Tumor Cells with Organ-specific Metastatic Ability Show Distinctive Trafficking 
in Vivo: Analyses by Positron Emission Tomography and Bioimaging

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ABSTRACT

To elucidate the behavior of various metastatic tumor cells with different characteristics in the blood flow, we have developed a system to investigate real-time trafficking using positron emission tomography. In this study, positron-labeled cells, i.e., lung-metastatic RAW117 cells and two sublines of liver-metastatic RAW117 large cell lymphoma, were injected i.v., and the trafficking of these cells was noninvasively determined. All sublines tested accumulated in the lungs immediately after injection, presumably because the lungs were the first organ passed through after i.v. injection. The elimination of RAW117 cells from the lungs, however, was fast compared with that of B16BL6 cells. The latter showed a release rate from the lungs of less than 1%/min, whereas that of RAW117 cells was greater than 2%/min. Reflecting the elimination from lungs, RAW117 cells accumulated in the liver in a time-dependent manner. Biodistribution of metastatic cells was also analyzed by whole-body autoradiography after injection of [125I]iodo-2-deoxyuridine-labeled cells, using a bioimaging analyzer system. The method is invasive; however, it enables a precise determination of the biodistribution of metastatic cells. Bioimaging analyzer system analysis also showed the organ-specific accumulation of these metastatic cells. Furthermore, colonized distribution of B16BL6 cells in the lungs and that of RAW117 cells in the liver were observed. The present data suggest that the trafficking of metastatic tumor cells greatly influences the organ specificity of cancer metastasis.

INTRODUCTION

Metastasis occurs through a complex cascade of events including dissociation from the primary sites, intravasation, adhesion to and invasion of the target, and growth at the colonization sites (1–3). Tumor cell adhesion to the vascular endothelium in the target organ is thought to be an essential step, especially in blood-borne metastasis (4). Through a number of in vitro analyses, the role of adhesion and invasion properties of metastatic tumor cells to the target tissues and that of the growth capability of the cells in the organ microenvironment have become clear (5, 6). However, the presumptions of tumor cell trafficking during metastasis have not been fully confirmed, because there was no noninvasive technique available for the determination of real-time tumor cell trafficking in vivo. We recently developed a technique using PET to overcome such difficulties (7). In these experiments, positron-labeled cells were injected into host animals to mimic blood-borne metastasis. The real-time trafficking of the injected cells was determined by PET. The method, using high-resolution intravital videomicroscopy, also enables the determination of tumor cell trafficking in vivo (8, 9). Although it is invasive, this method is quite useful to analyze single-cell distribution in vivo, such as cells in venules or those extravasated in a specified tissue. The present method cannot detect the precise location of a single cell but enables the assessment of total cell trafficking in the whole body.

Previous results obtained by the use of this technique showed that highly lung-metastatic sublines of rat adenocarcinoma cells accumulated in lungs more intensively than did poorly metastatic ones (7). However, the mechanism of accumulation in the lungs was difficult to determine, because the mechanical trapping of the cells might have played a significant role in the accumulation because this organ is the first to be encountered after an i.v. injection. Furthermore, accumulation due to specific adhesion of the cells might not be detectable separately from the mechanical trapping. On the contrary, the accumulation of liver-metastatic cells after i.v. injection might not be due to mechanical trapping (10). In this study, we investigated the trafficking of various tumor cells having differential organ specificity. The findings indicate that the organ-specific accumulation of metastatic cells through a highly specific mechanism can be successfully determined by PET.

