In Vitro Autoradiographic and In Vivo Scintigraphic Localization of Somatostatin Receptors in Human Lymphatic Tissue


Receptors for the neuropeptide somatostatin (SS) were evaluated in vitro and in vivo in various human lymphatic tissues, ie, thymus, spleen, and lymph nodes; thymic carcinoids and thymomas were also tested. The receptors were measured in vitro using receptor autoradiography on tissue sections incubated with the SS analog 125I-[Tyr3]-octreotide or 125I-[Leu8, D-Trp28, Tyr31]-SS-28. All tissues were SS-receptor positive for either radioligand, except the thymomas. In thymic tissue, the receptors were diffusely located in the medulla, presumably on epithelial cells. In the spleen, the red pulp was strongly labeled. In the lymph nodes, the germinal centers were preferentially labeled. In all tissues, the receptors were of high affinity (kD thymus, 0.84 nmol/L; kD spleen, 1.6 nmol/L; kD lymph node, 0.62 nmol/L) and specific for SS. Displacement by nanomolar concentrations of SS-14, SS-28, and octreotide was observed, as was guanosine triphosphate dependency. The in vivo visualization of somatostatin receptors was performed after injection of 111In-DTPA-octreotide and 125I-cameral scintigraphy. The spleen, but not thymus or lymph nodes, were visualized. These data suggest an important role for SS in regulating immune functions through SS receptors in thymus, spleen, and lymph nodes. Furthermore, SS may regulate neuroendocrine functions in the thymus. © 1993 by The American Society of Hematology.

Several regulatory peptides found in the brain and the gastrointestinal tract have also been localized in the lymphatic tissues, and were shown to act on cells of the immune system. This has been reported for the vasoactive intestinal peptide (VIP), substance P (SP), and somatostatin (SS), which may act separately or interact with each other.1,3 SS has been shown to inhibit murine lymphocyte proliferation,4-6 Ig synthesis,4 and the release of colony-stimulating factor (CSF) from activated lymphocytes.7 Moreover, SS enhances the formation of leukocyte-migration inhibiting factor in activated lymphocytes.4 High-affinity SS receptors mediating SS effects were described in murine and human lymphatic tissue.8,10 We have recently identified high-affinity SS receptors in the human gut-associated lymphatic tissue (GALT), preferentially located within germinal centers.11 Furthermore, some human lymphomas have increased uptake of radiolabeled SS analogs, a finding that suggests that lymphomas express SS receptors.12

In the present study, we have evaluated the presence of SS receptors in other human lymphatic tissues, including thymus of newborns and adults, spleen and lymph nodes of adults, as well as in a thymoma and in thymic carcinoids. SS receptors were investigated in vitro using SS receptor autoradiography and in vivo in the patient with SS analog scintigraphy.13-15

Materials and Methods

Samples. All samples of thymic tissues (listed in Table 1) and of lymph nodes (Table 2) were collected at the University Hospital in Berne and Kantonsspital Lucerne (Switzerland). In addition, five spleens were obtained from the Erasmus University Hospital in Rotterdam. All samples were obtained during surgical intervention performed for diagnostic or therapeutic reasons, with informed consent of all patients or their parents, and in accord with the Helsinki Doctrine on Human Experimentation. With the exception of the six thymic neoplasms, the tissue samples were histopathologically normal, or displayed mild, reactive changes. All tissue samples were taken fresh at operation and stored frozen at −70°C.

SS receptor autoradiography. Ten-micron and 20-μm thick cryostat sections of the tissue samples were processed for SS receptor autoradiography as described in detail previously.16 The radioligands used were the SS analogs 125I-[Tyr3]-octreotide and 125I-[Leu8, D-Trp28, Tyr31]-SS-28, known to specifically label SS receptors.17,18 Both ligands were iodinated, purified on high-pressure liquid chromatography (HPLC) column (specific activity, 2,000 Ci/mmol) and characterized in standard binding assays as described previously.17,18

