Biochemical and Biophysical Research Communications 452 (2014) 191–196

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

Stromal cell-derived factor-1α attenuates oleate-induced acute lung injury in rabbits

Weixin Guo [a,1], Zhihong Li [b,1], Xiaoyun Xie [c,1], Tao Tan [d], Shouhong Wang [a], Nanzi Xie [c], Minghuan Fu [d], Hua Zhu [d], Tiehe Qin [a,*]

[a] Guangdong Geriatrics Institute, Guangdong General Hospital, Guangdong Academy of Medical Sciences, No. 106 Zhongshan Road, Guangzhou 510100, China
[b] Division of General Surgery, Chenzhou First People's Hospital, Chenzhou, Hunan 423000, China
[c] Division of Geriatrics, Tongji Hospital, Tongji University, School of Medicine, Shanghai 200065, China
[d] Department of Surgery, Davis Heart and Lung Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH 43210, United States

ARTICLE INFO

Article history:
Received 2 July 2014
Available online 11 July 2014

Keywords:
SDF-1
CXCR4
Acute lung injury
Bcl-2
Bcl-xl

ABSTRACT

The stromal cell-derived factor-1α/C-X-C chemokine receptor 4 (SDF-1/CXCR4) axis is involved in various aspects of tissue repair, regeneration and development. However, the role of SDF-1/CXCR4 in acute lung injury (ALI) remains largely unknown. The aim of the present investigation is to examine pathological changes in a rabbit model with ALI induced by oleic acid (OA) and to explore the protective effect of SDF-1α on ALI. Intravenous application (i.v.) of oleic acid (0.1 ml/kg/h for 2 h) provoked pulmonary hemorrhage, edema, and protein leakage, resulting in severe ALI. When the rabbit received an infusion of SDF-1α (20 μg/kg/24 h) for 30 min before OA treatment, SDF-1α seemed to significantly improve the pathologies associated with OA-induced ALI. While dissecting the molecular mechanisms underlying the beneficial effects of SDF-1α, we found that SDF-1/CXCR4 is expressed in uninjured lung tissues but is greatly reduced after OA treatment. Interestingly, intravenous delivery of SDF-1α could target an injured lung and rescue expression of CXCR4, which in turn activates anti-apoptotic proteins, Bcl-1 and Bcl-xl, but does not affect pro-apoptotic proteins, such as Bad and Bax. These data suggested that SDF-1α could protect rabbit lungs from AIL. The molecular mechanism might be associated with upregulating anti-apoptosis family expression through CXCR4. Thus, SDF-1/CXCR4 signaling pathway may be a promising target for treatment of patients with ALI.

1. Introduction

Acute lung injury (ALI) and its more severe stage of acute respiratory distress syndrome (ARDS) are caused by a variety of reasons both within and outside of the lung characterized by progressive dyspnea and refractory hypoxemia. They are acute syndromes caused by the body's excessive inflammatory response [1,2]. The mortality rate in patients with ARDS is still more than 50% despite recent advances in intensive care. However, no clear reasons and effective treatment of, ALI have been addressed [3].

SDF-1 (also known as CXCL12) is a peptide chemokine initially identified in bone marrow-derived stromal cells and has now also been recognized to express in stromal tissues in multiple organs [4,5]. SDF-1 is composed of over 40 chemokines which have 18 known receptors. The SDF-1 receptor, C-X-C chemokine receptor 4 (CXCR4), is highly specific for SDF-1. The SDF-1/CXCR4 ligand-receptor pair is very specific without crosstalk with other chemokines or receptors [6]. The SDF-1/CXCR4 axis has been shown to be involved in broad aspects of tissue repair, regeneration, development and cancer [7–9]. It has been speculated that SDF-1 may promote cell survival through two distinct mechanisms: post-translational inactivation of the cell death machinery (e.g., increase anti-apoptotic and decrease pro-apoptotic proteins) and increased transcription of cell survival genes [10–12]. Thus, we hypothesized that SDF-1 might be a potential candidate for protection of ALI.

In the present study, by using a rabbit model of OA-induced ALI, we tested whether SDF-1α protected against ALI *in vivo*. In this report, we demonstrated the expression of SDF-1α and CXCR4 was tightly associated with pathological changes during ALI and present evidence to suggest the potential therapeutic benefits of SDF-1α in ALI model group might be due to activation of anti-apoptosis family proteins expression through CXCR4.

* Corresponding author.
E-mail address: tieheqin@126.com (T. Qin).
[1] Weixin Guo, Zhihong Li, Xiaoyun Xie contributed equally to this work.

http://dx.doi.org/10.1016/j.bbrc.2014.07.033
0006-291X/

2. Materials and methods

2.1. Animals

Male, New Zealand White rabbits (2.1–2.5 kg) were purchased from the Animal Center of Zhongshan School of Medicine, Sun Yat-sen University (Guangzhou, China). All animals were caged at room temperature and allowed to eat and drink *ad libitum*. The current study was conducted according to the guidelines of the Animal Care Review Board of the Guangdong general hospital Committee on Animal Care.

