Blocking of the Response by Human T-Lymphocytes to Extracts of Autologous Cancer by Monoclonal Antibody to Class-I Major Histocompatibility Complex Gene Products in the Leukocyte Adherence Inhibition Assay

George Shenouda and D. M. P. Thomson
Division of Clinical Immunology, Montreal General Hospital, Montreal, Quebec H3G 1A4, Canada

ABSTRACT

In the leukocyte adherence inhibition (LAI) assay, about 34% of adherent T-cells from patients with breast cancer exhibit nonadherence to glass when incubated with extracts of autologous cancer but not with HLA-A, -B, and -C mismatched extracts of breast cancer. To determine whether the recognition by T-cells of tumor antigen was major histocompatibility complex restricted, major histocompatibility complex antigens in the cancer extracts or on the T-cells were coated with monoclonal antibody (MAb) to nonpolymorphic determinants. Nonadherence of T-cells was antagonized by coating the target cancer extracts with MAb to a common framework determinant of Class I HLA-A, -B, and -C antigens or to the nonpolymorphic β2-microglobulin, which is noncovalently associated with Class I antigens. By contrast, a MAb to a monomorphic determinant on HLA-DR antigens did not change the positive T-cell response. Moreover, coating the T-cells with MAb to HLA-A, -B, and -C did not inhibit the positive T-cell response. The positive LAI response ofuffy coat peripheral blood leukocytes from patients with breast cancer to extracts of allogeneic breast cancer was not affected by coating the cancer extracts with the same MAb, indicating that the antibody-dependent LAI response ofuffy coat peripheral blood leukocytes was not major histocompatibility complex restricted. The results indicate that HLA-A, -B, and -C antigens in extracts of autologous breast cancer restrict the LAI response to tumor antigens of T-cells from patients with breast cancer.

INTRODUCTION

T-cells reacting to foreign non-MHC cell surface antigens such as viral, hapten-modified, and minor histocompatibility antigens are MHC restricted, i.e., they will only react to cells expressing both the immunizing antigen and the appropriate self-MHC gene products (2, 16, 53, 69). The major MHC codes for cell membrane glycoproteins, which are recognized by thymus-derived T-lymphocytes during their induction and the performance of their effector function. The classical Class I MHC transplantation antigens are expressed on all adult cells, exemplified by the murine H-2K, and D and the human HLA-A, -B, and -C antigens, and are involved in CTL recognition. Class-II MHC gene products, which are coded by the I region in mice and the D region in humans, are expressed mainly on B-cells and macrophages and are recognized by helper T-cells (45). Although the basis for the requirement of dual recognition of foreign antigen and MHC molecules is not known, MHC restriction of T-helper and T-killer function came to light in the years 1973 and 1974 and was a significant breakthrough in the understanding of the function of the MHC (70).

Whether MHC antigen recognition is also necessary for T-cell interaction with tumor cells has been more controversial (7). Most studies of animal tumors induced by viruses have shown that for optimal cytotoxicity the tumor must share Class I MHC antigens with the cytotoxic T-cell (3, 4, 6, 12–15, 44, 46–49, 55, 61). However, a few studies have found contradictory results (22, 60). For chemically induced tumors evidence from F1 parent chimeras has shown H-2 restriction of the T-cell response (33); and in H-2 loss, variant sublines of a chemically induced sarcoma which expressed the same tumor-specific transplantation antigen, T-cells are H-2 restricted in growth inhibition (1). Moreover, anti-H-2 antibodies are able to block the antitumor response (10, 52). In studies of cytotoxicity against human cancer, specific cytotoxicity is found most often when the tumor cells and lymphocytes are autologous (9, 35, 62–64, 68).

Tumor-specific immunity to human cancers can be measured by the antigen-induced LAI phenomenon (19, 21). The nonadherence of leukocytes to glass depends on immunological recognition of tumor antigen in extracts and synthesis from the leukocytes' membrane phospholipids of leukotriene-like metabolites (57, 59), which increase the nonadherence ofboth the cell producing the metabolites as well as bystander cells (5). In experimental animal tumors, there is evidence for both T-cells andarmed macrophages recognizing tumor antigen (11, 23, 26, 27, 42, 50). In human cancer, our results show that armed monocytes by an antibody-dependent mechanism recognize tumor antigen in extracts ofautologous and allogeneic cancer provided that the tumor is of the same organ and histogenesis (18, 37). On the other hand, T-cells react to only autologous cancer in the LAI assay (54), which raises the possibility that tumor antigen recognition is MHC restricted. In this study, MAb to MHC structures was used to block T-cell recognition of MHC antigens. The results of the LAI experiments indicate that Class I MHC antigens restrict T-cell recognition of human cancer antigens in breast cancer extracts.

