Intracellular Localization of the 74- and 53-kDa Forms of L-Histidine Decarboxylase in a Rat Basophilic/Mast Cell Line, RBL-2H3*

(Received for publication, November 19, 1997, and in revised form, January 12, 1998)

Satoshi Tanaka, Ken-ichi Nemoto, Eriko Yamamura, and Atsushi Ichikawa‡

From the Department of Physiological Chemistry, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, Japan

To clarify the process of post-translational modification of L-histidine decarboxylase (HDC), we investigated the conversion of the 74-kDa form of HDC into the 53-kDa form in specialized organella of a rat basophilic/mast cell line (RBL-2H3). With treatment of streptolysin-O, RBL-2H3 cells released approximately 40% of HDC activity accompanied by over 90% of lactate dehydrogenase activity. Only the 74-kDa form of HDC was detected in the leaked fraction by SDS-polyacrylamide gel electrophoresis. The 74-kDa form in the homogenate of pulse-labeled cells was recovered in both the supernatant and particulate fractions, while the 53-kDa form was detected only in the particulate fraction containing marker proteins of microsomes, Golgi, and lysosomal granules. Confocal microscopic observation using double staining immunofluorescence with anti-GST fusion HDC antiserum showed that most of the HDC coexists with protein-disulfide isomerase, a typical marker of the luminal space of the ER. With treatment of digitonin, RBL-2H3 cells released only 74-kDa HDC. Trypsin digestion of digitonin-permeabilized cells resulted in the disappearance of the 74-kDa form but not the 53-kDa form. From these results, it is assumed that the 74-kDa form of HDC, synthesized in the cytosol, is translocated into the lumen of the ER, where it is converted to the 53-kDa form.

L-Histidine decarboxylase (HDC); EC 4.1.1.22 catalyzes decarboxylation of L-histidine to histamine. It is the only enzyme that forms histamine in mammals. Histamine is well known to act as an important physiological modulator (1–12). HDCs have been purified from the soluble fraction of various tissues and found to be a dimer consisting of two identical 53-kDa subunits (13–16), while the size of CDNA- deduced HDC is around 74 kDa (17–19). The recombinant 74-kDa form expressed in the particulate fraction of Sf9 cells had a low activity, while the recombinant 54-kDa form that lacks the C-terminal region of the 74-kDa form had a full activity (20, 21). Furthermore, the particulate recombinant 74-kDa form was converted into soluble 53-kDa form with a high catalytic activity by porcine pancreatic elastase in vitro (22). These results suggest that the translated HDC is post-translationally processed to active mature form. Very recently, we have shown the existence of the converting enzyme-like activity in the extract of mouse tissues (23). Like the role of post-translational processing of proteins, the intracellular translocation of proteins is known. However, the intracellular localization of HDC remains to be clarified. In addition to the soluble form of HDC, membrane-associated HDC activity has been reported in various tissues, such as rat hypothalamus (24) and rat brain (25–28). However, these reports did not refer to the molecular size of the membranous HDC. The aim of this study was to investigate the conversion of the 74-kDa form into the 53-kDa form in specialized organella of rat basophilic/mast (RBL-2H3) cells.

EXPERIMENTAL PROCEDURES

Materials—Anti-NADPH-cytochrome P-450 reductase (anti-FP2) antiserum was the generous gift of Dr. R. Masaki (Kansai Medical University, Osaka, Japan). Anti-GST fusion HDC antiserum was prepared as described previously (29). The following materials were purchased from the sources indicated: Amberlite CG-50 (Type 1, 200–400 mesh) from Rohm and Haas (Philadelphia, PA); leupeptin, aprotinin, and digitonin from Wako Pure Chemicals (Tokyo, Japan); polyvinylidene difluoride membranes from Millipore Corp. (Tokyo, Japan); fluorescein isothiocyanate-conjugated anti-rabbit goat IgG antibody and rhodamine-conjugated anti-mouse goat IgG antibody from Leinco Technologies, Inc. (St. Louis, MO); biotinylated anti-mouse IgG antibody and ABC kit from Vector Laboratories (Burlingame, CA); anti-protein-disulfide isomerase antibody from Stress Gen Biotechnologies Corp. (Victoria, Canada); anti-mannosidase II antibody from Babco (Richmond, CA); [35S]methionine (1000 Ci/mmol) from NEN Life Science Products; and streptolysin-O, Protein A-Sepharose CL-4B, and Percoll from Amersham Pharmacia Biotech. All other chemicals were commercial products of reagent grade.