2.2. Animal model

The rabbits were randomly grouped into 6 groups (4 animals per group): one control (PBS treatment) group, one OA treated group, three OA+SDF-1α treated groups (with different doses of SDF-1α) and one OA+SDF-1α+AMD3100 (a CXCR4 inhibitor) group. Rabbits were initially anesthetized with ketamine hydrochloride (25 mg/kg, i.v.; Rogar/STB, Montreal, PQ, Canada), and then maintained by continuous infusion of ketamine at a rate of 0.5 mg/kg/h during OA and/or SDF-1α. The OA treatment group received 0.1 ml/kg/h, i.v. of OA (Sigma–Aldrich Corp.) for 2 h [13]. The control group received 0.1 ml/kg/h, i.v. of PBS for 2 h. The OA+SDF-1α treatment animals were treated with different doses of SDF-1α (10 μg/kg/24 h, 20 μg/kg/24 h and 40 μg/kg/24 h) (Antigenix America Inc.) three times during the procedure. The first treatment of SDF-1α was 30 min before OA infusion. Second and third administrations of SDF-1α were delivered 24 and 48 h after OA infusion [14]. Based on the previous study, AMD3100 (200 μg/kg/24 h) was delivered at the same time as SDF-1α administrations in the OA+SDF-1α+AMD3100 treated group [15].

2.3. Histopathological examination

The lungs were embedded in paraffin and the sections were stained with hematoxylin and eosin (H&E). Two qualified pathologists, blinded with the treatments, scored the lung injury, according to combined assessments of alveolar congestion, hemorrhage, edema of Immunostaining assays.

2.4. Immunohistochemical analysis

After deparaffinization, slides were incubated with target retrieval solution (DAKO, Carpentaria, CA). Staining was performed with the ImmunoCruz staining system (Santa Cruz, CA) according to the manufacturer's protocol. SDF-1α antibody (Santa Cruz, CA) and CXCR4 antibody (Santa Cruz, CA) was used at 1:1000. Normal IgG was used as a negative control. The secondary antibody was used at 1:500. DAPI was used as a nuclear stain. Slides were viewed using a Nikon ECLIPSE TE2000-U inverted microscope connected to a RT Slider Spot digital camera (Diagnostic Instruments, Sterling Heights, MI). Images were acquired using SPOT software version 3.2 [16].

2.5. Western Blot analysis

Tissues were harvested in Western blot lysis buffer and the lysates were cleared by centrifugation at 12,000×*g* for 10 min at 4 °C. The proteins were separated by 10% SDS–PAGE and transferred to polyvinylidene difluoride (PVDF) membranes, then probed with one of the following primary antibodies against SDF-1α, CXCR4, Bcl-2, Bcl-xl, Bad and Bax. All these antibodies were polyclonal antibodies from Santa Cruz Biotechnology (Santa Cruz, CA). The primary antibodies bound to the target proteins were then detected by horseradish peroxidase-conjugated anti-rabbit IgG (Promega, Madison, WI) and visualized with enhanced chemiluminescent detection (Pierce Biotechnology, Rockford, IL). Intensities of all target bands were normalized with that of the protein loading control GAPDH band calculated by the FluorChem 8900 software system (Alpha Innotech, San Leandro, CA) [17].

2.6. Statistical analysis

Data were presented as mean ± SD. SPSS software version 11.0 (SPSS, Inc., Chicago, IL) was used for statistical analyses. Statistical significance among mean values was evaluated by one-way ANOVA tests for measurement data, and LSD-t test for comparison between each other. Differences were considered significant when P value was $P < 0.05$.

3. Results

3.1. SDF-1α improves the pathologies of rabbit lungs following ALI

A recent study showed that the lung is the organ most vulnerable to the effects of OA [18]. In this study we chose a model of OA-induced ALI in New Zealand White rabbit because the rabbit is an extensively used model that remains relevant in the study of lung injury mechanism. In this study the changes induced by OA resembles ALI in many morphological, histological and physiological aspects, included edema, hemorrhage and atelectasis in ALI group (Fig. 1A), indicating our ALI model was successfully generated. Interestingly, the treatments of SDF-1α with different doses significantly improved pathologies associated with OA-induced ALI (Fig. 1A). Pathological scores further demonstrated that SDF-1α significantly reduced interstitial edema, hemorrhage, atelectasis and total lung injury histology scores (Fig. 1B). Since there was no obviously difference in protection effect of SDF-1α in ALI between 20 μg/kg/24 h and 40 μg/kg/24 h. Twenty μg/kg/24 h was used to for the following study.