MATERIALS AND METHODS

Cell Culture and Characterization of Metastatic Potentials. B16BL6 cells, a highly lung-metastatic subline of murine B16 melanoma, were cultured in DMEM and Ham’s F12 (1:1) medium supplemented with 10% FCS (JRH Biosciences, Lenexa, KS) under a humidified atmosphere of 5% CO2 in air. RAW117 parental line (RAW117-P) and a highly liver-metastatic variant subline (RAW117-H10) were cultured in hG-DMEM supplemented with 5% FCS. All these cells were gifts from Dr. G. L. Nicolson (Institute for Molecular Medicine, Irvine, CA). The growth curve of these cells was determined as follows: 4 X 10^6 cells/ml were seeded into each of several 35-mm culture dishes, and the number of cells was determined every 12 h. The growth of B16BL6, RAW117-P, and RAW117-H10 cells reached confluence at 96, 72, and 61 h, respectively. The doubling time of these cells was determined from the growth phase of the growth curves. The size of the cells was determined by measuring more than 100 cells using calipers on photomicrographs taken at a selected magnification; in the case of B16BL6 cells, they were trypsinized to obtain a single-cell suspension before the photomicrographs were taken.

The metastatic potential of the cells tested was determined as follows: 2 X 10^6 cells/mouse were injected i.v. into 7-week-old female C57BL/c mice (n = 6; Japan SLC Inc., Hamamatsu, Japan), and colonization in lungs and other tissues was tested at day 14 after injection. In the case of RAW117 cells, 10^6 cells were injected i.v. into 7-week-old female BALB/c mice (n = 6). The weights of the liver, spleen, and other tissues were determined at day 14 after injection instead of counting colonies, because the colonies of RAW117 cells were hard to count.

Cell Adhesion Assay. LEs or HSEs were seeded on a 24-well culture dish (2 X 10^5 cells/well) precoated with gelatin and incubated overnight. RAW117 parental line (RAW117-P) and a highly liver-metastatic variant subline (RAW117-H10) were cultured in hG-DMEM supplemented with 5% FCS. All these cells were gifts from Dr. G. L. Nicolson (Institute for Molecular Medicine, Irvine, CA). The growth curve of these cells was determined as follows: 4 X 10^6 cells/ml were seeded into each of several 35-mm culture dishes, and the number of cells was determined every 12 h. The growth of B16BL6, RAW117-P, and RAW117-H10 cells reached confluence at 96, 72, and 61 h, respectively. The doubling time of these cells was determined from the growth phase of the growth curves. The size of the cells was determined by measuring more than 100 cells using calipers on photomicrographs taken at a selected magnification; in the case of B16BL6 cells, they were trypsinized to obtain a single-cell suspension before the photomicrographs were taken.

The metastatic potential of the cells tested was determined as follows: B16BL6 cells (10^6 cells/mouse) were injected i.v. into 7-week-old female BALB/c mice (n = 6; Japan SLC Inc., Hamamatsu, Japan), and colonization in lungs and other tissues was tested at day 14 after injection. In the case of RAW117 cells, 10^6 cells were injected i.v. into 7-week-old female BALB/c mice (n = 6). The weights of the liver, spleen, and other tissues were determined at day 14 after injection instead of counting colonies, because the colonies of RAW117 cells were hard to count.

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2 The abbreviations used are: PET, positron emission tomography; hG, high glucose; HSE, hepatic sinusoidal microvesSEL endothelial cell; LE, lung endothelial cell; FDG, 2-fluoro-2-deoxy-D-glucose; [125I]IUdR, 5-[125I]iodo-2'-deoxyuridine; BAS, bioimaging analyzer system.
Preparation of Cell Suspensions for PET Analysis. The cells were labeled with [2-18F]FDG as described previously (7). In brief, B16BL6 cells were washed with glucose-free medium and incubated with [2-18F]FDG for 30 min at 37°C. After the free [2-18F]FDG had been washed away, the cells were removed from the plate with EDTA solution to obtain a single-cell suspension. After free [2-18F]FDG had been removed by centrifugation, a single-cell suspension was obtained. Viability of the labeled cells was determined by the trypan blue dye exclusion method and was greater than 90% throughout the experiments.

