ELSEVIER

European Journal of Pharmacology 418 (2001) 23–28

ejp

www.elsevier.nl/locate/ejphar

Expression of 74-kDa histidine decarboxylase protein in a macrophage-like cell line RAW 264.7 and inhibition by dexamethasone

Noriyasu Hirasawa*, Akira Murakami, Kazuo Ohuchi

Laboratory of Pathophysiological Biochemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba Aramaki, Aoba, Sendai, Miyagi 980-8578, Japan

Received 14 December 2000; received in revised form 20 March 2001; accepted 23 March 2001

Abstract

Stimulation of RAW 264.7 cells with the Ca^{2+}-ATPase inhibitor thapsigargin increased histamine production. Immunoblot analyses revealed that thapsigargin increased the expression of 74-kDa histidine decarboxylase protein although rat mast cell line RBL-2H3 cells express both 74- and 53-kDa histidine decarboxylase proteins. The inhibition of histamine production by the mitogen-activated protein kinase-extracellular signal-regulated kinase kinase (MEK) inhibitors PD98059 (2′-amino-3′-methoxyflavone) and U0126 (1,4-diamino-2,3-dicyano-1,4-bis(2-aminophenylthio)butadiene) and by the p38 mitogen-activated protein (MAP) kinase inhibitor SB203580 (4-(4-fluorophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)1*H*-imidazole) was correlated with the inhibition of the expression of thapsigargin-induced 74-kDa histidine decarboxylase protein. The synthetic glucocorticoid dexamethasone inhibited thapsigargin-induced histamine production and 74-kDa histidine decarboxylase protein expression. The thapsigargin-induced activation of p42/p44 MAP kinase and p38 MAP kinase was also inhibited by dexamethasone. These findings indicate that the induction of histamine production by thapsigargin in RAW 264.7 cells is due to the increased expression of 74-kDa histidine decarboxylase protein and that dexamethasone inhibits thapsigargin-induced histidine decarboxylase protein expression and histamine production via inhibition of MAP kinase activation.

Keywords: Histidine decarboxylase; Dexamethasone; MAP (mitogen-activated protein) kinase; RAW 264.7 cell

1. Introduction

Histamine is produced by mast cells, basophils, macrophages (Takamatsu et al., 1996; Shiraishi et al., 2000a), neutrophils (Shiraishi et al., 2000b) and lymphocytes (Aoi et al., 1989). Mast cells and basophils constitutively express histidine decarboxylase of 74 and 53 kDa molecular masses (Tanaka et al., 1998) and store the produced histamine in their granules. Other types of cells produce histamine in response to various stimulants and release it piecemeal. The constitutive secretion of histamine is observed in rapidly growing tissues such as bone marrow, granulation tissues and tumor (Kahlson and Rosengren, 1968), and the released histamine plays multiple roles in inflammatory and immune responses (Beer et al., 1984). However, the regulation mechanism of histamine production by non-mast cells has not been fully clarified.

We found that the stimulation of murine macrophage-like cell line RAW 264.7 cells with thapsigargin, a Ca^{2+}-ATPase inhibitor, induces histidine decarboxylase mRNA expression and histamine production (Shiraishi et al., 2000a). Pharmacological analyses indicated that thapsigargin-induced histamine production is regulated mainly by p42/p44 mitogen-activated protein (MAP) kinase and partly by p38 MAP kinase (Shiraishi et al., 2000a). However, the precise regulation of histidine decarboxylase activity in RAW 264.7 cells remains to be elucidated.

In an air pouch-type allergic inflammation model in rats, we demonstrated that the steroidal anti-inflammatory drug dexamethasone inhibits histamine production in the late phase (Hirasawa et al., 1990). Because dexamethasone does not inhibit antigen-induced histamine release from subcutaneous mast cells in the anaphylaxis phase (Ohuchi et al., 1985), dexamethasone might have an inhibitory action on histamine production by non-mast cells such as macrophages. In the present study, to get further insight into the regulation mechanism for histamine production in macrophages, we analyzed the changes in 74- and 53-kDa histidine decarboxylase protein levels and the effects of

* Corresponding author. Tel.: +81-22-217-6861; fax: +81-22-217-6863.