3.2. Lung expression of SDF-1α and CXCR4

Since we found the beneficial effects of SDF-1α on ALI when it was applied in the extracellular space (blood circulation), one would speculate that there might be a receptor for SDF-1α on the cell surface to transduce the extracellular signal into intracellular cell actions. Thus, we hypothesized that the specific receptor for SDF-1α, CXCR4, would be an ideal candidate for this signaling cascade. In order to test our hypothesis that SDF-1α/CXCR4 axis plays an important role in SDF-1α-mediated ALI protection, we first examined whether there are endogenous SDF-1α and CXCR4 in normal lung and whether their expressions change associated with ALI and SDF-1α treatments. We first performed immunohistochemical analysis on lungs sections from uninjured controls and ALI groups to determine the expression of SDF-1α and its receptor CXCR4. We found that both SDF-1α (Fig. 2A, left panel) and CXCR4 (Fig. 2B, left panel) were strongly expressed in uninjured adult rabbits lung. These observations are in agreement with a previous report describing CXCR4 expression in lung [19] and implicate the SDF-1/CXCR4 axis in the functions of lungs. To further understand the underlying function of the SDF-1/CXCR4 axis in lung injure, SDF-1α and CXCR4 were stained in ALI groups. We found that both SDF-1α and CXCR4 expression were decreased in ALI group (Figs. 2A and B, middle panels). After SDF-1α treatment, we observed SDF-1α increased in injured lung tissue, indicating the exogenous SDF-1α can be delivered to lung (Fig. 2A, right panel). More importantly, SDF-1α treatment led to enhancement of CXCR4 expression in injured lungs (Fig. 2B, right panel), which

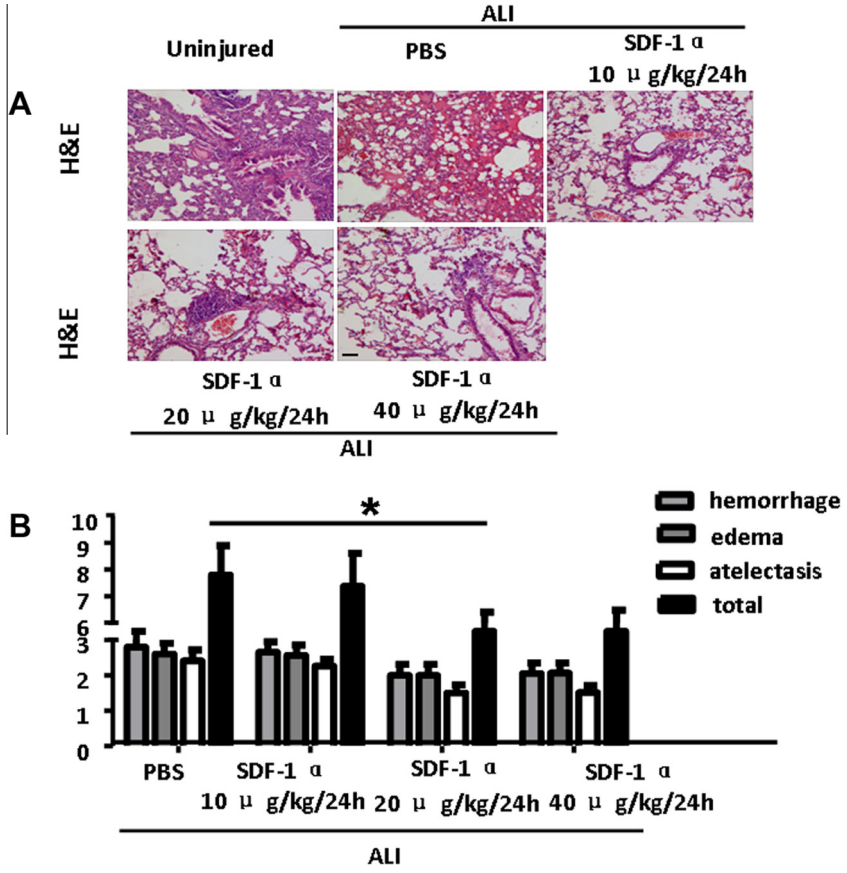

Fig. 1. SDF-1α treatment improves pathologies of lung associated with OA-induced ALI. (A) Representative figures for histochemical slides from different groups. Severe lung edema, hemorrhage were observed in ALI group. There was less damage in SDF-1α treatment group compared with the ALI group. (H&E, magnification×100). (B) Summary of lung injury scores in indicated groups. Data were presented as mean ± SEM, $^{*}P < 0.05$ in SDF-1α-treatment group vs. ALI group. The scale bar: 100 μm.