PET Analysis. The animal PET camera (SHR-2000; Hamamatsu Photonics) used in the experiment has an effective slice aperture of 3.25 mm and a resolution of 2.7 mm (11). The cells labeled with [2-18F]FDG (1 × 10^6 cells in 0.2 ml of medium) were injected into syngeneic 10-week-old female mice (C57BL/6 mice for B16BL6 cells and BALB/c mice for RAW117 cells) via a tail vein while under anesthesia with sodium pentobarbital after a 30-min transmission scan with 18.5 MBq of 68Ge/68Ga ring source. The emission scan of PET was started immediately after injection of the cells and was performed for 90 min. The initial 60 frames were taken at a rate of 1 every 1 min, and the next 12 frames were taken at a rate of 1 every 2.5 min. Thus, 72 frames were taken during the PET scan. PET images were simultaneously obtained in 14 slices of which the sixth slice was set at the xiphisternum.

The radioactivity in the form of coincidence γ photons was measured and converted to Bq/cm² of tissue volume by calibration after correction for decay and attenuation. The time activity curve was obtained from the mean pixel radioactivity in the region of interest of the composed PET images in which the injected dose was calibrated as 740 kBq. The release rate of cells from the lungs was calculated from the slope of 5–20-min accumulation changes of the time activity curves of 18F accumulation in lungs after injection of [2-18F]FDG-labeled cells. Each experiment was repeated at least twice, and similar results were obtained in repeated experiments, although each figure represents a typical result obtained from a single animal.

Bioimaging Analysis. Tumor cells were labeled with [125I]IUDR by the method originally established by Fidler (12). RAW117 cells (20 ml; 1 × 10^6 cells/ml) were incubated in the presence of 3.7 MBq of [125I]IUDR (Amersham) for 10 h in a CO2 incubator. After the cells had been washed with hG-DMEM, 1 × 10^6 cells/0.2 ml were injected i.v. into 10-week-old BALB/c mice via a tail vein. The animals were sacrificed after 15 and 120 min after injection of the cells and were immediately frozen with acetone dry ice. Frozen tissues were embedded in 8% barbituric acid and were cut into 30-μm thickness. The size of the tissues was determined using an image analysis system (Olympus). The size of the tumors was also measured using the same method.

RESULTS

Characterization of Cells. Before the PET study, characterization and metastatic potential of the cells used in this study were tested. As summarized in Table 1, B16BL6 cells were observed to metastasize to the lungs, whereas RAW117-H10 cells metastasized to the liver. Hypertrophy was also observed in the spleen. Histological observation of the lungs indicated that colonization of RAW117-H10 cells occurred in this organ in some animals, although the growth of these colonies was not as prominent as that in the liver. The mean cell sizes were determined by microscopy; the value for B16BL6 cells was obtained after trypsinization. The sizes of these cells are shown in Table 1. The two RAW117 cell types were not different from each other, although the B16BL6 cells were slightly larger than the former.

Fig. 1 shows the adhesion properties of RAW117 cells to LEs and HSEs. Both sublines of RAW117 cells adhered similarly to LEs, although RAW117-H10 cells adhered to HSEs more than RAW117-P cells did, consistent with the data reported previously (13).

Metastatic Tumor Cell Trafficking Determined by PET. The real-time trafficking of the three metastatic cell lines was determined by PET. Fig. 2 shows typical PET images obtained for B16BL6 cells in the present study. These images indicate the distribution of positron-labeled B16BL6 cells during the first 30 min after the initial i.v. injection. The corresponding X-ray computed tomography images are also shown. Intense accumulation of the cells was observed in the lung (four to six slices). Thus, the real-time trafficking of these metastatic cells could be determined, as shown in Fig. 3. The initial accumulation in the lungs and the time-dependent release of these cells from the lungs were clearly demonstrated. In the case of RAW117 cells, the number of cells retained in the lungs decreased rapidly. The time-activity curves of 18F in the lungs are shown in Fig. 4. Again, rapid removal of RAW117 from the lungs was observed, as compared with the slower loss of B16BL6 cells.

