Protection of Mice from Allergen-induced Asthma by Selenite

PREVENTION OF EOSINOPHIL INFILTRATION BY INHIBITION OF NF-κB ACTIVATION*

Received for publication, January 25, 2002, and in revised form, March 4, 2002
Published, JBC Papers in Press, March 15, 2002, DOI 10.1074/jbc.M200808200

Dae-won Jeong‡§, Min-Hyuk Yoo§†, Tae Soo Kim‡, Jae-Hong Kim‡, and Ick Young Kim‡¶

From the ‡Graduate School of Biotechnology, Korea University, Seoul 136-701, Korea and the ¶Department of Life
Science, Kwangju Institute of Science and Technology, Kwang-Ju 500-712, Korea

The potential anti-inflammatory effect of sodium selenite in a mouse model of asthma was investigated. Selenite was injected into the peritoneum of allergen (ovalbumin)-sensitized mice before allergen challenge. Ovalbumin challenge resulted in activation of the transcription factor NF-κB and an increase in the expression of cell adhesion molecules (intercellular adhesion molecule 1, vascular cell adhesion molecule 1, and E-selectin, which are encoded by NF-κB-dependent genes) in lung tissue as well as in the recruitment of eosinophils to lung airways. These effects of ovalbumin challenge were all inhibited by pretreatment of mice with selenite. Selenite administration also increased the activity of selenium-dependent glutathione peroxidase in lung tissue. Furthermore, supplementation of A549 human airway epithelial cell cultures with selenite increased glutathione peroxidase activity as well as inhibited both the generation of hydrogen peroxide and the activation of NF-κB induced by tumor necrosis factor α in these cells. Selenite also reversed in vitro the activation of NF-κB induced by this cytokine in intact A549 cells. These results suggest that selenite regulates the activity of NF-κB by increasing the activity of glutathione peroxidase, thereby removing potential activators of NF-κB, and possibly also by direct oxidation of critical sulfhydryl groups of this transcription factor. These effects of selenite likely underlie its anti-inflammatory action in asthma.

Asthma is a chronic respiratory disease characterized by three major symptoms: airway hyper-reactivity, airway obstruction, and lung inflammation. Numerous cytokines (including interleukins 4, 5, 9, 10, and 13), the chemokine eotaxin, and adhesion molecules such as intercellular adhesion molecule 1 (ICAM-1),† vascular cell adhesion molecule 1 (VCAM-1), and E-selectin contribute to the allergic inflammatory response associated with this condition (1–5). The expression of the genes for these various proteins in inflammation-related cells is induced as a result of activation of the transcription factor NF-κB (6–8) and is directly associated with the recruitment of eosinophils that is apparent early after pulmonary allergen challenge (9–11).

Dietary micronutrients and antioxidants such as vitamins A, C, and E, zinc, and selenium are implicated as determinants of the severity of bronchial asthma (12–14). Selenium is an essential biological trace element in mammals and is incorporated into selenoproteins in the form of selenocysteine, which is encoded in mRNA by the codon UGA (15). Mammalian selenoproteins include glutathione peroxidase (GPx), thioredoxin reductase, and thyroxine 5*-deiodinase (16–18). GPx is an antioxidant enzyme that scavenges H2O2 and organic hydroperoxides and whose expression level depends on selenium availability (16, 19–21).

The redox state of biological thiol groups regulates various intracellular signal transduction events in cells of the immune system. The activity of GPx is important for maintaining cellular thiol homeostasis. An increase in the amount of GPx in selenium-supplemented cells has been shown to inhibit both the activation of mitogen-activated protein kinases such as p38, JNK1 or JNK2, and ERK1 or ERK2 as well as the NF-κB-mediated signaling pathway (22–25).

Selenium has also been shown to prevent cancer in several animal models (26–30) as well as in humans (31). This chemopreventive effect is thought to result from modulation of cysteine residues in proteins by selenium. Selenium regulates the functions of many proteins by reacting with essential thiol groups to form S-Se-S (selenenulfide) or S-Se adducts (28). We and others have previously shown that proteins modulated as a result of thiol modification by selenium include the Na+/K*-dependent ATPase, the glucocorticoid receptor, pros-taglandin D synthase, the transcription factors AP-1 and NF-κB, the protease caspase-3, and the protein kinases Cdk2, protein kinase C, and JNK (32–40).