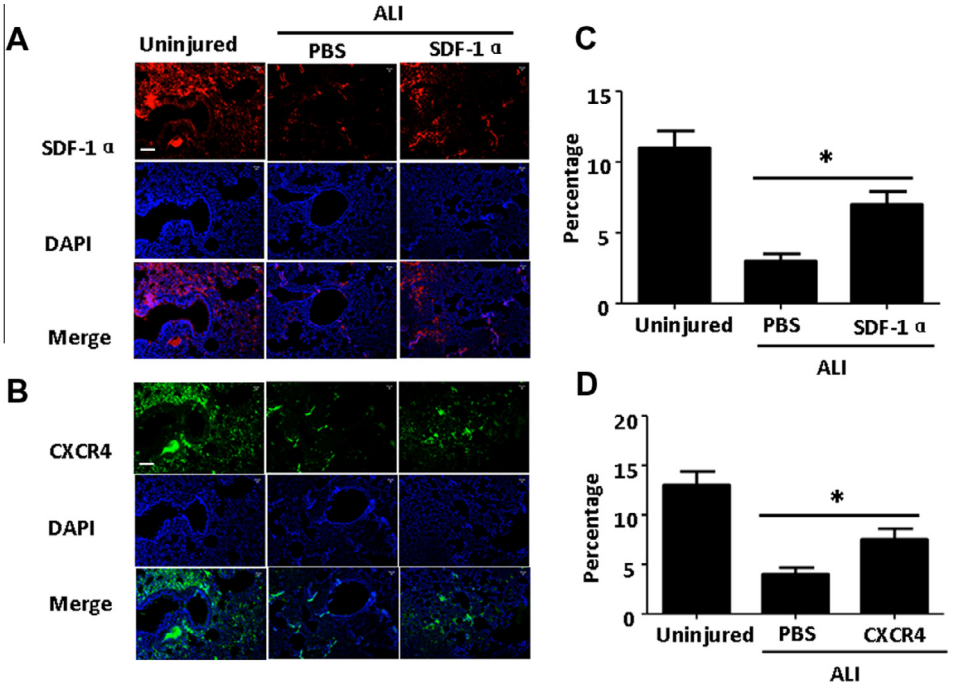

Fig. 2. SDF-1α rescues expression of CXCR4 in injured lungs. (A) SDF-1α staining in different groups. DAPI was used as staining of nucleus. (B) CXCR4 staining in different groups of lungs. Decrease in SDF-1α and CXCR4 expression were observed in ALI group, treatment of SDF-1α enhanced CXCR4 expression in the lung tissue of ALI rabbits. Quantitative measurement was expressed as percent of positive staining vs total per lung tissue area. (C and D) Data were presented by mean ± SEM. ($n = 3$ per each group, $^{*}P < 0.05$). The scale bar: 100 μm.

indicated that SDF-1α/CXCR4 axis might play a role in SDF-1α-mediated lung protection.

3.3. CXCR4 antagonist, AMD3100, inhibits the protective effect of SDF-1α on ALI

To determine the importance of SDF-1α/CXCR4 axis in protection of ALI, a CXCR4 antagonist, AMD3100, was used. Consistent with our immunohistochemical data, Western blotting results showed both SDF-1α and CXCR4 were significantly decreased in ALI group (Figs. 3A and B) and the levels of SDF-1α and CXCR4 were obviously increased after SDF-1α treatment (Fig. 3A and B). Interestingly, treatment with a small molecule CXCR4 antagonist, AMD3100, inhibited the effect of SDF-1α on upregulating CXCR4 (Fig. 3B). More importantly, the beneficial effects of SDF-1α on ALI was greatly lessened during co-administration with AMD3100. Thus, our results demonstrated that the protective effects of SDF-1α on ALI was through activation/upregulation of CXCR4.

3.4. SDF-1α/CXCR4 activates anti-apoptosis pathways for protection of lung injury

It has been shown that activation of CXCR4 can protect multiple tissue injuries by activating anti-apoptotic proteins or inhibiting pro-apoptotic pathways [7], and thus our next question was whether SDF-1α-mediated activation of CXCR4 plays a role in modulating apoptotic pathways in protecting against ALI. As shown in Fig. 4A, the expression levels of anti-apoptosis markers Bcl-2 and Bcl-xl (Fig. 4A) were reduced after ALI and recovered after SDF-1α treatment. Again, AMD3100 was able to inhibit SDF-1α-mediated activation of these anti-apoptotic proteins. However, although we observed activation of pro-apoptosis markers, Bad and Bax, after ALI, neither SDF-1α alone nor combination of SDF-1α and AMD3100 could modulate their expression (Fig. 4B).

Therefore, our studies suggested that the protective effects of SDF-1α/CXCR4 axis on ALI was through activation of anti-apoptotic pathway.

4. Discussion

The key finding in this study is that SDF-1α significantly ameliorated OA-induced ALI in rabbits, as evidenced by prevention of pulmonary edema, and a decrease in the leakage of proteins into alveolar airspaces. The molecular mechanism underlying the beneficial effects of SDF-1α might be involved in upregulating anti-apoptosis protein expression through increase of CXCR4. These results suggested that SDF-1α and CXCR4 might be a promising agent target for treatment of patients with ALI or ARDS.