For autoradiography, tissue sections were mounted on pre-cleaned microscope slides and stored at −20°C for at least 3 days to improve adhesion of tissue to the slide. Sections were then incubated for 2 hours at ambient temperature in the presence of the iodinated ligand (0.15 to 0.30 × 105 disintegrations per minute [dpm]/mL, approximately 80 to 160 pmol/L). The incubation solution was 170 mmol/L Tris-HCl buffer (pH 7.4) containing 1% bovine serum albumin (BSA), bacitracin (40 μg/mL), and MgCl2 (5 mmol/L) to inhibit endogenous proteases. Nonspecific binding was determined by adding a 1-μmol/L solution of unlabeled [Tyr3]-octreotide or SS-28. Incubated sections were washed twice for 5 minutes in cold incubation buffer containing 0.25% BSA and then in buffer alone, and were dried quickly. Compared with previous procedures of washing in distilled water,16 the present method of washing in buffer resulted in much better histologic preservation of the lymphatic tissues.11 Finally, the sections were exposed to 1H-Ulterofims (Cambridge Research Inc, Nussdorf, Germany) and exposed for 1 week in x-ray cassettes.

In selected cases, displacement experiments were performed in successive tissue sections using increasing concentrations of various biologically active or inactive peptides.19 In addition, saturation experiments using increasing concentrations of 125I-[Tyr3]-octreotide were performed on tissue sections.19 Moreover, the effect of nucleotides was tested on the 125I-[Tyr3]-octreotide binding using...
increasing concentrations (10^{-7} to 10^{-3} mol/L) of guanosine triphosphate (GTP). The autoradiograms were quantified using a computer-assisted image-processing system previously described.16 Tissue standards for iodinated compounds (Amersham Laboratories, Little Chalfont, UK) were used for this purpose. A tissue was defined as SS receptor positive when the optical density measured over an area in the total binding section was at least twice the optical density of the nonspecific binding section.16

Adjacent sections from selected samples of all tissues tested with 125I-[Tyr^3]-octreotide were tested for specific binding with the SS-28 radioligand 125I-[Leu^8, D-Trp^22, Tyr^25]-SS-28 to know if the two ligands identify comparable cellular elements. SS receptor scintigraphy was performed as described in detail previously.13-15 A dose of 7 to 10 μg of 111In-DTPA-octreotide corresponding to 185 to 259 MBq of radioactivity was administered as a single intravenous (IV) injection. Planar images were obtained with a large field of view γ camera (Counterbalance 3700 and ROTA II; Siemens, Hoffman Estates, IL). A standard protocol was used to scan the thorax and abdomen region in all patients. All cases had at least one antero-posterior and one postero-anterior scan of the thorax, including the neck region, and of the abdomen 24 hours after tracer injection. The acquisition parameters for planar images were 300,000 and 500,000 preset counts for the neck/chest and abdomen images, respectively.

RESULTS

Thymus, spleen, and lymph nodes express SS binding sites. In all three tissues these binding sites can be characterized as being of high affinity, specific for biologically active SS analogs, and GTP dependent (Tables 1, 2, and 3).

Normal thymus. All samples of normal thymus contained SS binding sites (Table 1). In young children as well as in adult individuals, the SS binding sites were located in the medulla (Fig 1). Because the medulla appears diffusely and homogeneously labeled and because the present autoradiographic technique does not allow us to assign the label to a given cell, SS binding sites may be located either on vascular epithelial cells, stroma, reticuloendothelial cells, or on lymphocytes. No significant labeling was observed in the cortex nor in Hassal’s corpuscles. Saturation experiments with increasing concentrations of 125I-[Tyr^3]-octreotide showed that the SS binding in the thymic medulla from a newborn child is saturable and of high affinity. Scatchard plots of the data showed a dissociation constant (K_d of 0.84 nmol/L and total number of sites (B_max) equivalent to 83 fmol/mg protein (Fig 2). This binding was specific because SS and bioactive SS analogs, ie, octreotide, were able to displace the radioligand in the high-affinity range, whereas the biologically inactive analog SS-28 (1-12) did not dis-

Table 1. Incidence of SS Binding Sites in Normal and Diseased Human Thymic Tissue

<table>
<thead>
<tr>
<th>Tissue</th>
<th>No. of Cases</th>
<th>Incidence of Cases With SS Binding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal thymus from children (age: 0-6 yr)</td>
<td>4</td>
<td>4/4 (100%)</td>
</tr>
<tr>
<td>Normal thymus from adults</td>
<td>8</td>
<td>8/8 (100%)</td>
</tr>
<tr>
<td>Thymomas</td>
<td>4</td>
<td>0/4 (0%)</td>
</tr>
<tr>
<td>Thymic carcinoids</td>
<td>2</td>
<td>2/2 (100%)</td>
</tr>
</tbody>
</table>