E-mail address: hirasawa@mail.pharm.tohoku.ac.jp (N. Hirasawa).

0014-2999/01/$ - see front matter © 2001 Published by Elsevier Science B.V.
PII: S0014-2999(01)00931-1

dexamethasone on thapsigargin-induced histamine production in RAW 264.7 cells.

2. Materials and methods

2.1. Cell culture

RAW 264.7 cells obtained from the Riken Cell Bank (Tsukuba, Japan) were used. The cells were suspended at 5×10^5 cells/ml in Eagle's minimum essential medium (EMEM) containing 10% (v/v) heat-inactivated fetal bovine serum (EMEM (+)). One milliliter of the cell suspension was seeded in each well of 12-well plastic tissue culture plates (Costar, Cambridge, MA, USA) and incubated for 20 h at 37°C in an atmosphere of 5% CO_2–95% air. After three washes with EMEM, the cells were incubated for the periods indicated at 37°C in 1 ml of EMEM (+) containing drugs.

2.2. Drug treatments

The drugs used were thapsigargin (Wako, Osaka, Japan), the MAP kinase-extracellular signal-regulated kinase kinase 1 (MEK 1) inhibitor PD98059 (2′-amino-3′-methoxyflavone, New England Biolabs, Beverly, MA, USA) and U0126 (1,4-diamino-2,3-dicyano-1,4-bis(2-aminophenylthio)butadiene, Calbiochem-Novabiochem, San Diego, CA, USA), and the p38 MAP kinase inhibitor SB203580 (4-(4-Fluorophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)1*H*-imidazole, Calbiochem-Novabiochem).

The cells were preincubated at 37°C in EMEM (+) containing PD98059, U0126 or SB203580 for 1 h or dexamethasone for 24 h, then further incubated at 37°C in EMEM (+) containing thapsigargin (20 nM) in the presence of drugs for the period indicated.

2.3. Determination of histamine contents

After incubation, the conditioned medium was collected and centrifuged at $220 \times g$ and 4°C for 3 min. Histamine contents in the supernatant fraction of the conditioned medium were determined fluorometrically as described by Shore et al. (1959).

2.4. Immunoblot analysis

Two-milliliter aliquots of the cell suspension (1.5×10^6 cells/ml) were seeded into plastic dishes (35-mm diameter, Corning, Grand Island, NY, USA) and incubated for 24 h at 37°C. After three washes with EMEM, the cells were further incubated for the period indicated at 37°C in 2 ml of EMEM (+) containing the indicated concentrations of drugs. After incubation, the cells were washed with ice-cold phosphate-buffered saline (pH 7.4) and lysed in 150 μl of ice-cold lysis buffer (20 mM HEPES, pH 7.3, 1% (v/v) Triton X-100, 1 mM EDTA, 50 mM NaF, 2.5 mM *p*-nitrophenylphosphate, 1 mM Na_3VO_4, 10 μg/ml leupeptin and 10% (v/v) glycerol). The cell lysates were centrifuged at $14{,}000 \times g$ and 4°C for 20 min, and 120 μl of the supernatant fractions was obtained. Proteins in the cell lysates were separated by sodium dodecyl sulfate-