Cell Culture—RBL-2H3 cells were grown in RPMI 1640 medium supplemented with 10% fetal calf serum (complete medium) in 5% CO2 at 37 °C in a fully humidified atmosphere. Exponentially growing cells were used in all experiments.

Biosynthetic Labeling—Cells were starved for 30 min in methionine-free RPMI 1640 medium supplemented with 10% dialyzed fetal calf serum and then pulse-labeled with [35S]methionine (10 μCi/ml) for designated periods. In chase experiments after pulse labeling, cells were rinsed in the complete medium once and incubated for appropriate periods.

Immunoprecipitation—[35S]Methionine-labeled cells were harvested and washed in PBS twice. The cell pellet was suspended in 1 ml of RIPA buffer (30 mM HEPES-NaOH, pH 7.3, containing 150 mM sodium chloride, 1% Triton X-100, 1% deoxycholate and 0.1% SDS) and homogenized by sonication. A 50-μl aliquot of the supernatant was centrifuged at 8,000 × g for 5 min at 4 °C. Anti-GST fusion HDC antiserum was added (1:200), and then the mixture was incubated for 4 h at 4 °C. After centrifugation at 10,000 × g for 10 min at 4 °C, the resulting supernatant was centrifuged at 8,000 × g for 5 min at 4 °C.

This paper is available on line at http://www.jbc.org
min at 4 °C, and the resulting precipitate was washed five times with 1 ml of RIPA buffer. The pellet was resuspended in an equal volume of 2× SDS-sample buffer (125 mM Tris-HCl, pH 6.8, containing 4% SDS, 10% 2-mercaptoethanol, 20% glycerol, and 0.1% bromphenol blue) and boiled for 15 min. The sample was subjected to SDS-PAGE according to Laemmli (30). The gel was dried and analyzed with a Fujix BAS 2000 Bio-Imaging Analyzer.

Subcellular Fractionation—Cells (1.5 × 10⁶ cells) were prelabeled with [³⁵S]methionine for 30 min and were harvested and homogenized in 10 ml HEPES-NaOH, pH 7.3, containing 1.5 mM MgCl₂, 10 mM KCl, 0.5 mM dithiothreitol, 1 mM EDTA, 1 mM EGTA, and the mixture of protease inhibitors described above. The homogenate was centrifuged at 10,000 × g for 10 min at 4 °C. The resultant supernatant was re-centrifuged at 100,000 × g for 1 h at 4 °C, and the supernatant fraction was designated as the S1 fraction. In contrast, the precipitate fraction at 10,000 × g was dissolved in buffer H (20 mM HEPES-NaOH, pH 7.3, containing 25% glycerol, 0.5 mM NaCl, 1.5 mM MgCl₂, 1 mM EDTA, 1 mM EGTA, and the mixture of protease inhibitors) and was re-centrifuged at 100,000 × g for 1 h at 4 °C. The resultant supernatant fraction was designated as the S2 fraction, and the precipitate was designated as the P1 fraction. The fraction precipitated at 1000 × g for 10 min was dissolved in buffer H and centrifuged at 10,000 × g for 30 min at 4 °C. The supernatant was designated as the S3 fraction, and the precipitate was named the P2 fraction. Each fraction (S1, S2, S3, P1, and P2) was separated and precipitated with anti-GST fusion HDC antiserum and analyzed with SDS-PAGE as described above.