Table 2. Localization, Diagnosis, and In Vitro Presence of SS Binding Sites in 15 Human Lymph Node Biopsies

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Patient/ Age (yr)/Sex</th>
<th>Localization (biopsy)</th>
<th>Diagnosis at Biopsy</th>
<th>SS Binding Sites* In Vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LF/43/F</td>
<td>Inguinal</td>
<td>Lymphoid hyperplasia</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>AR/25/M</td>
<td>Axillar</td>
<td>Lymphoid hyperplasia, follicular and diffuse</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>WS/33/F</td>
<td>Nuchal</td>
<td>Follicular lymphoid hyperplasia</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>KU/52/M</td>
<td>Cervical</td>
<td>Follicular lymphoid hyperplasia</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>SA/35/M</td>
<td>Cervical</td>
<td>Granulomatous lymphadenitis with microabscesses†</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>BT/47/M</td>
<td>Axillar</td>
<td>Granulomatous lymphadenitis with microabscesses†</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>JC/16/M</td>
<td>Submental</td>
<td>Follicular lymphoid hyperplasia</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>FM/29/M</td>
<td>Cervical</td>
<td>Lymphoiditis, Piringer-Kuchinka type</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>KP/40/F</td>
<td>Cervical</td>
<td>Lymphoid hyperplasia, diffuse</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>ZP/42/F</td>
<td>Axillar</td>
<td>Lymphoid hyperplasia, diffuse</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>KC/19/M</td>
<td>Inguinal</td>
<td>Granulomatous lymphadenitis with microabscesses†</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>KC/19/M</td>
<td>Inguinal</td>
<td>Granulomatous lymphadenitis with microabscesses†</td>
<td>+</td>
</tr>
<tr>
<td>13</td>
<td>MA/40/F</td>
<td>Mediastinal</td>
<td>Anthracosis, epithelioid cell reaction</td>
<td>+</td>
</tr>
<tr>
<td>14</td>
<td>HA/51/M</td>
<td>Cervical</td>
<td>Lymphoid hyperplasia</td>
<td>+</td>
</tr>
<tr>
<td>15</td>
<td>MM/49/F</td>
<td>Axillar</td>
<td>Lymphoid hyperplasia Piringer-Kuchinka lymphadenitis</td>
<td>+</td>
</tr>
</tbody>
</table>

* Detected with receptor autoradiography (see Materials and Methods for details).
† "Cat scratch lymphadenitis."
Table 3. Inhibition of Specific $^{125}$I-[Tyr$^3$]-Octreotide Binding by Various GTP Concentrations in Thymus, Spleen, and Lymph Nodes

<table>
<thead>
<tr>
<th>GTP Concentration</th>
<th>Specific binding (dpm/mg tissue; mean ± SEM, n = 3*)</th>
<th>% Inhibition</th>
<th>Specific binding (dpm/mg tissue; mean ± SEM, n = 3*)</th>
<th>% Inhibition</th>
<th>Specific binding (dpm/mg tissue; mean ± SEM, n = 3*)</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1,006 ± 60</td>
<td>—</td>
<td>2,040 ± 102</td>
<td>—</td>
<td>1,345 ± 77</td>
<td>—</td>
</tr>
<tr>
<td>10$^{-7}$ mol/L</td>
<td>677 ± 44</td>
<td>33</td>
<td>NT</td>
<td>—</td>
<td>682 ± 48</td>
<td>49</td>
</tr>
<tr>
<td>10$^{-6}$ mol/L</td>
<td>351 ± 27</td>
<td>66</td>
<td>1,130 ± 16</td>
<td>44</td>
<td>457 ± 31</td>
<td>66</td>
</tr>
<tr>
<td>10$^{-5}$ mol/L</td>
<td>166 ± 12</td>
<td>84</td>
<td>829 ± 33</td>
<td>59</td>
<td>274 ± 26</td>
<td>79</td>
</tr>
<tr>
<td>Nonspecific binding</td>
<td>128 ± 19</td>
<td>362 ± 14</td>
<td></td>
<td></td>
<td>225 ± 18</td>
<td></td>
</tr>
</tbody>
</table>

Nonspecific binding = total binding of $^{125}$I-[Tyr$^3$]-octreotide in presence of 10$^{-6}$ mol/L [Tyr$^3$]-octreotide.

