauge catheter was inserted into the trachea. The right carotid artery was cannulated with a 24-gauge Angiocath (Becton Dickinson, Franklin Lakes, NJ) for mean arterial pressure (MAP) measurement, blood withdrawal, and resuscitation. The tail vein was catheterized with a 22-gauge Angiocath (Becton Dickinson) for continuing anesthesia, and resuscitation. The tail vein was further maintained for another 15 min by additional blood withdrawal if MAP was <35 mmHg. Shed blood was collected into tubes containing citrate. After 30 min of hypotension, animals were resuscitated by transfusion of the shed blood mixed with Ringer lactate (RL) (1:1 in volume), for the next 30 min.

The rat sepsis model (LPS) used in our experiments has also been previously reported (54). Rats were anesthetized and operated, as described above, and then received an intravenous injection of LPS (Escherichia coli O55:B5; Sigma Chemical, St. Louis, MO) at a dose of 5 mg/kg in 200 μl of saline solution. After 60 min of hypotension, where MAP was maintained around 65 mmHg, animals were resuscitated with RL to restore MAP to 90 mmHg.

After the first insult of HS or LPS, rats were randomized to mechanical ventilation (Flexi Vent, SCIREQ, Montreal, PQ, Canada) for 4 h with either a high-volume strategy (HV), consisting of a tidal volume (VT) of 12 ml/kg, zero positive end-expiratory pressure (PEEP), respiratory rate (RR) of 50–60 breaths/min, and inspired O2 fraction of 35%, or a low-volume strategy (LV), consisting of VT of 6 ml/kg, PEEP of 5 cmH2O, RR of 50–60 breaths/min, and inspired O2 fraction of 35%. RR was adjusted to maintain arterial PCO2 in a range of 35–45 Torr. Sham-operated animals underwent the same surgical procedures and mechanical ventilatory strategies without HS or LPS. Four animals were used in each group. MAP was continuously recorded throughout the 4 h of mechanical ventilation in all animals. Changes in lung elastance were recorded every hour as following: elastance = (Pplat − PEEP)/VT, where Pplat is plateau pressure. The changes of lung elastance were defined as the percent increase over the baseline values. Body temperature was maintained at 37°C with a heating pad throughout the experimental period. All animals were killed at completion of the experiments by an overdose of pentobarbital sodium administered intravenously. The left lung was excised for histological evaluation, and the right cardiac lobe for measurement of lung wet-to-dry weight ratios. The rest of the right lung was immediately frozen in liquid nitrogen and stored at −80°C until it was used for future measurements.

Histological and immunohistochemical evaluation. For fixation, the lungs were intratracheally instilled with 10% formalin from 20 cm height, immersed in 10% formalin for at least 24 h, and then embedded in paraffin. After deparaffinization and dehydration, the sections (5 μm) were stained with hemotoxylin and eosin. The degree of lung injury was scored by two investigators in a blinded manner, based on the following four parameters: interstitial cellular infiltration, alveolar hyaline membrane formation, edema, and cellular exudates (52). Each parameter was graded from 0 to 3. The sum was used to reflect the severity of lung injury. Four animals per group were used, and 10 optical fields per animal were randomly chosen for assessment.

For immunohistochemical staining of PTX3, another set of deparaffinized and dehydrated lung tissue sections (4 μm) were immersed in 10 mM sodium citrate buffer, 0.05% Tween 20 (pH 6.0), for 5 min at 55–58°C, and then treated with 0.25% Triton X-100 for 5 min. After blocking with 5% bovine serum albumin at room temperature for 20 min, the slides were incubated at 4°C with a PTX3 polyclonal antibody (1:50 dilution; Santa Cruz Biotechnology, Santa Cruz, CA) overnight, and with a secondary antibody against rabbit IgG (1:600) at room temperature for 1 h. Detection was done by avidin-biotin