Streptolysin-O Treatment—Cells were treated with 1000 units/ml streptolysin-O (SLO) (preactivated by incubation for 15 min on ice with and analyzed with SDS-PAGE as described above. Separately immunoprecipitated with anti-GST fusion HDC antiserum and was named the P2 fraction. Each fraction (S1, S2, S3, P1, and P2) was separated and precipitated with anti-GST fusion HDC antiserum and analyzed with SDS-PAGE as described above.

Percol Density Gradient Fractionation—Percol density gradient fractionation was performed as described (31) with a minor modification. All steps were performed at 4 °C. Briefly, 5 × 10⁶ cells were resuspended in 1.5 ml of homogenization buffer consisting of 0.34 M sucrose, 10 mM HEPES, pH 7.3, 0.3 mM EDTA, and the mixture of protease inhibitors and homogenized by 40 strokes with a Dounce glass homogenizer (Kontes, Vineland, NJ). Remaining unbroken cells and nuclei were pelleted by centrifugation at 500 × g for 10 min, and the supernatant was layered onto 60% 20% Percoll containing 15 mM HEPES, pH 7.3, 0.25 M sucrose, and the mixture of protease inhibitors on top of 1 ml of saturated sucrose. Centrifugation was performed at 32,000 × g for 60 min, thus creating a density gradient. Fractions were collected 1 ml from the bottom using a peristaltic pump. (Fractions were collected 0.5 ml from the bottom in Fig. 3C.) For the enzyme assay, each fraction was diluted with an equal volume of 15 mM HEPES, pH 7.3, containing 0.2% Triton X-100, incubated for 1 h at 4 °C, and dialyzed against buffer K (10 mM potassium phosphate, pH 7.3, containing 1% pyridoxal-5-phosphate, 0.2 mM dithiothreitol, 2% polyethylene glycol 6000, 2 mM phenylmethlysulfonyl fluoride, and 0.1 mM benzamidine chloride) at 4 °C for 15 h. For immunoprecipitation with anti-GST fusion HDC antiserum, 1 ml of deioned water and 0.5 ml of 5× RIPA buffer were added to each fraction. Then the mixture was incubated for 1 h at 4 °C and centrifuged at 10,000 × g for 15 min at 4 °C. The resulting supernatant was immunoprecipitated with anti-GST fusion HDC antiserum as described above.

Histidine Decarboxylase Assay—Histidine decarboxylase activity was assayed as described previously (13). Briefly, the assay mixture (1 ml) comprised 0.8 μmol of L-histidine, 0.2 μmol of dithiothreitol, 0.01 μmol of pyridoxal-5-phosphate, 10 μg of polyethylene glycol 6000, 100 μmol of potassium phosphate (pH 6.8), and enzyme. The reaction was carried out at 37 °C and was terminated by adding 0.04 ml of 60% perchloric acid. Histamine formed was isolated on a column of Amberlite CG-50 and then measured by the o-phtalaldehyde method (32).

Protein Assay—The protein concentration was determined by the method of Lowry et al. (33) with bovine serum albumin as a standard.

Marker Enzyme Assay—Enzymatic activity of lactate dehydrogenase, NADPH-cytochrome c reductase, and β-hexosaminidase were assayed as described previously (36).

Immunoblot Analysis—SDS-PAGE was performed on slab gels (10%). A protein sample was subjected to SDS-PAGE, and the separated proteins were transferred electrophoretically to a polyvinylidene difluoride membrane in 25 mM Tris base containing 40 mM 6-aminohexanoic acid, 0.02% SDS, and 20% methanol at room temperature for 90 min at 15 V. The membrane was rinsed in Tris-buffered saline (TBS, 20 mM Tris-HCl, pH 7.5, containing 150 mM NaCl) and then preincubated overnight in TBS containing 5% nonfat milk at 4 °C. The membrane was then incubated with anti-FD antibody (1:1000) or anti-mannosidase II antibody (1:1000) in TBS containing 5% nonfat milk for 1 h at 37 °C. The membrane was washed three times with TBS containing 0.05% Tween 20 (TBB5) at room temperature. The membrane was incubated with biotinylated anti-mouse IgG antibody in TBSB for 1 h at room temperature and then stained with an ABC Kit.