The disruption of the alveolar-capillary barrier function in ALI and ARDS leads to diffuse pulmonary infiltration and increase pulmonary capillary permeability and lung hemorrhage [20]. A recent study showed that the lung is the organ most vulnerable to the effects of OA. Both endothelial and alveolar epithelial cells were markedly sensitive to OA injury [21]. In this study we are using the OA guided acute lung injury animal model. OA causes morphological and cellular changes similar to the findings seen in patients with ARDS, and has thus been extensively used to evaluate the

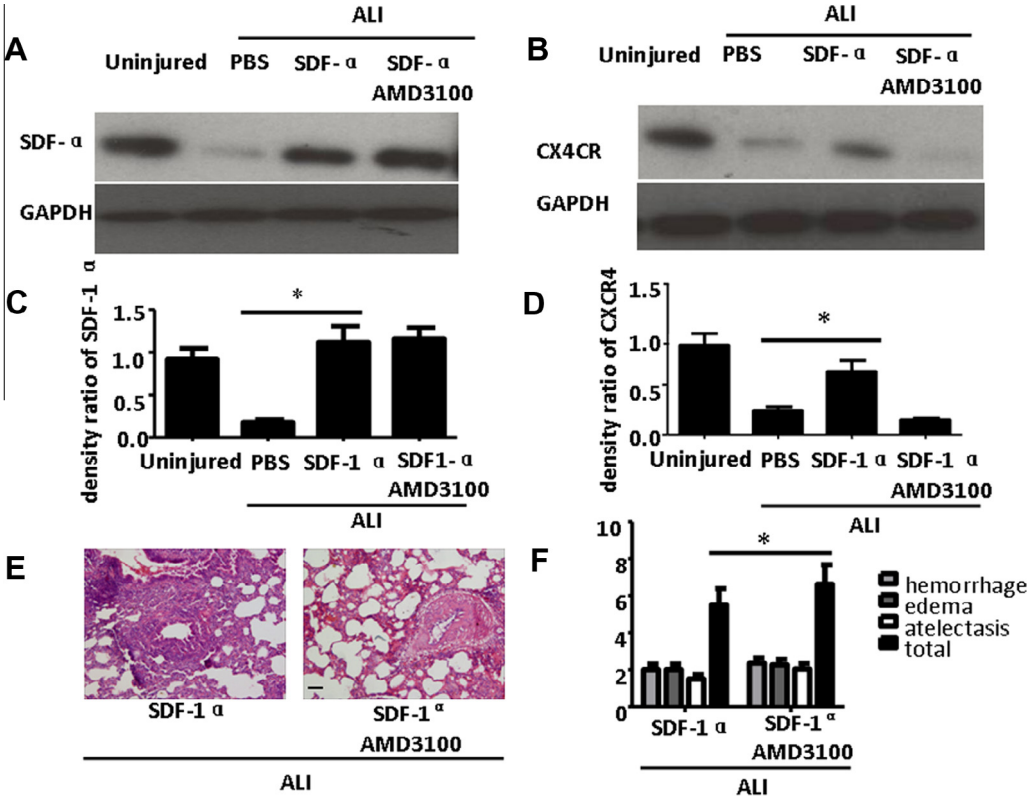

Fig. 3. Expression of SDF-1α and CXCR4 in different groups of lung tissues. (A) SDF-1α was significantly decreased in ALI group. The levels of SDF-1α were obviously increased with SDF-1α treatment in lung tissue. (B) CXCR4 was significantly reduced in ALI group and recovered by SDF-1α treatment. The CXCR4 inhibitor, AMD3100, significantly abolished the upregulation of CXCR4 by SDF-1α. GAPDH was used as an internal control. (C and D) Quantitative data were summarized from A and B, (E) the beneficial effects of SDF-1α on ALI was abolished by AMD3100 treatment. (F) Pathological scores of E. data were presented as mean ± SEM. ($n = 3$ per each group, $^{**}P < 0.01$, $^{*}P < 0.05$). The scale bar: 100 μm.