1 Supported by grants from the Medical Research Council of Canada and the National Cancer Institute of Canada.
2 Recipient of Medical Research Council Fellowship.
3 To whom requests for reprints should be addressed, at Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4, Canada.
4 The abbreviations used are: MHC, major histocompatibility complex; CTL, cytotoxic lymphocyte; LAI, leukocyte adherence inhibition; MAb, monoclonal antibody; NAI, nonadherence inhibition; PBL, buffy coat peripheral blood leukocytes; PGE2, prostaglandin E2.

Received October 5, 1983; accepted March 22, 1984.
HLA Restriction of Tumor-immune T-Cells

MATERIALS AND METHODS

Reagents. Heparinized Vacutainer tubes (Becton-Dickinson & Co., Mississauga, Ontario, Canada), PGE₂ (Sigma Chemical Co., St. Louis MO), Medium 199, fetal bovine serum (Flow Laboratories, Inc., Mississauga, Ontario, Canada), Ficol-Paque (Pharmacia Fine Chemicals Inc., Montreal, Quebec, Canada), Linbro multiwell plastic plate (35 × 10-mm flat-bottomed wells) (Flow Laboratories, Inc., McLean, VA), and nylon wool Leuko-Pack (Baxter Travenol; Fenwal Laboratories, Inc., Deerfield, IL) were purchased. MAb to T-cells, to human β₂-microglobulin (catalogue No. 5370; Becton-Dickinson, Sunnyvale, CA), to monocytes (catalogue No. 201-20207; Bethesda Research Laboratories, Bethesda, MD), to HLA-A,-B, and -C and to HLA-DR antigens (catalogue No. 0201-2007; Cappel Laboratories, Cochranville, PA) were purchased.

MAb. MAb (IgG₁) to a monomorphic determinant of HLA-A,-B, and -C is purified from ascites fluid by the supplier. The monoclonal antibody reacts with all HLA-positive cells and is directed against a common framework determinant on the M, 45,000 polypeptide which is associated with β₂-microglobulin. Peripheral blood cells (1 × 10⁶) are stained by 100 µl of a 1:12 dilution (0.8 µg). The MAb (IgG₁) to a monomorphic constant region of the bimolecular glycoprotein complex (molecular weight of 29,000 and 34,000) of HLA-DR is purified by the supplier from nude mouse serum and used at a dilution of 1:35 (0.3 µg). MAb to a non-polymorphic M, 12,000 human β₂-microglobulin is purified by the supplier by ion-exchange chromatography from serum and/or ascites fluid of tumor-bearing BALB/c mice and is used at a 1:100 dilution (0.6 µg).

Cancer Extracts. Solid tumor metastases in the liver were processed as described previously (19). Fresh primary breast cancers were obtained from patients having a mastectomy and were processed and used in the same manner as the extracts prepared from metastases in the liver. The extract of primary breast cancer was paired with a nonspecific control extract of malignant melanoma and was titrated and used at ~100 µg in the tube LAI assay. Leukocytes from control subjects were equally nonadherent to the 2 extracts.

Preparation of PBL. Venous blood from patients with breast cancer or unrelated diseases was drawn into heparinized Vacutainer tubes. PBL were isolated by sedimentation, and RBC were lysed (19). In all experiments, 1 × 10⁶ PBL were incubated with 2.5 × 10⁻⁶ M PGE₂ at 20° for 5 min, PBL or T-cells from patients with breast cancer or control subjects were diluted to 1.0 ml and plated at 1 × 10⁶/ml/test tube to which was added ~100 µg in 0.1 ml of extracts of either autologous or allogeneic breast cancer in one set of tubes and malignant melanoma to the other set; Medium 199 was added to bring the final volume to 0.5 ml. After 2-hr incubation horizontally at 37° in 5% CO₂, the tubes were placed vertically, and a sample of nonadherent cells in each tube was plated on to a hemocytometer and counted with a × 10 objective over 4 fields by computerized image analysis. The computer-linked instruments calculated the mean number of nonadherent cells and expressed the results in terms of the percentage of change in nonadherence compared with that of the nonadherent cells in control tubes (19) or percentage of difference in nonadherent cells between control and experimental tubes:

\[ \text{NAI} (\%) = \frac{A - B}{B} \times 100 \]

where A equals the number of nonadherent cells in the sample after incubation with the breast cancer extract, and B equals the number of nonadherent cells in the sample after incubation with the malignant melanoma extract. This difference in nonadherence has been expressed as a proportional change (NAI) rather than an absolute change. In previous studies, leukocytes from more than 95% of subjects without breast cancer had proportional changes (NAIs) of less than 30, distributed normally about zero, whereas leukocytes from most patients with early cancer had NAIs >30 (36). In this study, the percentage of difference in nonadherent cells is also calculated.

Blocking of T-Cell Response with MAbs. One mg of both specific and nonspecific cancer extracts were incubated for 1 hr at 4° with the MAb in a final volume of 1 ml. The MAb to HLA-A,-B, and -C, to HLA-DR antigen, and to human β₂-microglobulin were at 1:12, 1:35, and 1:100 dilutions, respectively, in the 1 ml. To each LAI tube in 100 µl was added 1 × 10⁶ leukocytes or T-cells, 300 µl medium, and 100 µl of the mixture containing ~100 µg of the cancer extract and the diluted MAb. The final dilution of the MAb in the LAI assay was 1:80 for MAb to HLA-A, -B, and -C, 1:175 for MAb to HLA-DR, and 1:500 for MAb to β₂-microglobulin. The MAbs were used at dilutions that were equipotent in coating HLA-A, -B, and -C molecules, HLA-DR molecules, or β₂-microglobulin molecules on the cell surface of 10⁶ PBL by indirect immunofluorescent techniques. In addition, 1 × 10⁷ T-cells were incubated in 1 ml of medium containing MAb to HLA-A, -B, and -C diluted 1:12 for 30 min at 4°, washed 3 times in Medium 199 to remove excess MAb, and then resuspended at 1 × 10⁶ cells/ml in Medium 199 before being plated in the tube LAI assay at 1 × 10⁶ cells/0.1 ml to which was added the cancer extracts (100 µg in 100 µl) and 300 µl of medium.

6 D. M. P. Thoman. Reversible abnormal nonadherence to glass and responsiveness to chemotactants of leukocytes from patients with advanced cancer, submitted for publication.
G. Shenouda and D. M. P. Thomson

RESULTS

Methodological Considerations. Leukocytes, including T-cells, from different patients show variations in nonadherence when incubated with control cancer extracts. To control for this, leukocytes are always incubated with 2 different cancer extracts. The response of the leukocytes is determined by the percentage of change (NAI) or percentage of difference in nonadherence in experimental tubes compared with the same leukocytes in the control tubes. In this manner, it is possible to be certain that changes in glass-adherent properties of leukocytes under differing experimental conditions is not nonspecific. The variation in nonadherent leukocytes is related both to fluctuations of innate nonadherence and to the actual measurements because of plating of cells and reading of nonadherent cells. For this reason, the number of nonadherent cells might be somewhat different in different experimental pairings; nonetheless, the percentage of change or percentage of difference in nonadherent cells is highly reproducible in paired tubes.