Immunofluorescence—Cells were grown to a low density on round cover glasses in 12-well culture dishes under standard conditions. Cells treated with or without SLO were rinsed with PBS and fixed in 100 mM sodium phosphate, pH 7.5, containing 2% paraformaldehyde, 0.1% glutaraldehyde, and 3% sucrose on ice for 30 min. Then they were permeabilized with 100 mM sodium phosphate, pH 7.5, containing 0.5 M sodium chloride, 0.1% Tween 20, and 0.1% Triton X-100 at room temperature for 10 min three times, incubated in PBS containing 0.05% Tween 20 (TBB5) with 2% normal goat serum at room temperature for 30 min, and incubated in TBB5 with anti-GST fusion HDC antibody (1:500) or anti-FD antibody (1:500) and with anti-FD antibody (1:500) at 4 °C overnight. Thereafter, they were once rinsed with 100 mM sodium phosphate, pH 7.5, containing 0.5 M sodium chloride and 0.1% Tween 20 for 5 min and then stained by incubation for 1 h at room temperature with fluorescein isothiocyanate-conjugated goat anti-rabbit IgG antibody (1:200) and rhodamine-conjugated goat anti-mouse IgG antibody (1:150). The stained cells were viewed with a fluorescence microscope, and original photographs were obtained with Ektachrome 400HC film. Digitonin Permeabilization and Trypsinization—Digitonin permeabilization and trypsinization of the cells labeled with [³⁵S]methionine were performed according to Macrì and Adeli (37). Briefly, the cells labeled with [³⁵S]methionine were washed and incubated in CSK buffer (0.3 M sucrose, 0.1 M KCl, 2.5 mM MgCl₂, 1 mM sodium-free EDTA, 10 mM PIPES, pH 6.8) with 100 μg/ml digitonin for 10 min at room temperature or with 1% Triton X-100 for 30 min at 4 °C. Permeabilized cells were once washed in CSK buffer and the soluble fractions obtained by centrifugation at 800 × g were incubated in the presence and absence of trypsin (200 μg/ml) prepared in CSK buffer for 10 min at room temperature. The reaction was stopped by adding 5× RIPA buffer containing the mixture of protease inhibitors (described above), and the reaction mixture was subjected to immunoprecipitation as described above.

RESULTS

Evidence for the Soluble 74-kDa and the Particulate 53-kDa Forms of HDC—In contrast with the expressed recombinant
Intracellular Localization of Histidine Decarboxylase

TABLE I
Leakage of enzymatic activity of HDC upon streptolysin-O treatment

|             | HDC activity |             | LDH activity |
|-------------|--------------|-------------|--------------|
|             | None         | SLO         | None         | SLO         |
|             | pmol/min/10^7 cells | pmol/min/10^7 cells |
| Total       | 64.3 ± 0.376 | 61.5 ± 1.08 | 1.25 ± 0.0808 | 1.50 ± 0.0917 |
| Leakage     | 4.29 ± 0.105 | 25.1 ± 1.39 | 0.111 ± 0.00666 | 1.31 ± 0.0520 |
| Percentage of total | 6.67 ± 0.149% | 40.8 ± 1.56% | 8.88 ± 0.382% | 87.3 ± 2.51% |

Fig. 2. Leakage of the 74-kDa form of HDC on selective permeabilization of plasma membrane with streptolysin-O treatment. Cells (1 x 10^6 cells/lane) were pulsed for 30 min with [35S]methionine and treated with (lanes 3 and 4) or without (lanes 1 and 2) streptolysin-O (1000 units/ml) as described under “Experimental Procedures.” The leaked fraction (lanes 1 and 3) and the cells that were washed once time after the treatment (lanes 2 and 4) were then immunoprecipitated with anti-GST fusion HDC antiserum, respectively. The 74- and 53-kDa forms of HDC are indicated by arrows.

74-kDa HDC in SF9 cells (20), we found that the 74-kDa form of RBL-2H3 cells was largely present in the soluble fraction (Fig. 1A, lane 1). Only a little 74-kDa HDC was found in the 100,000 x g particulate fraction. However, the 53-kDa form was essentially localized in the particulate fraction (lanes 3 and 5).