In remains unclear, however, whether a low dietary intake of selenium and reduced GPx activity are associated with an increased risk of asthmatic inflammation. Given that the activities of GPx and NF-κB are determined by selenium availability, we have now investigated the effects of the activity levels of these proteins on allergen-induced asthmatic reactions both in selenite-treated mice and in selenite-supplemented airway cells. We now show that the increased GPx activity in selenite-treated mice is associated with inhibition of allergen-induced NF-κB activation as well as of consequent inflammatory gene expression and eosinophil recruitment to the airways. In addition, NF-κB activity in A549 airway epithelial cells supplemented with selenite was directly inhibited as a...
result of thiol modification of this transcription factor. Furthermore, selenite-supplemented A549 cells were shown to scavenge reactive oxygen intermediates (ROI), such as H$_2$O$_2$, that contribute to NF-κB activation.

**EXPERIMENTAL PROCEDURES**

**Cell Culture** — The human airway epithelial cell line A549 was cultured under a humidified atmosphere of 5% CO$_2$ at 37°C in Ham’s F-12 medium supplemented with 10% of fetal bovine serum, 100 units/ml of penicillin G, 100 units/ml of streptomycin, and 0.25 μg/ml of amphotericin.

**Sensitization and Challenge of Mice** — The sensitization and challenge of mice were achieved by a modified version of the method described by Kanekirio et al. (4). In brief, mice (6 weeks of age) were injected intraperitoneally with 500 μg of ovalbumin (Sigma) and 2 mg of aluminum (Feruc). A second intraperitoneal injection of 20 μg of ovalbumin adsorbed to aluminum hydroxide gel was administered 10 days after the first injection. After an additional 10 days, the mice were exposed to an aerosol of 1% ovalbumin in phosphate-buffered saline (PBS) for 30 min at 1-day intervals for 3 days. Two days after the final exposure to the aerosol of 1% ovalbumin, the animals were challenged with a nebula of 10% ovalbumin in PBS. Nebulization was performed in a plastic chamber connected to an ultrasonic nebulizer (Omron, Vernon Hills, IL) that allows entry of an ovalbumin aerosol. For competition experiments, 3 pmol of unlabelled ovalbumin was mixed with 35 pmol of [3H]ovalbumin adsorbed to aluminum hydroxide gel. The homogenate was centrifuged at 12,000 g for 10 min, and the resulting supernatant was then collected as cytosolic extract of lung tissue (as described for immunoblot analysis) was incubated with 1 unit of glutathione reductase (Sigma), after which the reaction was initiated by the addition of tert-butyldihydroperoxide to a final concentration of 35 μM. GPx activity was monitored by measuring the decrease in absorbance at 340 nm, reflecting the oxidation of NADPH.

**RESULTS**

**Inhibition by Selenite of Airway Obstruction and Eosinophil Infiltration of the Lung** — The effect of selenite on airway inflammation was examined by intraperitoneal injection of this compound 1 and 24 h before challenge of sensitized mice with ovalbumin. Histological analysis of lung sections stained with hematoxylin-eosin revealed that ovalbumin challenge of mice resulted in an increase in muscle mass and airway obstruction, compared with control sensitized mice that were challenged with PBS (Fig. 1). These effects of ovalbumin challenge were prevented by pretreatment with selenite. Pretreatment of mice with N-acetylcysteine (NAC), a glutathione precursor and ROI scavenger with antioxidant activity, also greatly reduced the effects of ovalbumin challenge. Examination of BAL fluid collected from mice 48 h after ovalbumin challenge revealed a marked increase in the number of eosinophils (Fig. 2). Thus, whereas the number of eosinophils in BAL fluid from naive control mice or from PBS-challenged sensitized mice was less...
also examined as a control. The data are the means +/−SD of three independent experiments. Magnification was ×200, B, the number of eosinophils in BAL fluid of mice treated as in A was determined as a percentage of the total cells. Naive mice were also examined as a control. The data are the means ± S.E. of values obtained from seven animals/group. ∗, p < 0.0001 versus control (Student’s t test). OVA, ovalbumin; Se, selenite.