Table 1. The initial rate of elimination of B16BL6 and RAW117 cells as well as that for rat 13762NF mammary adenocarcinoma cells (MTLn3 and MTC), the latter of which metastasizes to the lungs and accumulates there as described previously (7), from the lungs was calculated from the corresponding time-activity curves. As shown in Table 2, the elimination rate of the highly lung-metastatic B16BL6 melanoma cells was 0.75%/min. The biological half-life of these cells in the lungs was 66.8 min. The elimination rate of rat 13762NF mammary adenocarcinoma cells, namely, highly lung-metastatic MTLn3 and poorly metastatic MTC cells, was also low.

Table 1 Characterization and metastatic potential of various metastatic tumor cells

<table>
<thead>
<tr>
<th>Cells</th>
<th>Cell size (μm)</th>
<th>Doubling time (h)</th>
<th>Metastatic potential to:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lung</td>
</tr>
<tr>
<td>Control</td>
<td>13.4 ± 1.4</td>
<td>9.5</td>
<td>0.175 ± 0.018</td>
</tr>
<tr>
<td>RAW 117-P</td>
<td>13.8 ± 1.4</td>
<td>9.2</td>
<td>0.155 ± 0.013</td>
</tr>
<tr>
<td>RAW 117-H10</td>
<td>13.8 ± 1.4</td>
<td>9.5</td>
<td>0.241 ± 0.008</td>
</tr>
<tr>
<td>B16BL6</td>
<td>17.6 ± 1.6</td>
<td>11.5</td>
<td>0.137 ± 0.02</td>
</tr>
</tbody>
</table>

\( ^a\) Significant difference between two cell lines.

\( ^b\) Significant difference against control (no tumor cells injected).

\( ^c\) \(P < 0.01\).

\( ^d\) \(P < 0.001\).
On the other hand, the rate of elimination of RAW117-P and RAW117-H10 cells from the lungs was much greater than that of lung-metastatic cells, with the values being 2.78%/min and 2.05%/min, respectively, for these cells.

**Metastatic Tumor Cell Trafficking in Liver Determined by PET.** The trafficking of various metastatic cells in the liver was determined considering that RAW117 cells, especially RAW117-H10 cells, are known to metastasize to the liver. Fig. 5 shows the accumulation patterns of B16BL6, RAW117-P, and RAW117-H10 cells in liver tissue. Although B16BL6 cells were detected in the liver, specific accumulation of these cells was not observed. The time course of the level of radioactivity in the liver of mice injected with RAW117 cells was different. The number of labeled cells increased gradually for 75 min after the injection. Accumulation was more prominent with RAW117-H10 cells than it was with RAW117-P cells. The liver:lung accumulation ratios are shown in Table 2. The values indicate that the patterns of accumulation of lung-metastatic cells and liver-metastatic cells are distinct.

**Biodistribution of Metastatic Tumor Cells Determined by BAS.** PET analysis shows the real-time biodistribution of metastatic cells; however, it is difficult to determine the intraorgan distribution by this method. Therefore, we examined the precise intraorgan distribution of metastatic tumor cells by whole-body autoradiography. Fig. 6 shows a specimen slice of a RAW117-H10-injected mouse and the autoradiography. Accumulations of cells in lungs and liver are shown in Figs. 7 and 8, respectively, after whole-body autoradiography. As shown in Fig. 7, RAW117 cells accumulated less than B16BL6 cells in lung tissue at 15-min postinjection. The intralung distribution of these cells was rather homogeneous, although the cells were distributed as colonies throughout the lung tissue. The accumulation of the
cells in the liver is shown in Fig. 8. The accumulation seemed to be rather homogeneous in the liver (dark area, Fig. 8a). A colony distribution was also observed in liver for both B16BL6 and RAW117 cells. At 120-min postinjection, radioactivity was observed in the spleen (black area, Fig. 8b, L-4 mm to L-7 mm). Fig. 9 shows the typical views of B16BL6 accumulation in lung tissue and RAW117-H10 accumulation in the liver at 2 h after injection. The colony distribution of the cells is obvious, although the precise number of cells in each colony is unknown due to halation during exposure. Table 3 shows the distribution concentration of the cells in various tissues. Although the values do not show the total distribution in various tissues but show the distribution concentration in their tissues, B16BL6 was clearly distributed in the lungs more than RAW117 cells were.