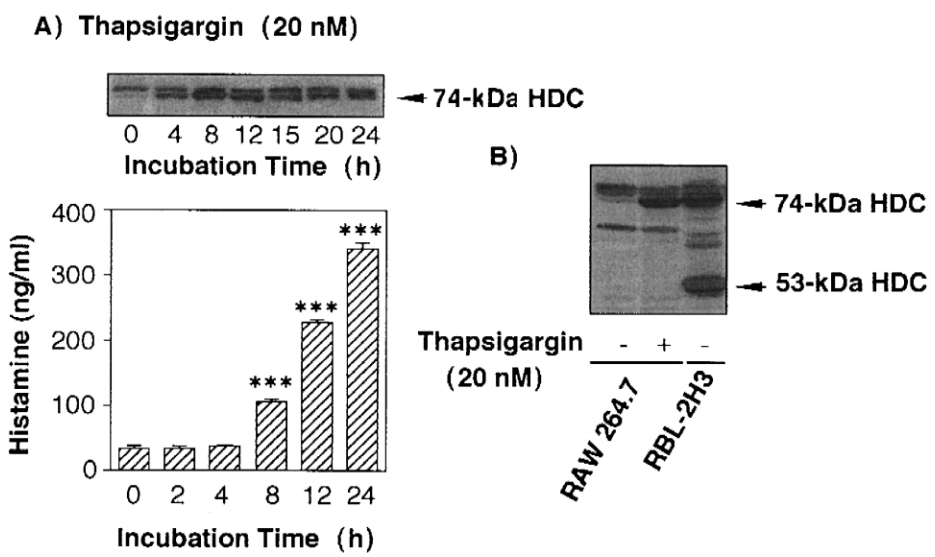

Fig. 1. Expression of 74-kDa histidine decarboxylase protein and histamine production in thapsigargin-stimulated RAW 264.7 cells. (A) RAW 264.7 cells (5×10^5 cells) were incubated for the period indicated in EMEM (+) in the presence of thapsigargin (20 nM). Histidine decarboxylase protein levels in the cells and the histamine content of the conditioned medium were determined. Vertical bars indicate S.E.M. of four samples. Statistical significance: $^{***}P < 0.001$ vs. time 0. (B) Histidine decarboxylase proteins in unstimulated and thapsigargin-stimulated (12 h) RAW 264.7 cells (1×10^5 cells) and in unstimulated RBL-2H3 cells (1×10^5 cells) were detected by immunoblotting. Histidine decarboxylases (74 and 53 kDa) are indicated by arrows. The band above 74-kDa histidine decarboxylase is a non-specific band.

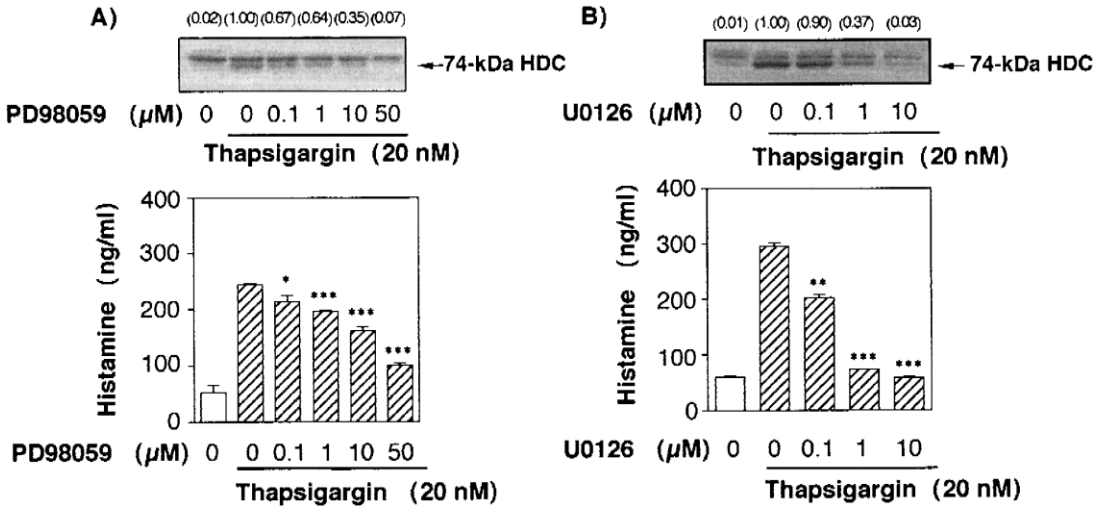

Fig. 2. Effects of the MEK inhibitors on the thapsigargin-induced expression of histidine decarboxylase protein and histamine production. RAW 264.7 cells (5×10^5 cells) were pretreated for 1 h with PD98059 (A) or U0126 (B) at the indicated concentrations, and incubated for 12 h in the presence of thapsigargin (20 nM) and the corresponding concentrations of the inhibitors. The levels of histidine decarboxylase protein in the cells and the histamine content of the conditioned medium 12 h after stimulation were determined. Vertical bars indicate S.E.M. of four samples. Statistical significance: $^{*}P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$ vs. the thapsigargin-stimulated control. Numbers in parentheses indicate the relative density of 74-kDa histidine decarboxylase protein as determined by densitometric analysis. The value of the thapsigargin-stimulated control is set to 1.0.