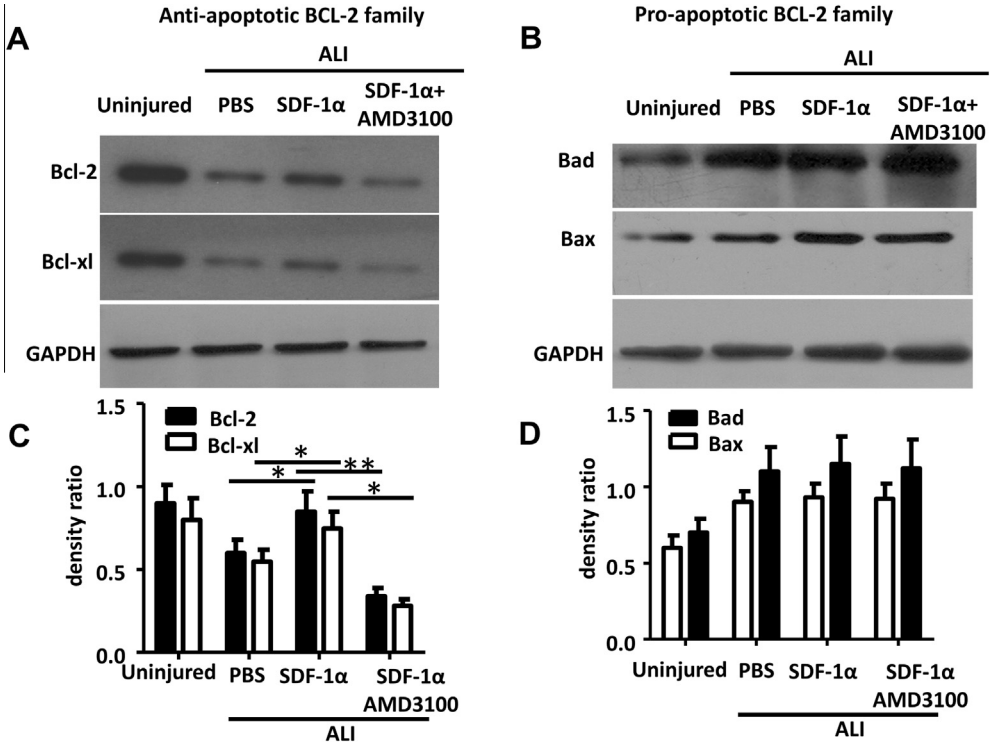

Fig. 4. Treatment of SDF-1α specifically activates anti-apoptotic proteins. (A) Tissue immunoblots for anti-apoptotic proteins (Bcl-2 and Bcl-xL). (B) Tissue immunoblots for pro-apoptotic proteins (Bax, Bad). GAPDH was used as internal control. (C and D) Summary of anti-apoptotic and pro-apoptotic family expression in three groups. The data were present as mean ± SEM ($n = 3$ $^*P < 0.05$).

efficacy of various treatment strategies in patients with ARDS. Therefore, we believed the OA induced ALI was an ideal animal model for study of ALI.

The SDF-1/CXCR4 axis has been shown to play important roles in development, tissue repair and regeneration [22]. Previous studies have suggested that SDF-1α pre-treatment or over-expression promotes the survival of rat and proliferation of human bone marrow stem cells after exposure to a variety of internal and external poptosis-inducing factors such as cytokine IL-4 and H_2O_2 [23,24]. In light of the reports of the critical role of the SDF-1/CXCR4 signaling axis in maintaining survival and proliferation of cell populations in the BM, we hypothesized that SDF-1α may ameliorate OA-induced ALI in rabbits. Determining how to restore the alveolar-capillary barrier function is the key to therapeutics for acute lung injury. We found that SDF-1α treatment significantly protected rabbits from OA-induced ALI, resulting in less interstitial edema, hemorrhage, atelectasis. We demonstrated in our results that SDF-1α expression in uninjured lung tissues decreased under the basal levels after treatment with OA. Hence, our studies suggested that SDF-1α may be a promising target for therapy of ALI.

It has been shown that SDF-1α can modulate the chemokine receptor CXCR4 on CML cells, thus increasing the function of SDF-1/CXCR4 axis [25–27]. Our studies have shown that CXCR4 was expressed in tissue derived uninjured lung but its expression were greatly decreased in ALI. ALI decreased the levels of both SDF-1α and its receptor CXCR4. Growing evidence implicates that SDF1 and its receptor CXCR4, which normally control neural crest development, have important roles in tissues growth and angiogenesis. This led us to investigate the effect of SDF-1α on the expression of CXCR4 in ALI. As illustrated in our results, SDF-1α upregulated the expression of CXCR4. These changes were accompanied by less interstitial edema, hemorrhage, atelectasis in ALI lung tissues. To further explore signal transduction mechanisms of the SDF-1/CXCR4 axis in ALI lung tissues, studies were carried out using AMD3100, which can specifically block CXCR4. The levels of interstitial edema, hemorrhage, atelectasis, measures of ALI, were increased when treated with AMD3100. We speculated that the mechanisms underlying the SDF-1α protection effect on ALI is mediated, at least partly, by CXCR4.

It was shown that SDF-1/CXCR4 signaling axis can regulate the levels of anti-apoptotic molecules and decrease the levels of pro-apoptotic family in many kinds cells and tissues [24,25,28]. Pro- and anti-apoptotic proteins of the Bcl-2 family play a pivotal role in the regulation of apoptotic cell death in mammalian cells. Modulation of proteins such as Bax and Bcl-xl can cause permeabilization of the mitochondrial outer membrane, leading to the release of soluble molecules responsible for activation of the apoptosis. These findings led to the investigation of the mechanisms underlying the SDF-1-dependent protection benefits in ALI animals. We analyzed both Pro- and anti-apoptotic proteins of the Bcl-2 family following treatment after SDF-1α. Treatment of SDF-1α promoted anti-apoptosis family both Bcl-2 and Bcl-xl expression and had no influence on pro-apoptosis family Bax and Bad. Anti-apoptosis family activation plays a central role in the execution and completion of apoptosis. In addition, AMD3100 inhibited the activation of the anti-apoptosis family. The results indicated that SDF-1α protection benefit of AIL is also associated with upregulating anti-apoptosis family expression, most probably through a CXCR4-dependent manner.

Evidently, our studies cannot address every aspect of the beneficial effects of SDF-1α; there are limitations in our current studies which requires future investigations. For example, our observations show SDF-1α/CXCR4 axis might be associated with anti-apoptosis proteins in ALI. The questions we should address are what molecular mechanisms are involved in this regulation, and how SDF-1α/CXCR4 axis crosstalk with anti-apoptotic protein family and regulate their activities in the setting of ALI? By answering these critical questions, we hope to gain additional insights into

the pathological changes during the progression of ALI as well as potential therapeutic targets for treatment of ALI.