Table 1. Primer sequences for quantitative RT-PCR

<table>
<thead>
<tr>
<th>Gene</th>
<th>Forward Primer (5′–3′)</th>
<th>Reverse Primer (5′–3′)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTX3</td>
<td>TCAAAGCCACAGAAGTTATCAAAGAA</td>
<td>AAACACTAGGAGCTGGAACATTAGG</td>
</tr>
<tr>
<td>IL-1β</td>
<td>CTCGACAGACCCCAAAAGATTAAGG</td>
<td>CTTUTGCAGATGTGCTGTGA</td>
</tr>
<tr>
<td>TNF-α</td>
<td>CCAGCGTCTCTTCAOGGGAGACAAA</td>
<td>TTGCAAGAGGAGCGCTGAATC</td>
</tr>
<tr>
<td>HMBS</td>
<td>GAGGCTGTAGCCTGAGCTTAG</td>
<td>TTAGATGCTATCTGAGCCATC</td>
</tr>
</tbody>
</table>

PTX3, pentraxin 3; HMBS, hydroxymethylbilane synthase.
complex system (Vecstain ABC-kit, Vector Laboratories, Burlingame, CA), with Vector red phosphatase alkaline substrate as chromogen. The slides were counterstained with 1% methyl green for 10 s. The specificity of staining was determined by replacing the primary antibody with nonimmune serum, or preincubating the primary antibody with PTX3 (N-18), a specific blocking peptide from Santa Cruz Biotechnology, following the instruction from the manufacturer. No staining was found under these negative control conditions (data not shown).

Reverse transcription of RNA and real-time RT-PCR. Total RNA was isolated from frozen lung tissues using TRIzol Reagent (Sigma) and purified using RNase Mini Kit (Qiagen, Mississauga, Ontario, Canada) following the manufacturer’s protocols. Taqman Reverse

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Fig. 1. Acute lung injury (ALI) was induced in rats by high-volume strategy (HV), hemorrhagic shock (HS), and lipopolysaccharide (LPS). Changes of lung elastance, defined as the percent increase over the baseline (A), wet-to-dry lung ratios (B), and arterial Po2 (PaO2; C) at the end of 4-h mechanical ventilation, are shown as means ± SD (n = 4 rats/group). HV is high-volume ventilation with tidal volume (VT) of 12 ml/kg and zero positive end-expiratory pressure (PEEP). Low-volume strategy (LV) is low-volume ventilation with VT of 6 ml/kg and PEEP of 5 cmH2O. Significances are expressed as follows: +P < 0.05 vs. sham + LV; #P < 0.01 vs. sham + LV; ##P < 0.05 vs. sham + HV; +++P < 0.05 vs. HS + LV; and ^P < 0.05 vs. LPS + LV.

Fig. 2. Pentraxin 3 (PTX3) expression was upregulated during ALI. A: quantitative RT-PCR was performed with total RNA from each animal, and PTX3 mRNA expression in the lung was shown as a ratio over a housekeeping gene [hydroxymethylbilane synthase (HMBS)] in the same sample. PTX3 protein expression was determined by ELISA in the lung (B) and in the serum (C). Data shown are means ± SD from 4 rats/group. Significances are expressed as follows: +P < 0.05 vs. sham + LV; #P < 0.01 vs. sham + LV; ##P < 0.05 vs. sham + HV; +++P < 0.05 vs. HS + LV; and ^P < 0.05 vs. LPS + LV.
Transcription Reagent kit (Applied Biosystems, Foster City, CA) was used for reverse transcription (RT). The reaction mixture (20 μl) for RT contained 2.0 μl of 10× Taq Man RT buffer, 4.4 μl of 25 mM MgCl₂, 4.0 μl of 50 mM random hexamers, 0.4 μl of 20 U/μl RNase inhibitor, 0.5 μl of 50 U/μl MultiScribe Reverse Transcriptase, and 7.7 μl of RNase-free water with 500 ng of total RNA. The mixture was incubated at 25°C for 10 min, at 48°C for 30 min for RT, and at 95°C for 5 min for reverse transcriptase inactivation. The cDNA products were diluted to 60 μl with RNase-free water and stored at −20°C. The PCR amplification mixture (20 μl) contained 2 μl of the template cDNA, 10 μl of 2× reaction buffer from QuantiTect SYBRgreen PCR kit (Qiagen), and 2 μl of each the forward and reverse primer. Conditions for PCR included 95°C for 15 min and 40 cycles of 94°C for 15 s and 60°C for 60 s (ABI PRISM 9700HT, Applied Biosystems). All assays were performed in duplicate. Primers (Table 1) were designed using the Primer Express 1.5 software (Applied Biosystems) and synthesized by ACGT (Toronto, Ontario, Canada). Each assay included a standard curve of five serial dilutions from a known concentration of genomic DNA and a nontemplate control. The expression levels of genes of interests were first calculated as relative intensity values against the standard curve for each gene and then normalized as ratios over the level of a housekeeping gene, hydroxymethylbilane synthase, in each sample.