T-Cell Nonadherence to Glass and the Effect of MAb to HLA-A, -B, and -C and to HLA-DR Antigens Incubated with the Cancer Extracts. T-cells from patients with breast cancer repeatedly exhibited increased nonadherence when incubated with extracts of autologous but not allogeneic breast cancer in this and in a previous study (54) (Table 1). Of the 524 ± 16 T-cells counted immediately after plating in the tubes, about 227 were nonadherent with the control malignant melanoma extract after 2 hr; of the remaining 297 (524 - 227) adherent T-cells, about 100, or 34% (100/297), were nonadherent with the autologous cancer extract (Table 1). To investigate whether the response was MHC restricted, the MHC antigens in the target cancer extracts were coated with MAb specific for common determinants on all HLA-A, -B, and -C antigen or HLA-DR antigen molecules. Pretreatment of the cancer extracts with MAb to HLA-A, -B, and -C inhibited the positive LAI response of T-cells to the autologous cancer extract, with the NAIs of the T-cells falling from 45 ± 6 to 2 ± 2. The effect of the MAb on the target cancer extracts was dose dependent; 1:12, 1:18, and 1:24 dilutions of the MAb on the stock extract produced 90, 72, and 12% inhibition of the T-cell LAI response, respectively. By contrast, MAb to HLA-DR antigen did not affect the positive response to autologous breast cancer; the LAI response of T-cells gave an NAI of 55 ± 11 (Table 1). T-cells from patients with breast cancer exhibited no increased nonadherence to extracts of allogeneic breast cancer compared to malignant melanoma, and neither MAb added to the extracts changed the response. Likewise, T-cells from control subjects showed no LAI to the breast cancer extracts compared to the malignant melanoma extract, and neither MAb added to the extracts affected the response (Table 1).

Effect of MAb on T-Cells. In the above experiments, not all the MAb may have been bound by the cancer extracts, and free MAb may have bound to the T-cells. To rule out the possibility that the MAb to HLA-A, -B, and -C was inhibiting the LAI response by binding to T-cells, T-cells were preincubated with MAb to HLA-A, -B, and -C antigens and washed and plated in the LAI assay. The NAI of T-cells tested without MAb pretreatment was 48 ± 6 and after treatment the NAI was 35 ± 4 (p > 0.2) (Table 2). Although there was a slight decrease in the response, T-cells still showed significantly more nonadherence with the extracts of autologous breast cancer compared to malignant melanoma indicating that MAb to HLA-A, -B, and -C inhibited the T-cell LAI response to autologous cancer by coating HLA-A, -B, and -C antigens in the target cancer extract.

T-Cell Nonadherence to Glass and the Effect of Coating Cancer Extract with MAb to Human β2-Microglobulin. To add further support to the importance of Class-I MHC antigens in the LAI T-cell response, we examined the effect of coating with MAb the noncovalently bound M, 12,000 β2-microglobulin of the Class-I MHC antigen in the target cancer extracts. When MAb to human β2-microglobulin was incubated with the extracts of autologous breast cancer, it also inhibited the LAI response of T-cells from patients with breast cancer (Table 3). As a control, MAb to human β2-microglobulin showed no effect on the nonadherence of T-cells from patients with breast cancer or control subjects when incubated with the extracts of allogeneic breast

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effect of coating MHC molecules of the cancer extracts with MAb to HLA-A, -B, and -C or HLA-DR antigens on the nonadherence to glass of T-cells from patients with breast cancer incubated with autologous cancer extract</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor of T-cells</th>
<th>Pretreatment of cancer extract</th>
<th>Primary breast cancer</th>
<th>Malignant melanoma</th>
<th>% Δ in non-adherence (NAI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>None</td>
<td>200 ± 30</td>
<td>225 ± 30 (29)^d</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Autologous</td>
<td>Anti-HLA-A, -B, and -C</td>
<td>235 ± 21</td>
<td>232 ± 22 (2)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>None</td>
<td>Anti-HLA-DR</td>
<td>327 ± 30</td>
<td>216 ± 27 (34)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Allogeneic</td>
<td>None</td>
<td>292 ± 42</td>
<td>267 ± 42 (9)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>None</td>
<td>Anti-HLA-A, -B, and -C</td>
<td>224 ± 45</td>
<td>207 ± 24 (8)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>Control subject</td>
<td>None</td>
<td>233 ± 9</td>
<td>204 ± 20 (12)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>None</td>
<td>Anti-HLA-A, -B, and -C</td>
<td>253 ± 3</td>
<td>262 ± 20 (4)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>None</td>
<td>Anti-HLA-DR</td>
<td>248 ± 44</td>
<td>233 ± 31 (6)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>None</td>
<td>Anti-HLA-DR</td>
<td>226 ± 26</td>
<td>191 ± 13 (15)</td>
<td>&gt;0.3</td>
</tr>
</tbody>
</table>

^a Student’s dependent t test.
^b NAI >30 is positive, <30 is negative.
^c Mean ± S.E. There were 524 ± 16 cells nonadherent immediately after 1 × 10^6 T-cells were plated.
^d Numbers in parentheses, percentage of difference.
^e Student’s independent t test (p < 0.01).
^f Student’s dependent t test (p < 0.01).
^g Student’s dependent t test (p > 0.2).
cancer and malignant melanoma (Table 3).