In conclusion, SDF-1α and CXCR4 were markedly decreased in lung tissues after OA treatment, and this decrease correlated well with the severity of lung injury. Treatment with SDF-1α was efficacious, clearly indicating that SDF-1α is a crucial factor in OA-induced lung injury. This can be explained partly by its increase of anti-apoptosis molecules Bcl-2 and Bcl-xl through CXCR4. In fact it has been reported that SDF1 not only stimulates CXCR4 signaling but also regulates its expression by positive feed back mechanism. Therefore, further investigation is required to understand the mechanism underlying the positive regulation of CXCR4 by SDF-1α.

Acknowledgments

This work was supported by Natural Science Foundation of Guangdong Province of China (Grant No. 1015008008000008) to Tiehe Qin, by Medical Scientific Research Foundation of Guangdong Province of China (Grant No. B2010001) to Weixin Guo, by the National Natural Science Foundation of China (Grant No. 81200 244) to Xiaoyun Xie, by the Shanghai Natural Science Foundation (Grant No. 12ZR1428400) to Xiaoyun Xie, by Science and Technology Department of Hunan Province (Grant No. 2013FJ3061) to Zhihong Li, Chenzhou Science, Technology Bureau (Grant No. CZ2013081) to Zhihong Li and by American Heart Association (12SDG12070174) to Hua Zhu. We thank Ms. Susu D'Andrea for her English editing support.