**ELISA measurements for PTX3, IL-1β, and TNF-α.** Lung tissues were homogenized and centrifuged (22, 31). Tissue lysates and sera were assayed in duplicate with ELISA kits from Alexis (San Diego, CA) for PTX3 and from BioSource (Camarillo, CA) for IL-1β and TNF-α, respectively. The optical density was read from each well at 450 nm, and the concentrations were calculated by converting the optical density against a standard curve of each molecule tested.

**Statistical analysis.** Statistical analysis was performed using JMP5 Statistical Discovery Software (SAS Institute, Cary, NC). All data are expressed as means ± SD. Differences between groups were compared by analysis of variance followed by Tukey-Kramer posttest. The strength of correlation was calculated by Pearson’s product-moment correlation. Statistical significance was accepted at *P* < 0.05.

**RESULTS**

"Two-hit” induces ALI. To determine the effects of mechanical ventilation on PTX3 expression, two clinically applicable ventilation regimens were used, either alone or in combination with HS or LPS challenge. All animals in this study survived and remained hemodynamically stable during the 4 h of mechanical ventilation. In HS groups, there were no significant differences in the blood volume withdrawn between HV and LV (HS HV: 11.4 ± 0.7 ml; HS LV: 12.1 ± 0.5 ml). In LPS groups, there were no significant differences in the amount of RL administered to restore MAP to 90 mmHg (LPS HV: 18.7 ± 0.8 ml; LPS LV: 18.2 ± 1.3 ml). Compared with other groups, sham + LV revealed the lowest degree of lung injury with the least change of lung elastance (Fig. 1A), the lowest wet-to-dry lung ratio (Fig. 1B), and the highest arterial PO₂ (PaO₂) (Fig. 1C). HV ventilation alone significantly increased lung elastance (Fig. 1A) and wet-to-dry lung ratio (Fig. 1B) and reduced PaO₂ (Fig. 1C). HS + LV group did not show any significant differences with sham + LV group, whereas LPS alone induced significantly higher wet-to-dry lung ratio (Fig. 1B) and lower PaO₂ (Fig. 1C). HV
ventilation further increased LPS-induced elevation of lung elastance and wet-to-dry lung ratio (Fig. 1, A and B). The \( \text{PaO}_2 \) in LPS + HV or HS + HV group was significant lower than that in sham + HV group (Fig. 1C). These physiological measures demonstrate an additive effect between HV ventilation and LPS challenge or HS, supporting the “two-hit” hypothesis in the pathogenesis of ALI. Histological study with hematoxylin and eosin staining showed more severe lung injury in groups with HV ventilation. However, the semiquantitative lung injury scores did not reach statistical significance (data not shown), which may be due to the small sample size, or suggesting that ALI was still at its early stage. We then used these models to further evaluate PTX3 expression in the lung and its relationship with the lung injury.

High-volume ventilation increases PTX3 expression in the lung. PTX3 expression was measured at mRNA level by quantitative real-time RT-PCR in the lung tissues and at protein level by ELISA in the lung tissue lysates and sera. Compared with sham + LV, HV increased PTX3 mRNA and protein expression significantly in the lung tissues (Fig. 2, A and B). In LV groups, PTX3 expressions were also significantly enhanced by LPS but not by HS. However, in HV + HS group, PTX3 expressions in the lung tissues were significantly increased compared with the sham + HV group; HV also significantly enhanced LPS-induced PTX3 expression (Fig. 2, A and B). In contrast, circulating levels of PTX3 were only enhanced by systemic LPS treatment (Fig. 2C).