Abbreviation: NT, not tested.

* Calculated from optical density values obtained from autoradiograms in successive tissue sections incubated with the ligand $^{125}$I-[Tyr$^3$]-octreotide and a corresponding concentration of GTP (see Materials and Methods for details).

place the radioligand (Fig 3). Furthermore, SS binding was GTP-dependent (Table 3). The binding characteristics obtained in child thymus were also obtained in adult thymus. The present results are similar to the SS binding characteristics found in other SS target tissues. In addition, one thymus from a patient with myasthenia gravis was positive for SS binding sites, again with the label preferentially located in the medullary area.

Thymic neoplasms. Table 1 shows the results of the evaluation of SS binding sites in six human thymic neoplasms. Whereas the four thymomas were negative, the two thymic carcinoids were positive.

In vivo scintigraphy with $^{111}$In-[DTPA]-octreotide performed in more than 800 patients suffering from various types of mostly neuroendocrine tumors never did identify hot spots in the thymus region. However, one patient with a thymic carcinoid was scanned in vivo and showed accumulation of the radioligand in the primary tumor and its mediastinal metastases.

Spleen. In all five spleens tested, SS binding sites were preferentially located in the red pulp, as seen in the autoradiography picture of Fig 4. Binding was specific and of high affinity because both SS and bioactive SS analogs such as octreotide were able to displace the radioligand in the nanomolar range, whereas the biologically inactive SS-28 (1-12) was not (Fig 3). In a case of lymphatic hyperplasia, the $k_a$ calculated from Scatchard plot was 0.62 nmol/L and the estimated $B_{max}$ was 128 fmol/mg protein. Binding was GTP-dependent (Table 3). Similar binding characteristics of lymph nodes were found in lymphatic hyperplasia and in granulomatous lymphadenitis caused by cat scratch disease.

The lymph nodes, thymus, and spleens labeled in vitro with $^{125}$I-[Tyr$^3$]-octreotide could also be labeled with $^{125}$I-[Leu$^6$,D-Trp$^{22}$,Tyr$^{25}$]-SS-28 radioligand. Figure 7 shows an example of a lymph node and a spleen containing binding sites labeled with $^{125}$I-[Leu$^6$,D-Trp$^{22}$,Tyr$^{25}$]-SS-28.

Interestingly, in vivo scintigraphy of more than 250 patients without evidence of lymphatic pathology did not identify lymph nodes labeled with $^{111}$In-[DTPA]-octreotide.

DISCUSSION

The present study describes for the first time the presence of SS binding sites in human lymphatic tissues such as newborn and adult thymus, spleen, and lymph nodes. This observation relates to a previous study describing SS receptors in the human GALT. As in the GALT, the SS binding sites in the presently investigated tissues may be specific SS receptors because a GTP-dependency could be observed. Moreover, they appear to belong to the SS1 receptor subtype, because the SS octapeptide octreotide as well as SS-14 or SS-28 show high-affinity binding to the receptor. Recently, the genes encoding three human SS-receptor subtypes have been cloned and sequenced; one of these, the SSTR2 type, shows high affinity not only for SS-14 but also for small synthetic SS analogs such as MK 678 or octreotide; recent data suggest that it is identical to the pharmacologically characterized SS1 receptor subtype. Therefore, lymphatic tissues investigated in the present report probably express the SSTR2 subtype; however, we cannot completely
exclude the possibility that a further subtype, different from SSTR1 and SSTR3, is also expressed.

**Thymus.** The human thymic medulla of both newborn and adult contains high-affinity SS receptors. It is presently not possible to assign these receptors to a defined cell type in the medulla. The very weak staining of the cortex suggests that the cells located predominantly in this area, ie, lymphatic cells, have no SS receptors. Thus, in the medulla, strong candidates for the expression of SS receptors could be the epithelial cells, densely packed in this region. Some of