References

[1] G.D. Rubenfeld, M.S. Herridge, Epidemiology and outcomes of acute lung injury, Chest 131 (2007) 554–562.
[2] A.P. Wheeler, G.R. Bernard, Acute lung injury and the acute respiratory distress syndrome: a clinical review, Lancet 9572 (2007) 1553–1564.
[3] W.L. Lee, G.P. Downey, Neutrophil activation and acute lung injury, Curr. Opin. Crit. Care 7 (2001) 1–7.
[4] M. Kucia, J. Ratajczak, M.Z. Ratajczak, Bone marrow as a source of circulating CXCR[4] tissue-committed stem cells, Biol. Cell 97 (2005) 133–146.
[5] A. Aiuti, I.J. Webb, C. Bleul, T. Springer, J.C. Gutierrez-Ramos, The chemokine SDF-1 is a chemoattractant for human CD34 hematopoietic progenitorcells and provides a new mechanism to explain the mobilization of CD34 progenitors to peripheral blood, J. Exp. Med. 185 (1997) 111–120.
[6] H. Peng, Y. Huang, J. Rose, D. Erichsen, S. Herek, N. Fujii, H. Tamamura, J. Zheng, Stromal cell-derived factor 1-mediated CXCR4 signaling in rat and human cortical neural progenitor cells, J. Neurosci. Res. 76 (2004) 35–50.
[7] Tatsuya Yano, Zhengyu Liu, Jennifer Donovan, Melissa K. Thomas, Joel F. Habener, Stromal cell-derived factor-1 (SDF-1)/CXCL12 attenuates diabetes in mice and promotes pancreatic cell survival by activation of the prosurvival kinase Akt, Diabetes 56 (2007) 2946–2957.
[8] L. Yuan, N. Sakamoto, G. Song, M. Sato, Low-level shear stress induces human mesenchymal stem cell migration through the SDF-1/CXCR4 axis via MAPK signaling pathways, Stem Cells Dev. 22 (2013) 2384–2393.
[9] W. Tristram Arscott, Annette E. LaBauve, Victor May, Umadevi V. Wesley, Suppression of neuroblastoma growth by dipeptidyl peptidas IV: relevance of chemokine regulation and caspase activation, Oncogene 28 (2009) 479–491.
[10] X. Liu, B. Duan, Z. Cheng, X. Jia, L. Mao, H. Fu, SDF-1/CXCR4 axis modulates bone marrow mesenchymal stem cell apoptosis, migration and cytokine secretion, Protein Cell. 2 (2011) 845–854.
[11] J.J. Lataillade, D. Clay, P. Bourin, F. Herodin, C. Dupuy, M.C. Le Bousse-Kerdilès, Stromal cell-derived factor 1 regulates primitive hematopoiesis by suppressing apoptosis and by promoting G(0)/G(1) transition in CD34(+) cells: evidence for an autocrine/paracrine mechanism, Blood 99 (2002) 1117–1129.
[12] H.E. Broxmeyer, L. Kohli, C.H. Kim, Y. Lee, C. Mantel, D.W. Clapp, Stromal cell-derived factor-1/CXCL12 directly enhances survival/antiapoptosis of myeloid progenitor cells through CXCR4 and G(alpha)i proteins and enhances engraftment of competitive repopulating stem cells, J. Leukoc. Biol. 73 (2003) 630–638.
[13] K. Kuwabara, S. Furue, Y. Tomita, M. Ueno, T. Ono, A. Matsukawa, M. Yoshinaga, K. Mikawa, K. Nishina, M. Shiga, H. Obara, Y. Hori, Effect of methylprednisolone on phospholipase A(2) activity and lung surfactant degradation in acute lung injury in rabbits, Eur. J. Pharmacol. 433 (2001) 209–216.
[14] A.N. Carr, B.W. Howard, H.T. Yang, E. Eby-Wilkens, P. Loos, A. Varbanov, A. Qu, J.P. DeMuth, M.G. Davis, A. Proia, R.L. Terjung, K.G. Peters, Efficacy of systemic administration of SDF-1 in a model of vascular insufficiency: support for an endothelium-dependent mechanism, Cardiovasc. Res. 69 (2006) 925–935.
[15] Yu Misao, Masazumi Arai, Takamasa Ohno, Hiroaki Ushikoshi, Hirohito Onogi, Hiroyuki Kobayashi, Genzou Takemura, Shinya Minatoguchi, Takako Fujiwara, Hisayoshi Fujiwara, Modification of post-myocardial infarction granulocyte-colony stimulating factor therapy with myelo-suppressives, Circ. J. 71 (2007) 580–590.
[16] F. Jin, S. Irshad, M. Belakavadi, M. Ittmann, C. Abate-Shen, J.D. Fondell, Med1 amplification in malignant prostate epithelium is associated with increased cellular proliferation and tumorigenicity, Mol. Cancer Res. 11 (2013) 736–747.
[17] F. Jin, J.D. Fondell, A novel androgen receptor-binding element modulates Cdc6 transcription in prostate cancer cells during cell-cycle progression, Nucleic Acids Res. 37 (2009) 4826–4838.
[18] Kenji Kuwabara, Shingo Furue, Yasuhiko Tomita, Masahiko Ueno, Takashi Ono, Akihiro Matsukawa, Masaru Yoshinaga, Katsuya Mikawa, Kahoru Nishina, Makoto Shiga, Hidefumi Obara, Yozo Hori, Effect of methylprednisolone on phospholipase A2 activity and lung surfactant degradation in acute lung injury in rabbits, Eur. J. Pharmacol. 433 (2001) 209–216.
[19] A. Suga, K. Ueda, Y. Takemoto, A. Nishimoto, T. Hosoyama, T.S. Li, K. Hamano, Significant role of bone marrow-derived cells in compensatory regenerative lung growth, J. Surg. Res. 183 (2013) 84–90.
[20] G.M. Matuschak, A.J. Lechner, Acute lung injury and the acute respiratory distress syndrome: pathophysiology and treatment, Mo. Med. 107 (2010) 252–258.
[21] K. Inoue, H. Takano, A. Shimada, R. Yanagisawa, M. Sakurai, S. Yoshino, T. Yoshikawa, Urinary trypsin inhibitor protects against systemic inflammation induced by lipopolysaccharide, Mol. Pharmacol. 67 (2005) 673–680.
[22] Z. Liu, V. Stanojevic, S. Avadhani, T. Yano, J.F. Habener, Stromal cell-derived factor-1 (SDF-1)/chemokine (C-X-C motif) receptor 4 (CXCR4) axis activation induces intra-islet glucagon-like peptide-1 (GLP-1) production and enhances beta cell survival, Diabetologia 54 (2011) 2067–2076.
[23] S. Herberg, X. Shi, M.H. Johnson, M.W. Hamrick, C.M. Isales, W.D. Hill, Stromal cell-derived factor-1β mediates cell survival through enhancing autophagy in bone marrow-derived mesenchymal stem cells, PLoS One 8 (2013) e58207.
[24] A. Kortesidis, A. Zannettino, S. Isenmann, S. Shi, T. Lapidot, S. Gronthos, Stromal-derived factor-1 promotes the growth, survival, and development of human bone marrow stromal stem cells, Blood 105 (2005) 3793–3801.
[25] S. Singh, A. Sadanandam, R.K. Singh, Chemokines in tumor angiogenesis and metastasis, Cancer Metastasis Rev. 26 (2007) 453–467.
[26] S.R. Chinni, S. Sivalogan, Z. Dong, J.C. Filho, X. Deng, R.D. Bonfil, M.L. Cher, CXCL12/CXCR4 signaling activates Akt-1 and MMP-9 expression in prostate cancer cells: the role of bone microenvironment-associated CXCL12, Prostate 66 (2006) 32–48.
[27] J.A. Burger, T.J. Kipps, CXCR4: a key receptor in the crosstalk between tumor cells and their microenvironment, Blood 107 (2006) 1761–1767.
[28] Fabrizio Vianello, Federica Villanova, Veronica Tisato, Stefania Lymperi, Ka-Kei Ho, Ana R. Gomes, David Marin, Dominique Bonnet, Jane Apperley, Eric W.-F. Lam, Francesco Dazzi, Bone marrow mesenchymal stromal cells non-selectively protect chronic myeloid leukemia cells from imatinib-induced apoptosis via the CXCR4/CXCL12 axis, Haematologica 95 (2010) 1081–1089.