polyacrylamide gel electrophoresis and immunoblotted by using the rabbit polyclonal antibodies to rat histidine decarboxylase (Euro-diagnostica, Malmo, Sweden), phospho-p44/p42 MAP kinase (Thr^{202}/Tyr^{204}) (New England Biolabs), phospho-specific p38 MAP kinase (Thr^{180}/Tyr^{182}) (New England Biolabs), rat MAP kinase R2 (Erk1-CT) (Upstate Biotechnology, Lake Placid, NY, USA), or p38 (C-20) (Santa Cruz Biotechnology, Santa Cruz, CA, USA). The recognized proteins were visualized by using a chemiluminescence detection system or an alkaline phosphatase reaction using nitroblue tetrazolium/5-bromo-4-chloro-3-indolyl-phosphate solution (Promega, Madison, WI, USA) as a substrate. Histidine decarboxylase protein from RBL-2H3 cells, a rat mast cell line (Japanese Cancer Research Resources Bank, Osaka, Japan), was also immunoblotted.

2.5. Statistical analysis

The statistical significance of the results was analyzed by Dunnett's test for multiple comparisons and Student's *t*-test for unpaired observations. The results were confirmed in at least three independent experiments.

3. Results

3.1. Induction of 74-kDa histidine decarboxylase protein by thapsigargin in RAW 264.7 cells

RAW 264.7 cells were incubated in medium containing thapsigargin (20 nM) for the periods indicated, and histidine decarboxylase protein in the cell lysates and histamine levels in the conditioned medium were determined. As shown in Fig. 1A, the level of 74-kDa histidine decarboxylase protein was very low before stimulation, but increased from 4 h with a maximum at 8 h after thapsigargin stimulation, which was followed by an increase in the histamine level in the conditioned medium. The increment of histamine content in the conditioned medium from 8 to 12 h was almost the same with that from 12 to 24 h

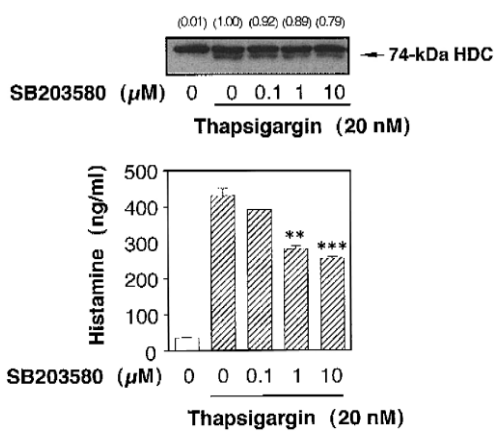

Fig. 3. Effects of the p38 MAP kinase inhibitor SB203580 on the thapsigargin-induced expression of 74-kDa histidine decarboxylase protein and histamine production. RAW 264.7 cells (5×10^5 cells) were pretreated for 1 h with SB203580 at the indicated concentrations, and incubated for 12 h in the presence of thapsigargin (20 nM) and corresponding concentrations of SB203580. The levels of histidine decarboxylase protein in the cells and the histamine content of the conditioned medium 12 h after stimulation were determined. Vertical bars indicate S.E.M. of four samples. Statistical significance: $^{**}P < 0.01$, and $^{***}P < 0.001$ vs. the thapsigargin-stimulated control. Numbers in parentheses indicate the relative density of 74-kDa histidine decarboxylase protein as determined by densitometric analysis. The value of thapsigargin-stimulated control was set to 1.0.