To determine the distribution of PTX3 expression in the lung, PTX3 immunohistochemistry staining was performed for all 24 animals. The representative pictures from each group are shown in Fig. 3. PTX3 immunoreactivity was minimally detectable in sham + LV group and clearly increased in all other groups (Fig. 3). The PTX3-positive staining (pink color) was mainly found on the alveolar walls (Fig. 3).

Cytokines are upregulated during ALI in the lung. We have recently demonstrated that treatment of human alveolar epithelial cells with IL-1β as well as TNF-α induced PTX3 production (28). These cytokines are known to be upregulated in patients with ALI (7). Therefore, the protein concentrations and mRNA expression levels of these two proinflammatory cytokines were measured both in the lung and in the serum. IL-1β mRNA expression was significantly higher in HV
PTX3 expression in the lung was correlated with the severity of lung injury. To determine whether increased protein levels of PTX3 in the lung were associated with the severity of lung injury, we examined the correlation between PTX3 expression and physiological data. PTX3 protein level in the lung significantly and positively correlated with the changes in lung elastance ($P < 0.0001$), and wet-to-dry lung ratios ($P < 0.0001$) (Fig. 5, A and B). A negative correlation was observed between PTX3 protein levels and $P_{aO_2}$ ($P < 0.0001$) (Fig. 5C).

Effects of injurious ventilation, HS, and LPS alone on PTX3 expression. In the first group of experiments, all animals were ventilated. It is necessary to determine the effects of HS/resuscitation or LPS alone on PTX3 expression. Furthermore, both ventilation regimens are commonly used clinically and are thus less injurious. It is important to determine the effect of injurious ventilation alone on PTX3 expression. We designed and performed a second group of studies, in which normal rats were used as control compared with rats treated with HS or LPS or ventilated with VT of 25 ml/kg without PEEP. Compared with normal control group, HS or LPS did not induce dramatic change in lung histology. In contrast, thickened alveolar wall, patchy alveolar edema and hemorrhage, intra-alveolar inflammatory cell infiltration, and enlarged alveolar space were observed in injurious ventilation group (Fig. 6A). Injurious ventilation significantly increased wet-to-dry lung ratio (Fig. 6B).

In normal rat lung, almost no PTX3 staining was detected. After HS/resuscitation, very weak staining was detected in the lung tissue. In the LPS group, the PTX3 staining was increased. Injurious ventilation significantly increased PTX3 staining along the alveolar wall (Fig. 7A). Since PTX3 is a soluble protein, other lung cells, such as endothelial cells, fibroblasts, and macrophages, may also produce PTX3. When the primary antibody was replaced with nonimmune serum, or preincubated with a specific PTX3 blocking peptide, no staining was found (data not shown). PTX3 expression determined by ELISA in the lung tissue was increased by LPS and very significantly increased by injurious ventilation (Fig. 7B).

**DISCUSSION**

PTX3 has been known to be very important in the innate immune responses as a soluble pattern-recognition receptor and in the acute inflammatory responses as a potential mediator (20). However, its role in mediating ALI/VILI is little known. In the present study, we found that PTX3 expression can be regulated by mechanical ventilation, either alone or in combination with other pathological processes. The PTX3 protein levels in the lung were strikingly correlated with lung injury parameters, which support our hypothesis that PTX3 may participate in the pathogenesis of ALI.

The present study was conducted to define the PTX3 expression patterns in multiple ALI models and its relationship with the lung injury. In a recent study, our laboratory performed in situ hybridization and immunohistochemistry studies on rat lung tissue collected after low-volume ventilation and LPS challenge and observed increased PTX3 gene and protein expression on alveolar wall (28). In the present study, increased PTX3 protein levels were found in the lung tissue by immunohistochemistry staining in multiple lung injury models and quantified with ELISA. These results indicate increased PTX3 expression as a major local response during ALI.