Inhibition by Selenite of Eosinophil Recruitment to Airways. A, BAL fluid was collected 48 h after challenge from mice treated as described in the legend to Fig. 1. The fluid was stained with Diff-Quick for microscopic detection of eosinophils (arrows). Magnification was ×200. B, the number of eosinophils in BAL fluid of mice treated as in A was determined as a percentage of the total cells. Naive mice were also examined as a control. The data are the means ± S.E. of values obtained from seven animals/group. ∗, p < 0.0001 versus control (Student’s t test). OVA, ovalbumin; Se, selenite.

Effects of Selenite on Allergen-induced Asthma

Fig. 1. Effects of selenite on the activation of NF-κB in lung tissues. The lungs were removed 48 h after challenge from mice treated as described in the legend to Fig. 1. Nuclear extracts were then prepared from the tissue and subjected to EMSA analysis of the DNA binding activity of NF-κB. Nuclear extract prepared from the lung tissue of a naive control mouse was similarly analyzed. The arrow indicates the specific DNA-probe complex. OVA, ovalbumin; Se, selenite.

Inhibition by Selenite of Inflammatory Mediator Gene Expression in the Lung. AQ, ICAM-1, VCAM-1, and E-selectin are expressed during asthmatic inflammation, and the genes that encode these proteins are regulated by NF-κB. We therefore examined the expression of adhesion proteins in cytosolic extracts prepared from the lungs of mice challenged with ovalbumin. Immunoblot analysis revealed that the abundance of ICAM-1, VCAM-1, and E-selectin in the lungs of ovalbumin-sensitized challenged mice was markedly increased compared with that in the lungs of naive control mice (Fig. 4). The expression of all three proteins was greatly inhibited by treatment of mice with selenite or with NAC before ovalbumin challenge. It has been well known that IgE is produced and secreted from B cells stimulated by cytokine during lung inflammation (41). Therefore, when horseradish peroxidase-conjugated mouse anti-IgG monoclonal antibody was used to probe a mouse anti-ICAM-1 or a mouse anti-E-selectin monoclonal antibody, heavy chain (molecular mass = ~55 kDa) of IgE originated from the lung of ovalbumin-challenged mice was detected as shown in Fig. 4 (A and C).

Inhibition by Selenite of TNF-α-induced NF-κB Activation in A549 Cells. To examine the possible effect of selenite on the DNA binding activity of NF-κB in vitro, we exposed A549 airway epithelial cells to TNF-α for 1 h to induce NF-κB activation and then subjected nuclear extracts prepared from the cells to EMSA analysis. Incubation of the nuclear extract with 3 μM selenite for 10 min before exposure to the 32P-labeled probe reversed the increase in the DNA binding activity of NF-κB induced by TNF-α (Fig. 5A). The DNA binding activity of NF-κB lost after treatment of nuclear extract with 10 μM selenite was completely recovered by subsequent exposure to 2 mM DTT. These results suggest that selenite is able to inhibit NF-κB activity in vitro by direct modification of thiol groups. The addition of 0.5 mM DTT was necessary for the full reduction of NF-κB but was not sufficient to recover NF-κB inactivated by selenite.

To determine the effect of selenite treatment in vivo on the DNA binding activity of NF-κB, we incubated A549 cells with 5 μM selenite for 6, 12, or 24 h before exposure of the cells to TNF-α for 1 h. The increase in the DNA binding activity of NF-κB induced by TNF-α was inhibited in a time-dependent manner by pretreatment of the cells with selenite (Fig. 5B). The specificity of the observed DNA binding activity was revealed by its sensitivity to competition by a 100-fold excess of unlabeled κB oligonucleotide and by its resistance to the addition of a mutant oligonucleotide.