The content of [35S]methionine-labeled 74-kDa HDC in pulse-labeled cells was abolished within 60 min, while the 53-kDa form appeared within 5 min and gradually increased in the presence of an excess amount of cold methionine. From these results, it was inferred that the 74-kDa form of HDC is immediately interconverted to the 53-kDa form in RBL-2H3 cells (Fig. 1B).

Localization of the 74-kDa HDC in the Cytosol—The molecular form of HDC in the soluble fraction of RBL-2H3 cells was extracted by SLO treatment, which is known to permeabilize plasma membrane selectively (38). The efficiency of the permeabilization was monitored by the amount of leakage of lactate dehydrogenase. Under conditions of approximately 90% leakage of lactate dehydrogenase activity, approximately 40% of HDC activity was discharged from the permeabilized cells when the cells were treated with SLO (Table I). After immunoprecipitation, the molecular sizes of released HDC were determined by SDS-PAGE. As shown in Fig. 2, only the 74-kDa form of HDC was detected in the cytosol of RBL-2H3 cells (lane 3). Although the 53- and 74-kDa forms of HDC resided in SLO-permeabilized cells after the washing (lane 4), the level of 74-kDa HDC remaining in the permeabilized cells was less than that in the control cells without SLO treatment (lane 2 versus lane 4).

Fractionation Study of the 74- and 53-kDa Forms of HDC—To determine the localization of the 74- and 53-kDa forms of HDC, the cells were pulse-labeled for 30 min, homogenized, and then fractionated by Percoll density gradient centrifugation. The immunoprecipitated radioactive HDC in each fraction was analyzed by SDS-PAGE to determine the molecular size. As shown in Fig. 3A, the 74-kDa form was mostly recovered in fractions 7 and 8, which contained more than 90% of the lactate dehydrogenase activity (Fig. 3D), whereas the 53-kDa form was in fraction 6, where microsomal NADPH-cytochrome c reductase activity and both the 55-kDa band of protein disulfide isomerase (PDI) and the 135-kDa band of mannosidase II were detected (Fig. 3D). Fig. 3B shows the result in the cells pulse-labeled over 90 min. The level of the radioactive 53-kDa form in fraction 6 was much higher than that obtained in cells pulse-labeled for 30 min (Fig. 3, A versus B). In addition, in cells pulse-labeled for 90 min, the 53-kDa form appeared in fraction 1 (Fig. 3B), where histamine and HDC activity and β-hexosaminidase activity co-existed (Fig. 3C).

Identification of HDC in the Particulate Fraction of RBL-2H3 Cells—To confirm the localization of HDC in specialized organelles of RBL-2H3 cells, immunofluorescence studies with anti-GST fusion HDC antiserum were performed (Fig. 4). Lane I indicates the staining of the cells fixed before the treatment with 0.1% Triton X-100. Lanes II and III indicate the stainings of cells pretreated with SLO fixed and treated with or without Triton X-100, respectively. With SLO treatment, more than 90% of the cells were found to be permeabilized, as monitored by propidium iodide (5 μg/ml) staining (data not shown). Compared with the whole cell staining pattern (lane I), the cells permeabilized with SLO exhibited no fluorescent signals when treated with anti-GST fusion HDC antiserum or anti-PDI antibody (Fig. 4A, lane II). However, the reticular pattern of signal was observed with anti-FP2 antisera (Fig. 4B, lane II). On the other hand, the cells permeabilized with SLO and then treated with Triton X-100 after fixation, exhibited reticular patterns of staining with either of the antiserum against GST fusion HDC, PDI, or FP2 (Fig. 4, A and B, lane III). These results indicate co-localization of HDC together with PDI and FP2. Furthermore, the fluorescent pattern of the signal of HDC indicates that the membrane topology of HDC is similar to that of PDI but not to that of NADPH-cytochrome P-450 reductase.

The co-localization of HDC and PDI was confirmed with confocal microscopy (Fig. 5).