**DISCUSSION**

Many factors are known to influence the outcome of cancer metastasis. Some of them are believed to determine the organ-specific aspect of metastasis. The adhesion of blood-borne tumor cells to the endothelium at distant organ sites is believed to be the first step to determine such organ specificity (14). To determine the organ specificity of tumor cell adhesion, cultured endothelial cells have been used. Although the information obtained by such experiments is useful, it is difficult to assess whether such mechanisms are actually involved in the process of organ colonization. A noninvasive method to determine tumor cell trafficking in vivo should be developed to close the gap between in vitro and in vivo experiments on metastasis. Biodistribution studies of tumor cells have been conventionally carried out using the following protocols: (a) the animals are injected with radioisotope-labeled tumor cells; (b) at given times, these animals are sacrificed; and (c) the radioactivities remaining in the removed organs are determined. In these experiments, a large number of animals need to be sacrificed to obtain different time points. Furthermore, cell trafficking in vivo may be affected by subtle changes in conditions (15, 16); excision of the animals may cause a serious

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Table 2: Release rate of the cells accumulated in the lungs and the accumulation ratio of cells in the liver and lungs

<table>
<thead>
<tr>
<th>Cells</th>
<th>Release from lungs (%/min)</th>
<th>Half-life in lungs (min)</th>
<th>Liver/lung ratio at 60 min postinjection</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAW 117-P</td>
<td>2.78</td>
<td>21.6</td>
<td>0.346</td>
</tr>
<tr>
<td>RAW 117-H10</td>
<td>2.05</td>
<td>30.6</td>
<td>0.326</td>
</tr>
<tr>
<td>B16BL6</td>
<td>0.75</td>
<td>&gt;90</td>
<td>0.097</td>
</tr>
<tr>
<td>MTLn3</td>
<td>0.72</td>
<td>&gt;90</td>
<td>0.030</td>
</tr>
<tr>
<td>MTC</td>
<td>1.01</td>
<td>70.4</td>
<td>0.147</td>
</tr>
</tbody>
</table>
change in cell-cell interactions in the animal body. Therefore, the present method using PET should be useful to noninvasively determine cell trafficking without changing the physiological conditions. Furthermore, only a small number of animals are required.

In this study, we compared the trafficking of lung-metastatic B16BL6 melanoma cells and liver-metastatic RAW117 lymphoma cells as well as that of two sublines of lung metastatic rat 13762NF mammary adenocarcinoma cells. As shown in Fig. 2, this method enables the determination of cell trafficking in specific organs. For example, B16BL6 cells were accumulated in the lungs. The lung is the target organ for B16BL6 cells, and it is also the first organ having microvasculature met by the cells after i.v. injection via a tail vein. Liver-metastatic RAW117 cells also accumulated in the lungs at a relatively early time period after injection. However, the initial accumulation in lungs was higher for B16BL6 than it was for RAW117 cells. Also, RAW117 cells were rapidly released from lungs; the rate of release was much greater than that of B16BL6 cells. When RAW117 sublines were compared, the release rate of RAW117-H10 cells was lower than that of RAW117-P cells. This fact may correspond to the metastatic potential of RAW117-H10 cells, which also metastasize to the lungs in addition to the liver after i.v. injection.