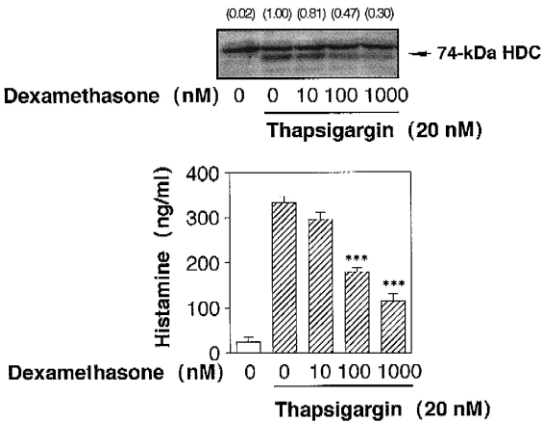

Fig. 4. Effects of dexamethasone on the thapsigargin-induced expression of histidine decarboxylase protein and histamine production. RAW 264.7 cells (5×10^5 cells) were treated for 24 h with dexamethasone at the indicated concentrations, and incubated for 12 h in EMEM (+) in the presence or absence of thapsigargin (20 nM) and corresponding concentrations of dexamethasone. The levels of histidine decarboxylase protein in the cells and the histamine content of the conditioned medium 12 h after the stimulation were determined. Vertical bars indicate S.E.M. of four samples. Statistical significance: $^{**}P < 0.01$, and $^{***}P < 0.001$ vs. the thapsigargin-stimulated control. Numbers in parentheses indicate the relative density of 74-kDa histidine decarboxylase protein as determined by densitometric analysis. The value of thapsigargin-stimulated control was set to 1.0.

indicating that the histamine-producing rate in the former period was higher than that in the latter period. Although 74- and 53-kDa histidine decarboxylase proteins were detected in unstimulated RBL-2H3 cells, a mast cell line, 53-kDa histidine decarboxylase protein was not detected in thapsigargin-stimulated RAW 264.7 cells (Fig. 1B).

3.2. Effects of the MEK inhibitors PD98059 and U0126 and the p38 MAP kinase inhibitor SB203580 on thapsigargin-induced histidine decarboxylase protein expression and histamine production

To clarify the roles of p42/p44 MAP kinase and p38 MAP kinase in the thapsigargin (20 nM)-induced expression of 74-kDa histidine decarboxylase protein and histamine production, the effects of MEK inhibitors and p38 MAP kinase inhibitors were examined. Both PD98059 and U0126, inhibitors of MEK, inhibited 74-kDa histidine decarboxylase protein expression and histamine production in a concentration-dependent manner (Fig. 2). In addition, the p38 MAP kinase inhibitor SB203580 reduced partially but significantly thapsigargin-induced histidine decarboxylase protein expression and histamine production (Fig. 3).

3.3. Inhibition by dexamethasone of thapsigargin-induced histidine decarboxylase protein expression and histamine production

RAW 264.7 cells were pretreated for 24 h with dexamethasone at the concentrations indicated, and stimulated by thapsigargin (20 nM) for 12 h in the presence of dexamethasone. The thapsigargin-induced expression of 74-kDa histidine decarboxylase protein and histamine pro-