A Possible Localization of 53-kDa HDC in the Luminal Compartment—The distinct signal pattern in double stainings of HDC with anti-PDI antibody and with anti-FP2 antiserum indicates the possible localization of HDC in the luminal area of the ER. To identify the molecular form of the luminal HDC, digitonin-permeabilized cells were treated with trypsin according to the method of Macri and Adeli (37). Under this condition, most of the lactate dehydrogenase activity but none of the PDI protein was observed to be released from the cells on the basis of the observation by immunoblot analysis (data not shown). In the extracellular fluid prepared from digitonin-permeabilized cells, the 74-kDa form of HDC was detected (Fig. 6, lane 1). Upon treatment of the digitonin-permeabilized cells with trypsin, the remains of the 74-kDa form disappeared, but the 53-kDa form of HDC was still detectable (lane 4). On the other hand, the treatment of Triton X-100 resulted in the solubilization of the 74- and 53-kDa forms of HDC (lanes 5 and 7), both of which were sensitive to the trypsin digestion (lanes 6 and 8).
DISCUSSION

Besides the 53-kDa form, known as a subunit of HDC-purified from various mammalian tissues (13–16), RBL-2H3 cells were found to contain the 74-kDa form, corresponding to the nascent HDC molecule. Most of the 74-kDa form in RBL-2H3 cells leaked out upon treatment of SLO, indicating that the 74-kDa form is localized primarily in the cytosol. Furthermore, [35S]methionine-labeled 74-kDa HDC is a short half-life protein as shown by its rapid degradation in the pulse-chase experiment. Since the 74-kDa form lacks an amino-terminal signal sequence that is cleaved after the translocation across the ER membrane (20), it may be synthesized by free ribosomes in the cytosol as a nonsecreted protein. Regarding the degradation of the 74-kDa form of HDC, very recently we demonstrated the involvement of the proteasome system by the finding that the degradation of the 74-kDa form is inhibited by proteasome inhibitors, such as carboxybenzyl-leucyl-leucyl-leucinal, n-acetyl-leucyl-leucyl-norleucinal, and lactacycin (39). Therefore, the amount of the cytosolic 74-kDa form of HDC may be regulated through post-translational steps including the proteasome system. It is notable that some of the 74-kDa form was also present in the particulate fraction, which has been revealed to exist in the ER, as judged from the distribution of the 74-kDa HDC and the PDI. The membrane topology of the 74-kDa form in the particulate fraction of RBL-2H3 cells was also analyzed by the technique of trypsin digestion of the permeabilized cells (Fig. 6). From these results, it is inferred that the 74-kDa form localizes on the surface of the ER. Regarding membrane-associated HDC activity, Snyder et al. (24) demonstrated a low
but significant amount of rat hypothalamic HDC activity associated with the membranous fraction, although the majority of the activity was found in the supernatant when subcellular particles were osmotically lysed. Furthermore, Martres et al. (25), Braudry et al. (26), and Toledo et al. (27) also reported membrane-bound HDC activity in rat brain. Toledo et al. (28) also reported that the membrane-bound HDC activity was solubilized by Ca\textsuperscript{2+}. However, these reports did not refer to the molecular size of the membrane-bound HDC. From our results, it is deduced that membrane-associated HDC activity reported previously originated from the membrane-associated 74-kDa form.

Since the 74-kDa form has not been purified, it is unknown whether it has full activity. In our previous report, the recombinant mouse 74-kDa form exhibited a low catalytic activity compared with purified HDC, comprising a dimer of the 53-kDa subunit (20). Yatsunami et al. reported that the 54-kDa monomer form of recombinant human HDC, being expressed in the cytosol fraction, has specific activity similar to that of the purified enzyme (21). In the present experiment, we observed that 40% of HDC activity in RBL-2H3 cells was discharged by SLO treatment (Table I), and this activity is inferred to chiefly originate from the 74-kDa form of HDC (Fig. 1). These results indicate that the 74-kDa form has significant enzymatic activity.