Although LPS administration induced PTX3 gene and protein expression in the rat lung, it did not induce PTX3 expression in human lung epithelial cells. In contrast, treating human
alveolar epithelial A549 cells, human normal bronchial epithelial BEAS-2B cells, primary human alveolar type 2 cells, and small airway epithelial cells with TNF-α induced a significant increase in PTX3 gene expression and protein production (28). When A549 cells were challenged with IL-1β, similar effects on PTX3 induction were observed (28). These cell culture studies suggest that PTX3 expression could be secondary to proinflammatory mediators. In the present study, we observed that both TNF-α and IL-1β were upregulated in the lung at both mRNA and protein levels. However, neither IL-1β nor TNF-α protein expression in the lung was significantly affected by HV. Therefore, the upregulated PTX3 expression in sham + HV group could be a combined effect of these two cytokines or together with other proinflammatory mediators. Alternatively, PTX3 may be more sensitive to HV ventilation in vivo.

In the first group of studies, HV ventilation induced more severe lung injury than LV ventilation, and HV enhanced the initial insult of HS or LPS in the lung. In these so-called HV groups, not only the VT was higher, but also the PEEP was set up at zero, which may also contribute to the lung damage (15). Nevertheless, both ventilation regimens are used clinically with relatively less injury. In the second group of studies when we used VT of 25 ml/kg without PEEP, ventilation alone induced much severe lung injury and significantly increased the expression of PTX3. In contrast, HS or LPS alone had much less effect on PTX3 expression, as well as on lung injury. It is known that mechanical force could activate intracellular signal transduction pathways (25, 27, 38). Mechanical stretch can directly stimulate release of cytokines (26, 42). Whether mechanical ventilation can directly induce PTX3 expression in lung cells merits further investigation.

The additive effects of HV ventilation with the primary insults, LPS or HS, suggest that the expression of PTX3 can be regulated by multiple intermediate factors. The additive effect of high VT ventilation with other injurious factors on lung injury has been reported previously. For example, high VT ventilation increases lung injury after acid aspiration (18, 29, 30), sepsis (10, 29), severe acute respiratory syndrome coronavirus (32), or LPS challenge (5). Combined injurious effects of these factors with mechanical ventilation may be responsible for the increased expression of PTX3 and many other inflammatory mediators. Alternatively, the increase in lung PTX3 and other inflammatory mediators may contribute to the severity of lung injury. Among many newly discovered inflammatory mediators (37, 44), PTX3 may be a good candidate for further investigation in VILI.

The potential function of PTX3 in the development of ALI is still unknown. It has been shown that PTX3 could recognize pathogens (21), regulate activation of complement system by binding C1q (8, 47), and mediate the clearance of apoptotic...
Moreover, it has been demonstrated that PTX3 could upregulate expression and activity of tissue factor in human endothelial cells and monocytes. Tissue factor-dependent activation of coagulation is an early event in the pathogenesis of ALI and organ dysfunction. Our observation that PTX3 expression was significantly correlated with the severity of lung injury suggests that an upregulation of PTX3 during ALI may be either a contributor of injury in the lung or a consequence of lung injury.

In a clinical setting, evidence has been shown that circulating levels of PTX3 increase in a series of human disorders, including ischemic heart disease, sepsis, and small-vessel vasculitis. Elevated PTX3 has been shown in critically ill patients with systemic inflammatory response syndrome due to septic shock and was associated with unfavorable outcomes. In the present study, only LPS elevated the serum level of PTX3, suggesting that organs other than the lung may also produce PTX3 due to the systemic challenge. PTX3 levels were higher in the plasma in all of the lung injury models compared with the sham + LV group, although the differences did not reach statistical significance. It is possible that the lung injury in that group of studies was still at an early stage and thus was not severe enough to significantly increase the release of PTX3 from the lung to the circulation.

In conclusion, we have shown that high-volume ventilation can induce PTX3 expression in the lung and can enhance the effect of other inflammatory insults on the PTX3 expression, which is associated with the severity of the lung injury. PTX3 might contribute to early local inflammatory responses during ALI, especially for VILI. More investigations on the biological activities of PTX3 will likely lead to new understanding for mechanisms of ALI.

REFERENCES


PTX3 EXPRESSION IN ACUTE LUNG INJURY