PBL Nonadherence to Glass and the Effect of MAb to HLA-A, -B, and -C and HLA-DR Antigens Incubated with Cancer Extracts. PBL, in contrast to T-cells from patients with breast cancer, react with extracts of allogeneic breast cancer (19). Previous studies indicated that the response depends on tumor antigen cross-linking cytophilic antibody on monocytes and releasing leukotriene-like metabolites (18, 37, 57-59). Table 4 shows experiments to further examine both the specificity of inhibition by MAB to HLA antigens and the difference in antigen recognition. When both cancer extracts had been pretreated with MAB to either HLA-A, -B, and -C or HLA-DR molecules, the positive LAI response of PBL from patients with breast cancer to the extracts of allogeneic breast cancer remained unchanged (Table 4). Moreover, a comparison of nonadherence of leukocytes from normal control subjects incubated with cancer extracts either containing MAB or not showed no change (Table 4).

DISCUSSION

The results of this study show that tumor-immune T-cells exhibit a marked preference for extracts of autologous cancer. Specific nonadherence of T-cells induced by HLA-A, -B, and -C mismatched extracts of breast cancer was not observed. The T-cell nonadherence to the autologous breast cancer extract was substantially antagonized in a dose-dependent fashion when the breast cancer extract was coated with MAB to a common framework determinant of Class I MHC antigens or β2-microglobulin, a molecule which noncovalently associates with HLA-A, -B, and -C. This provides direct evidence for the T-cell response in LAI being restricted by the necessity for dual recognition of tumor antigen and Class I MHC antigens. Monocyte antibody-dependent recognition of tumor antigen in LAI, in sharp contradiction, was not antagonized by MAB to MHC antigens.
indicating that it was independent of MHC restriction.

Nonadherence of leukocytes in the LAI assay is affected by leukotrienes and thromboxanes (54, 57, 59). Moreover, nonadherence is an active cellular event (59). Either authentic leukotrienes or similar metabolites and thromboxanes generated from membrane phospholipids of leukocytes, which have bound antigen immunologically, mediate the nonadherence (57–59). Not only do the cells that bind antigen and produce the leukotrienes and thromboxanes exhibit nonadherence, but so do bystander cells. Of the adherent leukocytes or T-cells in the LAI assay, about 29 to 34% exhibit nonadherence to either authentic chemoattractants or to immunologically generated leukotrienes or thromboxanes (54, 57, 59). Thus, for a positive T-cell response in LAI, it is necessary for a few T-cells to recognize antigen and these same few cells plus other cells to have their nonadherence affected by the synthesized leukotrienes and thromboxanes. T-cells of T8 and T4 phenotype show about 34% nonadherence to authentic leukotrienes, and thus, both cell types will show nonadherence to leukotrienes or thromboxanes generated immunologically from even a few T-cells.

In the experiments, serious consideration was given to the possible nonspecific effects of the MAbs on the T-cell nonadherence: (a) the nonadherence of normal T-cells to the extracts with or without added MAb was the same; (b) MAb bound to T-cells did not affect the LAI response to autologous cancer; (c) 2 independent MAbs, one binding to Class I MHC antigen and the other to noncovalently attached B2-microglobulin molecule of the target tissues, antagonized the response, whereas MAb to Class II MHC antigens in the target cancer extracts did not interfere with the response; and (d) the same MAb that inhibited the T-cell LAI response had no effect on the LAI response of PBL, which is antibody dependent, to an extract of allogeneic breast cancer. For these reasons, it seems unlikely that the binding of MAb to the HLA-A, -B, and -C antigens or to B2-microglobulin of the cancer extracts blocks the nonadherence response nonspecifically.