Fig 1. SS binding sites in the human thymus from children (A through C) and adults (D through F). (A, D) Hematoxylin-eosin stained sections. Bar = 1 mm. (B, E) Autoradiograms showing total binding of $^{125}$I-[Tyr$^2$]-octreotide. (C, F) Autoradiograms showing nonspecific binding of $^{125}$I-[Tyr$^2$]-octreotide (in presence of $10^{-6}$ mol/L [Tyr$^2$]-octreotide). All sections were incubated with $0.3 \times 10^6$ dpm/mL of tracer. Twelve slices were studied. In both tissues the SS binding sites are located in the medulla.
these epithelial cells can be labeled with A2B5, a monoclonal antibody (MoAb) directed against a complex neuronal ganglioside found on the cell surface of neurons and neuroendocrine cells. Interestingly, some of the medullary epithelial cells, including A2B5-positive cells, were shown to contain various thymic hormones, strongly suggesting that these cells have neuroendocrine characteristics. Because most normal neuroendocrine tissues, as well as the thymic carcinoids (which originate from neuroendocrine cells), are known to express SS, it is conceivable that these medullary "neuro-endocrine-like" epithelial cells also bear SS receptors. However, because of the diffuse and homogeneous labeling pattern, it is possible that the other nonneuroendocrine types of epithelial cells were also labeled, and it cannot be completely excluded that some mature medullary thymocytes or isolated B lymphocytes in the medulla do contain SS receptors.

In addition to being the primary lymphatic organ generating effectors of cell-mediated immunity, the thymus can be considered a major endocrine gland responsible for the secretion by its epithelial cells of a heterogeneous family of polypeptide hormones such as thymulin, thymosins, and thymopoietin. These peptides not only exert important

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**Fig 2.** Scatchard plot from a saturation experiment using increasing concentrations of $^{125}$I-[Tyr$^3$]-octreotide in successive sections of a newborn thymus using receptor autoradiography techniques. $K_d = 0.84$ nmol/L; number of sites ($B_{max}$): 93 fmol/mg protein.

**Fig 3.** Effect of peptides on SS binding in human lymphatic tissues. (A) Newborn thymus. Displacement curve of $^{125}$I-[Tyr$^3$]-octreotide in tissue sections incubated with 30,000 cpm/100 µL radioligand and increasing concentrations of octreotide (○), SS-14 (△), or 100 nmol/L of the biologically inactive SS analog SS-28 (1-12) (□). Each point represents the mean of triplicate determinations of the optical density. (B) Displacement curve of $^{125}$I-[Tyr$^3$]-octreotide in a human spleen using increasing concentrations of [Tyr$^3$]-octreotide (○), SS-28 (△), or 100 nmol/L LHRH (□). The data are averages from triplicate determinations in a single experiment and are representative of three separate experiments. (C) Displacement curve of $^{125}$I-[Tyr$^3$]-octreotide in a human lymph node using increasing concentrations of octreotide (○) or SS-14 (△) or 100 nmol/L of SS-28 (1-12) (□). The data are averages from triplicate determinations in a single experiment and are representative of three separate experiments.
The functional role of SS and SS receptors should probably be considered under the same point of view, despite the lack of experimental data. In epithelial cells, SS may regulate the secretion of thymic hormones, in a way similar to its well-known inhibition of hormone release in virtually all neuroendocrine cells in the body. Moreover, and in analogy to the described action of SS in other lymphatic tissue, we may speculate that an SS effect relates to lymphopoiesis, perhaps by regulating the proliferation and specific functions of lymphocytes. Endogeneous SS should be available locally for that purpose because it was recently shown that the thymic medulla of the rat contains both SS mRNA and immunohistochemically detectable SS.

Thymic neoplasms. Many well-differentiated neoplasms arising from SS receptor-positive tissues contain SS receptors. This principle does not seem to be valid for the four thymomas studied in this report. However, the two thymic carcinoids were SS receptor positive. This is not surprising, because these neoplasms are thought to arise from neuroendocrine cells located in the thymus, and is in keeping with our previous observation that most of the carcinoids, independently of their location, usually express SS receptors. Thymic carcinoids, as their gastrointestinal or bronchial counterparts, may therefore be detected by in

regulatory effects within the immune system, such as induction of proliferation and differentiation of T lymphocytes, but also regulate the neuroendocrine system and are themselves subject to control by various hormones (prolactin, growth hormone, thyroid hormones, adrenocorticotropic [ACTH], or opioids) through specific receptors located in the thymus. Thus, these peptides represent an important interface between the immune and neuroendocrine systems.