In contrast to the present study, we previously reported that the recombinant 74-kDa form of HDC expressed in S9 cells was mostly recovered in the particulate fraction, while the mutant 53-kDa HDC in the expressed cells was the soluble form (20, 21). Considering the solubilization of the precipitated 74-kDa HDC only on treatment with a mixture of 6 M guanidine
In intracellular localization of histidine decarboxylase

1. Beaven, M. A. (1978) *Histamine: Its Role in Physiological and Pathological Processes*, Karger, Basel, Switzerland
2. Code, C. F. (1965) *Fed. Proc.*, 24, 1311–1321
3. Schwartz, J. C., Pollard, H., and Quach, T. T. (1980) *J. Neurochem.*, 35, 26–33
4. Schneider, E., Piquet-Pellorce, C., and Dy, M. (1990) *J. Cell. Physiol.*, 143, 337–343
5. Cribel, S., Schneider, E., Lemoine, F. M., and Dy, M. (1995) *Blood*, 86, 531–539
6. Bartholyena, J., and Fozard, J. R. (1985) *Trends Pharmacol. Sci.*, 6, 123–125
7. Cricco, G. P., Davio, C. A., Martin, G., Engel, N., Fitzsimons, C. P., Bergec, R. M., and Rivera, E. S. (1984) *Agents Actions*, 17, 20–20
8. Bartholyena, J., and Fozard, J. R. (1984) *Cancer Res.*, 44, 639–645
9. Modlin, I. M., Zhu, Z., Tang, L. H., Kidd, M., Lawton, G. P., Miu, K., Powers, R. E., Goldenring, J. R., Parshkow, D., and Soroka, C. J. (1996) *Digestion*, 57, 310–321
10. Kolb, L., Wangberg, B., Ahlman, H., Modlin, I. M., Granérus, G., Theodorsen, E., and Nilsson, O. (1996) *Endocrinology*, 137, 4435–4442
11. Saxena, S. P., Brandes, L. J., Becker, A. B., Simons, K. J., LaBella, F. S., and Gerrard, J. M. (1989) *Science*, 243, 1056–1059
12. Liao, W., Rudling, M., and Angelin, B. (1997) *Endocrinology*, 138, 1863–1870
13. Ohmori, E., Fukui, T., Imanishi, N., Yatsunami, K., and Ichikawa, A. (1990) *Biochem. Tokyo*, 107, 834–839
14. Taguchi, Y., Watanebe, T., Kubota, H., Hayashi, H., and Wada, H. (1984) *J. Biol. Chem.*, 259, 5214–5221
15. Watabe, A., Fukui, T., Ohmori, E., and Ichikawa, A. (1992) *Biochem. Pharmacol.*, 43, 587–590
16. Martin, S. A. M., and Bishop, P. M. (1986) *Biochem. J.*, 234, 349–354
17. Joseph, D. R., Sullivan, P. M., Wang, Y. M., Koakz, C., Fensternacher, D. A., Behrendsen, M. E., and Zahnov, C. A. (1990) *Proc. Natl. Acad. Sci. U. S. A.*, 87, 733–737
18. Yamauchi, K., Sato, R., Tanno, Y., Ohkawa, Y., Maeyama, K., Watanebe, T., Satoh, K., Yoshizawa, M., Shihabara, S., and Takashima, T. (1990) *Nucleic Acids Res.*, 18, 5181
19. Yamamoto, J., Yatsunami, K., Ohmori, E., Sugimoto, Y., Fukui, T., Katayama, T., and Ichikawa, A. (1990) *FEBS Lett.*, 276, 214–218
20. Yamamoto, J., Fukui, T., Suzuki, K., Tanaka, S., Yatsunami, K., and Ichikawa, A. (1993) *Biochim. Biophys. Acta.*, 1216, 431–440
21. Yatsunami, K., Tsuchikawa, M., Kamada, H., Hori, K., and Higuchi, T. (1995) *J. Biol. Chem.*, 270, 3080–3087