Increase in GPx Activity in Selenite-supplemented A549 Cells and Selenite-treated Mice. Exposure of cultured cells to sele-
Effects of Selenite on Allergen-induced Asthma

Sensitized mice were pretreated (or not) with selenite (Se) or NAC before ovalbumin challenge. The cell extracts were subjected to immunoblot analysis with antibodies to ICAM-1, VCAM-1, or E-selectin; the blots were reprobed with antibodies to β-actin to confirm consistent application of samples. The positions of molecular size standards (in kDa) are indicated on the left.

Fig. 4. Immunoblot analysis of the effects of selenite treatment on the expression of ICAM-1 (A), VCAM-1 (B), and E-selectin (C) in the lungs of ovalbumin-challenged mice. Sensitized mice were pretreated (or not) with selenite (Se) or NAC before ovalbumin (OVA) challenge. The cell extracts were prepared from the lungs of the experimental mice 48 h after challenge as well as from the lung tissue of a naive control mouse. The extracts were subjected to immunoblot analysis with antibodies to ICAM-1, VCAM-1, or E-selectin; the blots were reprobed with antibodies to β-actin to confirm consistent application of samples. The positions of molecular size standards (in kDa) are indicated on the left.

Selenite has been shown to result in an increase in GPx activity capable of scavenging H₂O₂ (19–21). Incubation of A549 cells with 100 nM selenite for 3 days induced an approximately 3.3-fold increase in GPx activity measured in cell extracts (Fig. 6A). The GPx activity in the lung tissue of mice treated with selenite before ovalbumin challenge was also about twice that in the lungs of mice not treated with selenite before challenge or of naive control mice (Fig. 6B). Immunoblot analysis revealed that the increases in GPx activity in both A549 cells and mouse lung induced by selenite were accompanied by increases in the abundance of GPx protein (Fig. 6).

Inhibition by Selenite of the Intracellular Generation of H₂O₂ in A549 Cells—The intracellular generation of H₂O₂ in response to a variety of exogenous stimuli is thought to contribute to the activation of NF-κB (42). The overexpression of H₂O₂-scavenging enzymes such as GPx and catalase thus prevents activation of the NF-κB signaling pathway (43, 44). We measured the intracellular generation of H₂O₂ by flow cytometry in A549 cells loaded with the oxidant-sensitive dye 2',7'-dichlorofluorescein diacetate; 2',7'-dichlorofluorescein diacetate is converted inside cells to 2',7'-dichlorofluorescin, which is oxidized by H₂O₂ to the fluorescent 2',7'-dichlorofluorescein. The intracellular concentration of H₂O₂ was increased in a time-dependent manner by exposure of control A549 cells to TNF-α, reaching a maximum at 12 min (Fig. 7). In contrast, the generation of H₂O₂ in response to TNF-α was not detected in A549 cells that had been cultured in the presence of 100 nM selenite. Furthermore, the basal concentration of H₂O₂ in the selenite-supplemented cells was reduced compared with that in the control cells.

DISCUSSION

Although selenium has been implicated as a determinant of asthma severity (13, 14), the mechanism for such an association has been unclear. We have now investigated the anti-inflammatory effect of selenium on asthma by intraperitoneal injection of selenite in allergen-sensitized mice. Such treatment with selenite greatly reduced the extent of NF-κB activation, NF-κB–dependent inflammatory protein expression, and eosinophil infiltration in the lung induced by allergen challenge. Selenite treatment also increased GPx activity in the lung. Furthermore, supplementation of A549 airway epithelial cells with selenite also resulted in an increase in GPx activity as well as in removal of H₂O₂ and in inhibition of NF-κB

![Fig. 5. Effects of selenite on the DNA binding activity of NF-κB in nuclear extracts of A549 cells.](http://www.jbc.org/Downloadedfrom)
activation induced by TNF-α. Selenite also reversed in vitro the activation of NF-κB induced by TNF-α in A549 cells. Together, our results thus indicate that selenite regulates NF-κB activity by increasing the activity of GPx and possibly also by direct oxidation of essential sulfhydryl groups of this transcription factor, thereby greatly ameliorating the allergen-induced asthmatic response (Fig. 8).