Interestingly, the release rate from lungs was similar in both rat and mouse when lung metastatic tumor cells were used (Table 2). We previously examined the differential cell trafficking between MTLn3 and MTC cells and observed that the lung accumulation of MTC cells was less than that of highly metastatic MTLn3 cells just after injection, although the cell size of the highly metastatic subline (MTLn3) was significantly smaller than that of MTC cells (7). In vitro study on MTLn3 and MTC cells indicated that the highly metastatic MTLn3 cells were more adhesive than the latter to LEs (17); moreover, the difference between the two in adhesion to lung-derived subendothelial matrices was greater than the difference observed with endothelial monolayers (18). This suggests that the observed difference in lung accumulation was not due to mechanical trapping but was probably due to specific adhesion and/or invasion. Therefore, the initial difference of accumulation between B16BL6 and RAW117 cells may also be due to the differential adhesiveness of these cells to lung endothelium. An alternative explanation for the distinctive release rate of these cells from the lungs, other than differential adhesiveness, is differential deformability of the cells. RAW117 cells may have a capacity to migrate through small capillaries in the lungs.

Noninvasive analyses by PET demonstrated that trafficking of
Differential Metastatic Tumor Cell Trafficking

Fig. 7. BAS images of lung accumulation of $[^{125}]$IUDR-labeled B16BL6 melanoma and RAW117 lymphoma cells. BAS analysis of $[^{125}]$IUDR-labeled B16BL6 and RAW117 cells was performed as described in “Materials and Methods.” Images represent the accumulation in the lung at 15 (a) and 120 min (b) postinjection. The arrowhead indicates the meson, and the labels under the frames represent left (L) or right (R) distance from the meson. Similar results were obtained in two separate experiments.

Lung metastatic B16BL6 melanoma cells was different than that of liver metastatic RAW117 lymphoma cells. Because BAS analysis shows the colonial accumulation of the cells, we speculate that the mode of trafficking of metastatic cells is as follows. At first, each cell is trapped in the capillary vessel due to its narrow width compared with the cell size; this view is consistent with the observation by high-resolution intravital videomicroscopy (9). Then the cell gradually moves through the capillary vessel, if there are no specific interactions with the endothelial cells. This may be the case for RAW117 cells in the lungs. On the other hand, if there

Fig. 8. BAS images of liver accumulation of $[^{125}]$IUDR-labeled B16BL6 melanoma and RAW117 lymphoma cells. BAS analysis of $[^{125}]$IUDR-labeled B16BL6 and RAW117 cells was performed as described in “Materials and Methods.” Images represent the accumulation in the liver at 15 (a) and 120 min (b) postinjection. The arrowhead indicates the meson, and the labels under the frames represent left (L) or right (R) distance from the meson. Similar results were obtained in two separate experiments.
are specific interactions between the metastatic cell and endothelia, the cell becomes arrested in the tissue. This may occur for B16BL6 cells in the lungs and for RAW117 cells, which pass through the lungs, in the liver. The B16BL6 cells that fail to interact with the lungs continue through the bloodstream, and some of these cells are trapped during the next passage through the lung capillaries. If a former cell is arrested in the lungs, the cells coming after or in the second passage may interact more easily with the lung endothelium due to the slower blood flow, and such cycles result in colonial accumulation of the cells in the target organ, as was detected by BAS analysis. In the case of RAW117 cells, a similar process may occur in the liver.

For the specific interactions mentioned above, adhesion molecules such as integrins and selectins may play an important role. In fact, integrins are known to be related to metastatic potential (19, 20); and RAW117-H10 cells were reported to express integrin avb3, which may relate to their metastatic ability to enter the liver (21). Selectin ligands, sialyl Lewis X and sialyl Lewis a, are also reported to be important for metastatic potency (22). In fact, E-selectin was observed to redirect the site of metastasis in experiments using E-selectin transgenic mice (23). We observed that sialyl Lewis X suppressed the accumulation of B16BL6 melanoma cells in the lungs after i.v. injection (24). Other than integrins and selectins, annexin II on the surface of RAW117 cells was also proposed as an adhesion molecule interactive with liver endothelial cells (25).