22. Tanaka, S., Fukui, T., Yamamoto, J., Shihama, Y., Tsubo, O., and Ichikawa, A. (1995) *Biochim. Biophys. Acta.*, 1253, 9–12
23. Tanaka, S., Funakoshi, E., Kawaihara, A., Nometo, K., Fukui, T., Suzuki, T., Igarashi, K., and Ichikawa, A. (1995) *Methods Find. Exp. Clin. Pharmacol.*, 17, Suppl. C, 25–29
24. Snyder, S. H., Brown, B., and Kuhar, M. J. (1974) *J. Neurochem.*, 20, 37–45
25. Matsumura, M., Pope, P. M., and Schwartz, J. C. (1975) *Brain Res.*, 86, 261–275
26. Braudry, M., Martres, M. P., and Schwartz, J. C. (1975) *Agents Actions*, 3, 175–176
27. Toledo, A., Brandner, R., Brandner, J., Palacios, J. M., and Blanco, I. (1988) *J. Neurochem.*, 51, 1400–1406
28. Toledo, A., Brandner, R., Bariola, J., and Blanco, I. (1988) *J. Neurochem.*, 56, 380–384
29. Ashara, N., Crabbe, S., Shimada, S., Fukui, H., Kinoshita, Y., Kawanami, C., Watanebe, T., Tanaka, S., Ichikawa, A., Uchihama, Y., Narushima, Y., Takasawa, S., Okamoto, H., Tohyama, M., and Chiba, T. (1996) *Gastroenterology*, 111, 45–55
30. Lennmii, U. K. (1970) *Nature*, 227, 680–685
31. Gullberg, U., Lindmark, A., Nilsson, E., Persson, A., and Olsson, I. (1994) *J. Biol. Chem.*, 269, 25219–25225
32. Shore, P. A., Burkhalter, A., and Cohn, V. H. (1959) *J. Pharmacol. Exp. Ther.*, 127, 182–186
33. Lowry, O. H., Rosebrough, N. J., Farr, A. L., and Randall, R. J. (1951) *J. Biol. Chem.*, 193, 265–277
34. Joels, M., and Tjerneld, F. (1994) *Methods Enzymol.*, 228, 136–143
35. Omura, T., and Takesue, S. (1970) *J. Biochem. Tokyo*, 67, 249–257
36. Hultberg, B., Lindsten, J., and Sjöblad, S. (1976) *Biochem. J.*, 155, 599–605
37. Murti, J., and Adeli, K. (1997) *J. Biol. Chem.*, 272, 7328–7337
38. Ahnert-Hilger, G., Mach, W., Fehr, K. J., and Grattl, M. (1989) *Methods Cell Biol.*, 31, 63–90
39. Tanaka, S., Nometo, K., Yamamura, H., Ohmura, S., and Ichikawa, A. (1992) *FEBS Lett.*, 317, 293–297
40. Landford, R. E., Kennedy, R. C., Dressman, G. R., Eichberg, J. W., Notal, L., Luckow, V. A., and Summers, M. D. (1987) in *Viral Hepatitis and Liver Diseases* (Zuckerman, A., ed) pp. 372–378, Alan R. Liss, New York
41. Quemeneur, E., Guthapfel, R., and Gueguen, P. (1994) *J. Biol. Chem.*, 269, 5485–5498
42. Bar-Nun, S., Kreibich, G., Adesnik, M., Alterman, L., Negishi, M., and Sabatini, D. D. (1988) *Proc. Natl. Acad. Sci. U. S. A.*, 85, 965–969
Intracellular Localization of the 74- and 53-kDa Forms of l-Histidine Decarboxylase in a Rat Basophilic/Mast Cell Line, RBL-2H3
Satoshi Tanaka, Ken-ichi Nemoto, Eriko Yamamura and Atsushi Ichikawa

J. Biol. Chem. 1998, 273:8177-8182.
doi: 10.1074/jbc.273.14.8177

Access the most updated version of this article at http://www.jbc.org/content/273/14/8177

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 39 references, 14 of which can be accessed free at http://www.jbc.org/content/273/14/8177.full.html#ref-list-1