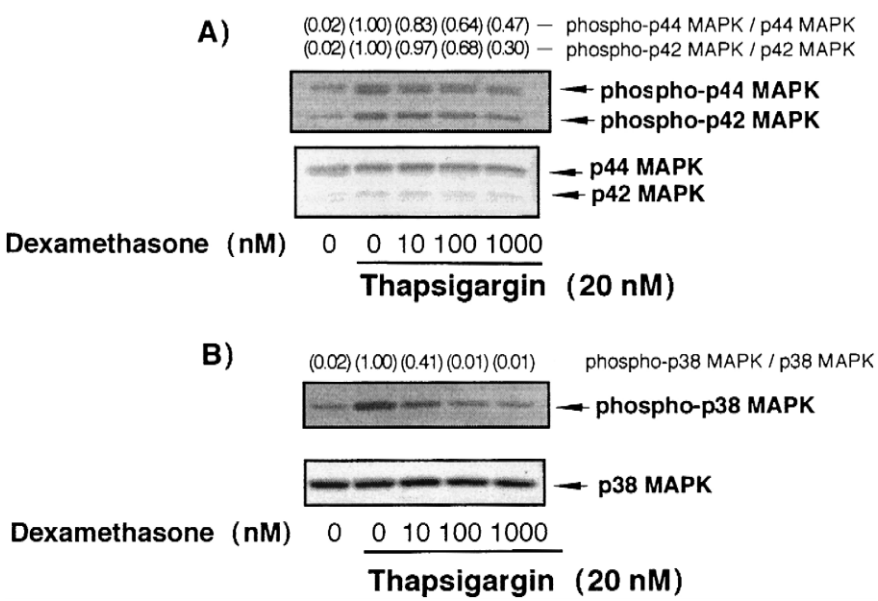

Fig. 5. Inhibition by dexamethasone of the thapsigargin-induced activation of p42/p44 MAP kinase and p38 MAP kinase. RAW 264.7 cells (5×10^5 cells) were treated for 24 h with dexamethasone at the indicated concentrations, and further incubated for 1 h in EMEM (+) in the presence or absence of thapsigargin (20 nM) and corresponding concentrations of dexamethasone. The phosphorylation of p42/p44 MAP kinase (A) and p38 MAP kinase (B) was determined by immunoblotting. Numbers in parentheses indicate the fold increase in phospho-MAP kinases as determined by densitometric analysis. The value of thapsigargin-stimulated control was set to 1.0.

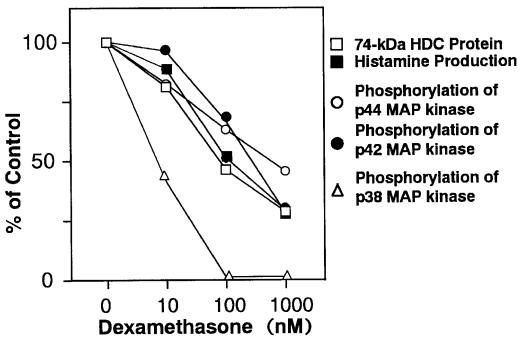

Fig. 6. Summary of the inhibitory effects of dexamethasone on thapsigargin-induced responses. The effects of dexamethasone on the phosphorylation of p42/p44 MAP kinase and p38 MAP kinase shown in Fig. 5 were compared with those for histamine production and 74-kDa histidine decarboxylase protein levels shown in Fig. 4. The control values obtained by 0 nM dexamethasone are expressed as 100%.

duction were reduced by dexamethasone in a concentration-dependent manner (Fig. 4). When the cells were stimulated by thapsigargin without dexamethasone pretreatment, histamine production was not inhibited (data not shown).

3.4. Inhibition of thapsigargin-induced activation of p42/p44 MAP kinase and p38 MAP kinase by dexamethasone

To clarify the mechanism by which dexamethasone inhibits histamine production, the effects of dexamethasone on the thapsigargin-induced activation of MAP kinases were determined. As shown in Fig. 5, dexamethasone inhibited the thapsigargin-induced phosphorylation of p42/p44 MAP kinase and p38 MAP kinase in a concentration-dependent manner. As summarized in Fig. 6, the thapsigargin-induced histamine production and 74-kDa histidine decarboxylase protein levels were decreased by dexamethasone in parallel with the decrease in the phosphorylation of p42/p44 MAP kinase.

4. Discussion

The present study shows that thapsigargin-induced histamine production in RAW 264.7 cells is regulated by the expression of 74-kDa histidine decarboxylase protein and that dexamethasone inhibits the thapsigargin-induced expression of histidine decarboxylase protein and histamine production via inhibition of the activation of MAP kinases. The present report is the first to describe the correlation between the expression of 74-kDa histidine decarboxylase protein and histamine production in macrophages.