Selenium is an essential trace element in mammals. It is incorporated into selenoproteins as selenocysteine, which is encoded by a UGA codon that normally functions as a signal for the termination of protein synthesis (15). Selenoproteins include the antioxidants GPx, selenoprotein P, and thioredoxin reductase as well as thyroxine 5′-deiodinase (45). The activity of these proteins thus depends on the concentration of selenium available for their biosynthesis (19–21).

In a mouse model of asthma, we have now shown that ovalbumin-induced asthmatic symptoms, such as lung obstruction and eosinophil recruitment to lung airways, were greatly reduced in animals pretreated with selenite. In investigating the mechanism of this anti-inflammatory effect, we showed by EMSA analysis that the increase in the DNA binding activity of NF-κB in lung tissue induced by ovalbumin challenge was markedly inhibited by pretreatment of mice with selenite. Selenite also inhibited the DNA binding activity of NF-κB in nuclear extracts prepared from A549 cells treated with TNF-α. This inhibition was reversed by the subsequent addition of 2

---

**Fig. 7.** Effect of selenite on the intracellular generation of H$_2$O$_2$ in A549 cells. A, the cells were cultured in medium containing 10% dialyzed fetal bovine serum for 7 days and incubated in the absence (open circles) or presence (closed circles) of 100 nM selenite (Se) for 3 days. They were then loaded with 20 μM 2′,7′-dichlorofluorescin diacetate for 30 min, washed with PBS, detached from the culture dish by exposure to trypsin, isolated by centrifugation, resuspended in medium containing 10% dialyzed fetal bovine serum, and subjected to flow cytometry (FACSCalibur, Becton Dickinson). 2′,7′-Dichlorofluorescein fluorescence was excited at 488 nm and measured at 530 nm. Base-line fluorescence was monitored for 2 min, after which the cells were exposed (arrows) to TNF-α (40 ng/ml). The data are presented as 2′,7′-dichlorofluorescein fluorescence index and are from a representative experiment. B, 2′,7′-dichlorofluorescein fluorescence index at 12 min after the addition of TNF-α was quantitated for cells pretreated or not with selenite and was then expressed as a percentage of the basal value for cells not exposed to selenite. The data are the means ± S.E. of values from three independent experiments. *, p < 0.01 versus the basal value for cells not exposed to selenite (Student’s t test).

**Fig. 8.** Proposed mechanism for the inhibitory effect of selenite on allergen-induced asthma.

---

**Fig. 6.** Effects of selenite on GPx activity in A549 cells (A) and mouse lung (B). A, A549 cells were maintained for 7 days in culture medium containing 10% dialyzed fetal bovine serum and were then incubated for 3 days in the absence (Control) or presence of 100 nM selenite (Se). Cytosolic extracts were then prepared and assayed for GPx activity. The data are expressed as nanomoles of NADPH oxidized/min/milligram of protein and are the means ± S.E. of values from five independent experiments. *, p < 0.0001 versus control (Student’s t test). B, sensitized mice were subjected to ovalbumin (OVA) challenge either with or without selenite pretreatment. The lung tissue was removed 48 h after challenge, and the cytosolic extracts were prepared from lung tissue and then analyzed as in A. Lung tissue from naive control mice was similarly processed. The data are the means ± S.E. of values from five animals/group. *, p < 0.001; †, p < 0.05 versus respective control (Student’s t test).
EF Selenite on Allergen-induced Asthma

Effects of Selenite on Allergen-induced Asthma

The NF-κB signaling pathway (43, 44, 46). We have now shown that the activity of selenium-dependent GPx was increased in the lungs of selenite-treated mice as well as in extracts of A549 cells cultured in the presence of selenite. These selenite-induced increases in GPx activity were accompanied by increases in the abundance of GPx protein. Moreover, the concentration of total glutathione in the blood of mice treated with selenite was twice that in mice not treated with selenite (data not shown). The rate of glutathione deple