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Fig 6. SS binding sites in a human lymph node with follicular lymphoid hyperplasia. (A) Hematoxylin-eosin-stained section showing germinal centers in the lymph node. Bar = 1 mm. (B) Autoradiogram showing total binding of \( ^{125}\text{I}-[\text{Tyr}^{2}] \)-octreotide. The germinal centers are preferentially labeled. (C) Nonspecific binding.

Spleen. The human spleen expresses high-affinity SS receptors located preferentially in the red pulp. The cell type bearing these receptors cannot be identified in the present study, for technical reasons. However, it is probable that some of the cells having SS receptors are lymphocytes, because rat spleen lymphocytes were shown to specifically react to SS(1); indeed, SS was able to inhibit the Ig synthesis as well as the proliferation of these cells. The presence of SS receptors in the human spleen suggests that SS could have similar functions in the human.

Lymph nodes. All large germinal centers in the lymph nodes tested in the present study were SS-receptor positive. This is in good agreement with our previous study on various tissues from the human GALT in which all germinal centers in tonsils, Peyer patches, appendix, and solitary follicles of the colon, were strongly SS receptor positive.\(^{11}\) In these tissues, as well as in the lymph nodes tested presently, it is likely that germinal center lymphatic cells are bearing these high-affinity SS receptors. The role of SS mediated through such SS receptors has not yet been investigated in the human tissues. In rats,\(^{18}\) proliferation and Ig synthesis of activated lymphocytes are inhibited by SS.

Correlation of in vitro and in vivo SS receptor assessment. The present study allows for a comparison between the visualization of SS receptors by in vitro methods on sections and by in vivo scintigraphy. There is an excellent correlation of the data for the spleen, showing that both methods show specific SS receptors. This confirms previous data from other normal organs of the human body, such as the pituitary, where also both methods identify specific SS receptors.\(^{33}\) Moreover, we have seen a highly significant correlation between the presence of SS receptors in vitro and in vivo in many human tumors.\(^{12,14,34,35}\) In most of these cases, we could establish that even tumors with a relatively low density of SS receptors or with a nonhomogeneous tissue distribution of SS receptors in vitro could be identified and localized by means of in vivo SS scintigraphy. Therefore, it is intriguing that SS receptor-positive lymph nodes as well as normal thymus have not been detected by in vivo scintigraphy. It is possible, but improbable, that the sensitivity of the in vivo method is not sufficient for the detection of these receptors, especially in regions with a higher background such as the abdomen or the skull base. However, a more attractive possibility is that such in vitro/in vivo discrepancies have a biologic origin. Hypothetically, the SS receptor turnover in lymphatic tissues could be much slower than in neoplasms and pituitary glands. This would mean that much less receptor-radioligand complex is being internalized in lymphatic tissue compared with internalization in neoplastic tissue and pituitary gland; this would result in a less intensive labeling of the tissue in vivo, which seems to depend not only on the receptor density but also on the capacity of internalization of the radioligand.\(^{14}\)

CONCLUSIONS
In the human, most lymphatic tissues express SS receptors. The function of these receptors is not yet established. In analogy to data obtained in animals,\(^{1,7}\) it is tempting to postulate that SS and SS analogs play a significant role in the regulation of the human immune system. However, despite the worldwide use of SS analogs such as octreotide for the
symptomatic therapy of certain cancers in humans, very few reports on immunologic side effects have appeared. However, preliminary data from one group of investigators support the existence of immunologic reactions to SS; clearly, the present results could stimulate more clinical studies in this direction.

Another conclusion of the present report relates to radiotherapy. The finding of a high number of SS receptors in various tumors recently generated the idea of targeting β-emitting isotope-linked SS ligands to “burn out” selectively such tumors. However, according to our present in vitro data, normal tissues bearing SS receptors, particularly “central” and “peripheral” lymphatic tissues, are likely to be affected by such an approach. Potential functional consequences should be carefully investigated.

ACKNOWLEDGMENT

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SOMATOSTATIN RECEPTORS IN LYMPHATIC TISSUE

2151

In vitro autoradiographic and in vivo scintigraphic localization of somatostatin receptors in human lymphatic tissue

JC Reubi, B Waser, U Horisberger, E Krenning, SW Lamberts, JO Gebbers, P Gersbach and JA Laissue

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