In mast cells such as RBL-2H3 cells, 74-kDa histidine decarboxylase protein is localized in the cytosol and is converted to the 53-kDa form in the luminal area of the endoplasmic reticulum (Tanaka et al., 1998). Although 74-kDa histidine decarboxylase protein is degraded rapidly, 53-kDa histidine decarboxylase protein is stable and forms homodimers. Since 53-kDa histidine decarboxylase protein shows a higher activity than 74-kDa histidine decarboxylase, processing of the 74-kDa form to the 53-kDa form is considered to be one of the activation mechanisms of histidine decarboxylase in mast cells (Tanaka et al., 1998). However, in RAW 264.7 cells, 53-kDa histidine decarboxylase protein was not detected even after stimulation with thapsigargin (Fig. 1). The level of 74-kDa histidine decarboxylase protein in unstimulated RAW 264.7 cells was very low but markedly increased by stimulation with thapsigargin (Fig. 1), and the change of histamine-producing rate was correlated with 74-kDa histidine decarboxylase protein levels in the cells. In addition, the correlation of 74-kDa histidine decarboxylase protein level and histamine production was confirmed by using the MEK inhibitors PD98059 and U0126 and the p38 MAP kinase inhibitor SB203580, which inhibit thapsigargin-induced histamine production and histidine decarboxylase mRNA expression (Shiraishi et al., 2000a). PD98059 and U0126, in concentrations that inhibit the phosphorylation of p42/p44 MAP kinase (Shiraishi et al., 2000a), inhibited the increase in 74-kDa histidine decarboxylase protein (Fig. 2). In addition, the inhibitor of p38 MAP kinase SB203580 partially reduced histidine decarboxylase protein expression, to an extent similar to that for inhibition of histamine production (Fig. 3). These results indicate that histamine production in thapsigargin-stimulated RAW 264.7 cells is regulated by the expression of 74-kDa histidine decarboxylase protein and is independent of its processing to 53-kDa histidine decarboxylase protein.

In the present study, we also found that dexamethasone inhibited thapsigargin-induced histamine production. As shown in Figs. 4 and 6, the inhibition by dexamethasone was correlated with the decrease in 74-kDa histidine decarboxylase protein, indicating that dexamethasone inhibits histamine production through inhibition of thapsigargin-induced histidine decarboxylase expression. Consistent with our previous report that dexamethasone inhibits antigen-induced activation of p42/p44 MAP kinase (Rider et al., 1996) and c-Jun N-terminal kinase (Hirasawa et al., 1998) in mast cells, dexamethasone inhibited thapsigargin-induced activation of p42/p44 MAP kinase and p38 MAP kinase in RAW 264.7 cells (Fig. 5). Although the thapsigargin-induced p38 MAP kinase activation was more prominently inhibited by dexamethasone than the thapsigargin-induced p42/p44 MAP kinase activation (Figs. 5 and 6), the inhibition by dexamethasone of histamine production was in parallel with the inhibition of the activation of p42/p44 MAP kinase but not with that of p38 MAP kinase (Fig. 6). These results suggest that the expression of histidine decarboxylase is mainly regulated by p42/p44 MAP kinase and only weakly by p38 MAP kinase. This conclusion is consistent with the finding that thapsigargin-induced histamine production was prominently inhibited by PD98059 and U0126 (Fig. 2), and partially inhibited by SB203580 (Fig. 3).

It is well known that dexamethasone suppresses the expression of cytokines, probably due to a direct interaction with transcriptional factors such as AP-1 (Jonat et al., 1990; Schule et al., 1990; Yang-Yen et al., 1990). In contrast, we reported that dexamethasone inhibited arachidonic acid release in antigen-stimulated mast cells via inhibition of the activation of p42/p44 MAP kinase (Rider et al., 1996). Therefore, the thapsigargin-induced expression of histidine decarboxylase protein in RAW 254.7 cells is another response that is inhibited by dexamethasone through inhibition of the activation of MAP kinases. Concentrations of dexamethasone required for the inhibition of thapsigargin-induced activation of p42/p44 MAP kinase in RAW 264.7 cells are higher than those required for the inhibition of antigen- and thapsigargin-induced activation of p42/p44 MAP kinase in RBL-2H3 cells (Rider et al., 1996). The difference in the concentration of dexamethasone required for inhibitory activity among the two types of cells might be due to differences in the sensitivity of the cells to glucocorticoids. The mechanisms by which dexamethasone inhibits p42/p44 MAP kinase and p38 MAP kinase and which cause the differences in cell sensitivity to glucocorticoids are under investigation.

Macrophages produce prostaglandins and cytokines that contribute to acute and chronic inflammation. Although the roles of histamine produced by macrophages are still undefined, histamine released continuously is involved in leukocyte differentiation (Schneider et al., 1990), rapid tissue growth (Kahlson and Rosengren, 1968) and immune responses (Beer et al., 1984). Therefore, the inhibition of histamine production by macrophages might be a novel mechanism by which dexamethasone regulates inflammation and immune responses.