Overexpression of GPx inhibits NF-κB-dependent signaling (46). We have now shown that the activity of selenium-dependent GPx was increased in the lungs of selenite-treated mice as well as in extracts of A549 cells cultured in the presence of selenite. These selenite-induced increases in GPx activity were accompanied by increases in the abundance of GPx protein. Moreover, the concentration of total glutathione in the blood of mice treated with selenite was twice that in mice not treated with selenite (data not shown). The rate of glutathione depletion in cells is increased by selenite supplementation, with the oxidized form of glutathione being released from the cells, and this increased rate of glutathione depletion is indicative of an increased GPx activity (21). The selenite-induced increase in GPx activity in the lungs of ovalbumin-challenged mice thus likely results in the rapid removal of ROI (such as H₂O₂) that contribute to the activation of NF-κB.

ROI generated in cells are thought to function as second messengers in the NF-κB signaling pathway (43, 44, 46–52). Our present data support this notion: (i) TNF-α induced the intracellular accumulation of H₂O₂ in A549 cells; (ii) preincubation of the cells with selenite prevented this effect of TNF-α; and (iii) the TNF-α-induced activation of NF-κB in A549 cells was blocked by pretreatment with buthionine sulfoximine, an inhibitor of glutathione synthesis that increases the basal concentration of peroxide (data not shown).

The NF-κB signaling pathway has been proposed as a promising target for therapeutic intervention in inflammatory diseases (53–56). Our results are consistent with this proposal. In summary, we have shown that GPx activity is increased in the lung of selenite-treated mice and in selenite-supplemented A549 cells. Furthermore, selenite blocks the TNF-α-induced generation of H₂O₂ and activation of NF-κB in A549 cells as well as the allergen-induced activation of NF-κB, inflammatory mediator gene expression, and eosinophil infiltration in the lungs of mice. Together, our data indicate that selenite ameliorates asthmatic symptoms and that ROI (such as H₂O₂) play a pivotal role in allergen-induced inflammatory signaling.

Acknowledgment—We thank Dr. Ho Zoon Chae (Chonnam National University, Kwangju, Korea) for kindly providing the antibodies to GPx.

REFERENCES
1. Feghali, C. A., and Wright, T. M. (1997) Front. Biosci. 2, 12–26
2. Hart, L., Lim, S., Adcock, I., Barnes, P. J., and Chung, K. F. (2000) Am. J. Respir. Crit. Care Med. 161, 224–231
3. Tomkinson, A., Dues, C., Cieslewicz, G., Pratt, J. C., Joetham, A., Shanafelt, M. C., Gundel, R., and Gelfand, E. W. (2001) J. Immunol. 166, 5792–5800
4. Kanehira, A., Kremura, T., Makena, M. J., Lahn, M., Joetham, A., Shanafelt, M. C., Gundel, R., and Gelfand, E. W. (2001) Am. J. Respir. Crit. Care Med. 163, 173–184
5. Webb, D. C., McKenzie, A. N., Matthaei, K. I., Rothenberg, M. E., and Foster, P. S. (2001) Immunol. Cell Biol. 79, 165–169
6. Oitzinger, W., Hofer-Warihne, K., Schmid, J. A., Koshelnik, Y., Binder, B. R., and de Martin, R. (2001) Blood 97, 1611–1617
7. Matsukura, S., Stellato, C., Pitt, J. R., Bickel, C., Miura, K., Georas, S. N., Casaloro, V., and Schleimer, R. P. (1999) J. Immunol. 163, 6876–6883
8. Kim, I. K., Moon, S. O., Kim, S. H., Kim, J. H., Koh, Y. S., and Koh, G. Y. (2001) J. Biol. Chem. 276, 7614–7620
9. Teixeira, M. M., Wells, T. N., Lukacs, N. W., Proudfoot, A. E., Kunelk, S. L., Williams, T. J., and Hell ovalbumin-challenged mice and that this increased expression is abolished by pretreatment with selenite. These data thus suggest that the transcription of the genes for these cell adhesion molecules in lung endothelium is controlled by NF-κB and that inhibition of NF-κB activation by selenite blocks their expression as well as the consequent recruitment of eosinophils to the lung airway.