Specific inhibition of the LAI response occurred despite the fact that the MAb does not bind to the polymorphic regions of HLA-A, -B, and -C antigen molecules which actually restrict T-cell function (29). In analogous results with cytotoxic T-cell recognition of influenza virus-infected cells, McMichael et al. (40) suggest that the inhibition reflects either a direct steric hinderance about the polymorphic site, because the IgG MAb molecule is about 2.5 times the size of an HLA molecule, or as may be more probable with MAb to B2-microglobulin structures, an antibody-induced conformational change in the HLA molecule (32). It has been demonstrated previously that steralic hinderence of MHC antigens with antibodies can block T-cell recognition of foreign cell surface antigens. Anti-H-2 antibodies directed against the serological specificities of the target inhibit the lysis of virally infected cells (28), virus-induced neoplastic cells (12, 13, 51), or neoplastic cells (8, 10, 52) by H-2-compatible CTL, whereas anti-H-2 antibodies to unrelated H-2 antigens and to non-H-2 antigens or coating of H-2 antigens on the effector T-cells does not interfere with the lytic event. In humans, MHC restriction of CTL was first described in secondary in vitro responses against influenza virus (30, 38, 39, 41). Certain genes of the HLA-B locus have been recently shown to regulate mumps virus-specific CTL (30). Lysis of influenza-infected target cells by sensitized CTL is blocked in a dose-dependent fashion by MAb to monomorphic HLA determinants on the target cells, indicating that HLA molecules are the restrictive element (40). Epstein-Barr virus-specific CTL recognize and kill only those virus-transformed B-cells derived from donors whose HLA-A and -B antigen type matches that of the effector cell donors (43), and experiments with blocking by MAb to common determinants of HLA-A, -B, and -C and to B2-microglobulin clearly demonstrate that the serologically defined HLA-A, -B, and -C region antigens on the virus-transformed cell surface are indeed the polymorphic elements which impose the genetic restriction (65, 66). The tumor antigen recognized by the antibody-dependent monocyte response is in the membrane (19, 56), and coisolates with B2-microglobulin after solubilization of the membrane proteins by limited papain digestion (56). Moreover, the tumor antigen, Class I HLA antigens and B2-microglobulin are shed from tissue-cultured cancer cells and are found in the top fraction after spent medium is centrifuged through KBr, as determined by blind LAI testing of the fractions from 2 unrelated tumors (25). The tumor antigen recognized by T-cells is unknown, and whether it is the same molecule as recognized by the antibody-dependent response is also unknown. However, it is probable that the antibody response is T-dependent and that tumor-immune T-cells are generated also to the same tumor antigen.

Our results indicate that tumor-immune T-cells are generated by the developing cancer and should be able to react in vivo with cancer cells. It is suggested that a paucity of HLA-A, -B, and -C antigen expression by tumor cells may allow some tumors to escape from immune attack (31). Although the primary tumors were not examined for expression of Class I antigens, our results indicate that expression of Class I antigens by the cancer cells did not limit T-cell recognition of the foreign tumor antigen. Whether metastatic cancer cells have undergone an immunoselection mechanism for Class I antigens is unknown. However, the antibody-dependent response in LAI is equal for most patients with advanced and early cancer (36, 57, 59).

ACKNOWLEDGMENTS

We thank Dr. W. P. Duguid, Pathologist-in-Chief, for portions of the cancer specimens. We also thank Drs. J. K. MacFarlane and other members of the Department of General Surgery for advising us of patients with cancer. We thank Mary Bergin for typing this manuscript.

REFERENCES


20. Guttman, R. D., and Poulsen, R. S. Fluorescence activated cell sorter analysis
14. Gooding, L. Specificity of killing by T lymphocytes generated against syngeneic
10. Germain, R. W., Dorf, M. E., and Benacerraf, B. Inhibition of T-lymphocyte
35. Lotze, M. T., Grimm, E. A., Maximuder, A., Straussner, J. L., and Rosenberg,
36. MacFarlane, J. K., Thomson, D. M. P., Phelan, K., Shenouda, G., and Scan-
in vitro detection of cell-mediated immunity to individual tumor-specific antigens

H1A Restriction of Tumor-immune Cells

1984 Association for Cancer Research.
G. Shenouda and D. M. P. Thomson


Blocking of the Response by Human T-Lymphocytes to Extracts of Autologous Cancer by Monoclonal Antibody to Class-I Major Histocompatibility Complex Gene Products in the Leukocyte Adherence Inhibition Assay

George Shenouda and D. M. P. Thomson


Updated version  Access the most recent version of this article at:  
http://cancerres.aacrjournals.org/content/44/7/2762

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.