Acknowledgements

This work was supported in part by a Grant-in-Aid for General Scientific Research (11470481) from the Ministry of Education, Science, Sports and Culture of Japan and by Nishinomiya Basic Research Fund (Japan).

References

Aoi, R., Nakashima, I., Kitamura, Y., Asai, H., Nakano, K., 1989. Histamine synthesis by mouse T lymphocytes through induced histidine decarboxylase. Immunology 66, 219–223.

Beer, D.J., Matloff, S.M., Rocklin, R.E., 1984. The influence of histamine on immune and inflammatory responses. Adv. Immunol. 35, 209–268.

Hirasawa, N., Funaba, Y., Hirano, Y., Kawarasaki, K., Omata, M., Watanabe, M., Mue, S., Tsurufuji, S., Ohuchi, K., 1990. Inhibition by dexamethasone of histamine production in allergic inflammation in rats. J. Immunol. 145, 3041–3046.

Hirasawa, N., Sato, Y., Fujita, Y., Mue, S., Ohuchi, K., 1998. Inhibition by dexamethasone of antigen-induced c-Jun N-terminal kinase activation in rat basophilic leukemia cells. J. Immunol. 161, 4939–4943.

Jonat, C., Rahmsdorf, H.J., Park, K.-K., Cato, A.C.B., Gebel, S., Ponta, H., Herrlich, P., 1990. Antitumor promotion and antiinflammation: down-modulation of AP-1 (Fos/Jun) activity by glucocorticoid hormone. Cell 62, 1189–1204.

Kahlson, G., Rosengren, E., 1968. New approaches to the physiology of histamine. Physiol. Rev. 48, 155–196.

Ohuchi, K., Hirasawa, N., Watanabe, M., Tsurufuji, S., 1985. Pharmacological analysis of the vascular permeability response in the anaphylactic phase of allergic inflammation. Eur. J. Pharmacol. 117, 337–345.

Rider, L.G., Hirasawa, N., Santini, F., Beaven, M.A., 1996. Activation of the mitogen-activated protein kinase cascade is suppressed by low concentrations of dexamethasone in mast cells. J. Immunol. 157, 2374–2380.

Schneider, E., Piquet-Pellorce, C., Dy, M., 1990. New role for histamine in interleukin-3-induced proliferation of hematopoietic stem cells. J. Cell. Physiol. 143, 337–343.

Schule, R., Rangarajan, P., Kliewer, S., Ransone, L.J., Bolado, J., Yang, N., Verma, I.M., Evans, R.M., 1990. Functional antagonism between oncoprotein c-*jun* and the glucocorticoid receptor. Cell 62, 1217–1226.

Shiraishi, M., Hirasawa, N., Kobayashi, Y., Oikawa, S., Murakami, A., Ohuchi, K., 2000a. Participation of mitogen-activated protein kinase in thapsigargin- and TPA-induced histamine production in murine macrophage RAW 264.7 cells. Br. J. Pharmacol. 129, 515–524.

Shiraishi, M., Hirasawa, N., Oikawa, S., Kobayashi, Y., Ohuchi, K., 2000b. Analysis of histamine-producing cells at the late phase of allergic inflammation in rats. Immunology 99, 600–606.

Shore, P.A., Burkhalter, A., Cohn, V.H., 1959. A method for the fluorometric assay of histamine in tissues. J. Pharmacol. Exp. Ther. 127, 182–186.

Takamatsu, S., Nakashima, I., Nakano, K., 1996. Modulation of endotoxin-induced histamine synthesis by cytokine in mouse bone marrow-derived macrophages. J. Immunol. 156, 778–785.

Tanaka, S., Nemoto, K., Yamamura, E., Ichikawa, A., 1998. Intracellular localization of the 74- and 53-kDa forms of L-histidine decarboxylase in a rat basophilic/mast cell line, RBL-2H3. J. Biol. Chem. 273, 8177–8182.

Yang-Yen, H.-F., Chambard, J.-C., Sun, Y.-L., Smeal, T., Schmidt, T.J., Drouin, J., Karin, M., 1990. Transcriptional interference between c-Jun and the glucocorticoid receptor: mutual inhibition of DNA binding due to direct protein–protein interaction. Cell 62, 1205–1215.