Taken together, the results obtained by PET provide new information suggesting that the trafficking of tumor cells in vivo is strongly influenced by tumor cell adhesion to the microvascular endothelium. Poorly adhering cells in the microvasculature of the lungs are rapidly released. Thus, being the first organ encountered after the administration of tumor cells may not be the only reason for such an organ to serve as the site of accumulation, although many experiments will be required to prove this hypothesis. For example, the effects of the site of injection should be carefully assessed. When B16BL6 cells were injected into tail veins, there was little accumulation of these cells in the liver. On the contrary, RAW117 cells accumulated in the liver in a time-dependent manner after i.v. injection into tail veins. The accumulation was slightly more intense for RAW117-H10 cells than it was for RAW117-P cells by PET analysis. This is consistent with the data that RAW117-H10 cells adhered more strongly than RAW117-P cells did to the HSEs (Fig. 1; Ref. 13). Therefore, the differential accumulation of RAW117 cells in the liver seems to reflect the adhesive ability of these sublines. A previous study that determined the accumulation of RAW117-H10 and RAW117-P by organ removal did not show the differential accumulation of these cells in such an early stage (26). This discrepancy might be explained by the possibility that the adhesion of some of these cells might be weak enough to permit cell dissociation during the process of an invasive method.

Table 3 Tissue distribution of [125I]IUDR-labeled metastatic tumor cells

ROI mean represents the percentage of radioactivity accumulated in 1 mg of tissue per total of injected labeled cells. Data indicate mean ± SD (n = 4). BAS analysis was performed as described in “Materials and Methods.” Imaging plates were exposed for 60 mm (for lung analysis) or 6 days (for other tissues) to the whole-body slice specimens taken from labeled cell-inoculated mice, and the autoradiographs were analyzed with a BAS2000II.

<table>
<thead>
<tr>
<th></th>
<th>Lung</th>
<th>Liver</th>
<th>Spleen</th>
<th>Kidney</th>
<th>Bone marrow</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. 15 min postinjection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAW117-P</td>
<td>985.8 ± 97.3</td>
<td>89.5 ± 15.2</td>
<td>37.5 ± 10.2</td>
<td>10.5 ± 0.2</td>
<td>8.7 ± 1.0</td>
<td>12.2 ± 3.0</td>
</tr>
<tr>
<td>RAW117-H10</td>
<td>1738.2 ± 1018.3</td>
<td>171.7 ± 30.1</td>
<td>52.2 ± 8.5</td>
<td>16.6 ± 1.2</td>
<td>20.9 ± 5.2</td>
<td>27.2 ± 2.7</td>
</tr>
<tr>
<td>B16BL6</td>
<td>5015.2 ± 640.1</td>
<td>102.4 ± 29.6</td>
<td>24.2 ± 8.2</td>
<td>17.9 ± 3.0</td>
<td>15.7 ± 4.2</td>
<td>94.7 ± 87.0</td>
</tr>
<tr>
<td><strong>B. 120 min postinjection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAW117-P</td>
<td>160.2 ± 10.6</td>
<td>220.0 ± 71.1</td>
<td>268.4 ± 11.2</td>
<td>109.1 ± 37.0</td>
<td>112.4 ± 39.7</td>
<td>81.9 ± 31.6</td>
</tr>
<tr>
<td>RAW117-H10</td>
<td>165.9 ± 62.8</td>
<td>195.6 ± 58.9</td>
<td>323.1 ± 90.9</td>
<td>79.6 ± 22.3</td>
<td>111.3 ± 25.3</td>
<td>77.5 ± 21.5</td>
</tr>
<tr>
<td>B16BL6</td>
<td>3263.0 ± 748.0</td>
<td>168.9 ± 13.7</td>
<td>95.3 ± 19.1</td>
<td>63.4 ± 7.3</td>
<td>73.4 ± 15.1</td>
<td>58.2 ± 11.1</td>
</tr>
</tbody>
</table>

Fig. 9. BAS images of colonized accumulation of [125I]IUDR-labeled B16BL6 melanoma and RAW117 lymphoma cells in each target organ. BAS analysis of [125I]IUDR-labeled B16BL6 and RAW117 cells was performed as described in “Materials and Methods.” Images represent the accumulation of B16BL6 cells in lung tissue (a) and that of RAW117-H10 cells in liver tissue (b) at 120 min postinjection.
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