References: 1. Feghali, C. A., and Wright, T. M. (1997) Front. Biosci. 2, 12–26 2. Hart, L., Lim, S., Adcock, I., Barnes, P. J., and Chung, K. F. (2000) Am. J. Respir. Crit. Care Med. 161, 224–231 3. Tomkinson, A., Dues, C., Cieslewicz, G., Pratt, J. C., Joetham, A., Shanafelt, M. C., Gundel, R., and Gelfand, E. W. (2001) J. Immunol. 166, 5792–5800 4. Kanehira, A., Kremura, T., Makena, M. J., Lahn, M., Joetham, A., Shanafelt, M. C., Gundel, R., and Gelfand, E. W. (2001) Am. J. Respir. Crit. Care Med. 163, 173–184 5. Webb, D. C., McKenzie, A. N., Matthaei, K. I., Rothenberg, M. E., and Foster, P. S. (2001) Immunol. Cell Biol. 79, 165–169 6. Oitzinger, W., Hofer-Warihne, K., Schmid, J. A., Koshelnik, Y., Binder, B. R., and de Martin, R. (2001) Blood 97, 1611–1617 7. Matsukura, S., Stellato, C., Pitt, J. R., Bickel, C., Miura, K., Georas, S. N., Casaloro, V., and Schleimer, R. P. (1999) J. Immunol. 163, 6876–6883 8. Kim, I. K., Moon, S. O., Kim, S. H., Kim, J. H., Koh, Y. S., and Koh, G. Y. (2001) J. Biol. Chem. 276, 7614–7620 9. Teixeira, M. M., Wells, T. N., Lukacs, N. W., Proudfoot, A. E., Kunelk, S. L., Williams, T. J., and Hell ovalbumin-challenged mice and that this increased expression is abolished by pretreatment with selenite. These data thus suggest that the transcription of the genes for these cell adhesion molecules in lung endothelium is controlled by NF-κB and that inhibition of NF-κB activation by selenite blocks their expression as well as the consequent recruitment of eosinophils to the lung airway.

References: 1. Feghali, C. A., and Wright, T. M. (1997) Front. Biosci. 2, 12–26 2. Hart, L., Lim, S., Adcock, I., Barnes, P. J., and Chung, K. F. (2000) Am. J. Respir. Crit. Care Med. 161, 224–231 3. Tomkinson, A., Dues, C., Cieslewicz, G., Pratt, J. C., Joetham, A., Shanafelt, M. C., Gundel, R., and Gelfand, E. W. (2001) J. Immunol. 166, 5792–5800 4. Kanehira, A., Kremura, T., Makena, M. J., Lahn, M., Joetham, A., Shanafelt, M. C., Gundel, R., and Gelfand, E. W. (2001) Am. J. Respir. Crit. Care Med. 163, 173–184 5. Webb, D. C., McKenzie, A. N., Matthaei, K. I., Rothenberg, M. E., and Foster, P. S. (2001) Immunol. Cell Biol. 79, 165–169 6. Oitzinger, W., Hofer-Warihne, K., Schmid, J. A., Koshelnik, Y., Binder, B. R., and de Martin, R. (2001) Blood 97, 1611–1617
Protection of Mice from Allergen-induced Asthma by Selenite: PREVENTION OF EOSINOPHIL INFILTRATION BY INHIBITION OF NF-κB ACTIVATION

Dae-won Jeong, Min-Hyuk Yoo, Tae Soo Kim, Jae-Hong Kim and Ick Young Kim

J. Biol. Chem. 2002, 277:17871-17876.
doi: 10.1074/jbc.M200808200 originally published online March 15, 2002

Access the most updated version of this article at doi: 10.1074/jbc.M200808200

Alerts:
• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 56 references, 18 of which can be accessed free at
http://www.jbc.org/content/277/20/17871.full.html#ref-list-1