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**Purpose:** As a first step for the development of a new cancer immunotherapy strategy, we evaluated whether antibody-mediated coating by MHC class I–related chain A (MICA) could sensitize tumor cells to lysis by natural killer (NK) cells.  
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**Results:** Flow cytometry analysis showed an efficient coating of MICA-negative human cancer cell lines with the Fab-rMICA conjugates. This was strictly dependent on the expression of the appropriate tumor-associated antigens in the target cells. Importantly, preincubation of the tumor cells with the appropriate Fab-rMICA conjugate resulted in NK cell–mediated tumor cell lysis. Antibody blocking of the NKG2D receptor in NK cells prevented conjugate-mediated tumor cell lysis.  
**Conclusions:** These results open the way to the development of immunotherapy strategies based on antibody-mediated targeting of MICA.

Since the Food and Drug Administration approval of anti-CD20 (rituximab) and anti-HER2 (trastuzumab) monoclonal antibodies (mAb) for the therapy of non-Hodgkin lymphomas and breast carcinomas, respectively, these antibodies, used alone or associated with chemotherapy, have been included as almost routine therapy for a vast number of patients suffering from these tumors. However, despite encouraging results, the percentage of complete remission remains low and there is a definitive need to improve the capacity of these mAbs to induce cytotoxicity against targeted tumor cells, e.g., by mutating their Fc part or by coupling radioisotopes (1), drugs (2), or cytokines (3). To this end, we (4, 5) and others (6, 7) recently described a new type of conjugate consisting of antitumor antibody Fab’ fragments chemically coupled or fused with soluble MHC class I molecules presenting antigenic viral peptides. These conjugates target tumor cells overexpressing the relevant membrane-bound antigen through the antibody part of the conjugate and coat the tumor cells with highly antigenic MHC class I/viral peptide complexes. Tumor target cells incubated with the relevant antitumor Fab-MHC class I/viral peptide were efficiently killed by the peptide/MHC–specific CTL in vitro (4, 5). This very attractive strategy also yielded some promising in vivo tumor therapy results (8, 9). However, the fact that MHC class I molecules are heterotrimERIC and highly polymorphic represents a limitation for clinical applications.

For these reasons, we have considered here the antibody-mediated tumor targeting of a nonclassic MHC class I molecule [i.e., the so-called MHC class I–related chain A (MICA)]. MICA is a stress-inducible molecule composed of α1, α2, and α3 MHC class I–like domains; however, it does not associate with β2 microglobulin and antigenic peptide (10). It is expressed in normal intestinal epithelium (11) and in diverse tumors of epithelial origin (12, 13). Although up to 54 different alleles of MICA have been described (14), there is a predominance of allele 008 with a frequency of 67% in the Caucasian population (15) and 31% in the Oriental population (16). MICA binds to the NKG2D receptor expressed in natural killer (NK) cells, as well as in γδ and activated αβ CD8+ T lymphocytes (17, 18). It can directly activate NK cells (17, 19) and coactivate CD8+ αβ CTL (20), representing a bridge between innate and acquired immunity. Indeed, NK cells are known to play an essential role in antitumoral immunity (21), especially to eliminate tumor cell variants that have lost MHC class I expression (22). Moreover, during tumor cell proliferation and tumor volume increase, a downregulation of MICA expression can occur due to liberation by the tumor cells of a soluble form of MICA (23, 24) and selection of MICA-negative tumor cells during the metastatic process (25).  

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**Cancer Therapy: Preclinical**

**MHC Class I–Related Chain A Conjugated to Antitumor Antibodies Can Sensitize Tumor Cells to Specific Lysis by Natural Killer Cells**  
Claire Germain,¹ Christel Labroutet,¹ Valérie Cesson,² Alena Donda,² Werner Held,³ Jean-Pierre Mach,² André Pèler grin,¹ and Bruno Robert¹

**Abstract**  
**Purpose:** As a first step for the development of a new cancer immunotherapy strategy, we evaluated whether antibody-mediated coating by MHC class I–related chain A (MICA) could sensitize tumor cells to lysis by natural killer (NK) cells.  
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Since the Food and Drug Administration approval of anti-CD20 (rituximab) and anti-HER2 (trastuzumab) monoclonal antibodies (mAb) for the therapy of non-Hodgkin lymphomas and breast carcinomas, respectively, these antibodies, used alone or associated with chemotherapy, have been included as almost routine therapy for a vast number of patients suffering from these tumors. However, despite encouraging results, the percentage of complete remission remains low and there is a definitive need to improve the capacity of these mAbs to induce cytotoxicity against targeted tumor cells, e.g., by mutating their Fc part or by coupling radioisotopes (1), drugs (2), or cytokines (3). To this end, we (4, 5) and others (6, 7) recently described a new type of conjugate consisting of antitumor antibody Fab’ fragments chemically coupled or fused with soluble MHC class I molecules presenting antigenic viral peptides. These conjugates target tumor cells overexpressing the relevant membrane-bound antigen through the antibody part of the conjugate and coat the tumor cells with highly antigenic MHC class I/viral peptide complexes. Tumor target cells incubated with the relevant antitumor Fab-MHC class I/viral peptide were efficiently killed by the peptide/MHC–specific CTL in vitro (4, 5). This very attractive strategy also yielded some promising in vivo tumor therapy results (8, 9). However, the fact that MHC class I molecules are heterotrimERIC and highly polymorphic represents a limitation for clinical applications.

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Here, we describe the production of a new type of conjugate, consisting of antitumor antibody Fab’ fragments coupled to recombinant MICA (rMICA), and show that they can specifically coat tumor cells and induce their lysis by NK cells.

Materials and Methods

Tumor and natural killer cell lines. Human acute monocytic leukemia THP-1 [expressing Fc receptors (Fcr) FcγRI and FcγRII], human breast carcinoma SK-BR-3 and human ovarian carcinoma SK-OV-3 (both expressing Fc receptors including FcγRII), and human B-cell lymphoma Raji cells (expressing CD20) were obtained from American Type Culture Collection (Rockville, MD) and maintained as described by the manufacturer. The murine C15.4.3(AP cell line (kindly provided by Dr. J. Primus, Department of Pathology, Vanderbilt University Medical Center, Nashville, TN; ref. 26) was obtained by transfection of the murine chemo-induced colon carcinoma MC38 (27) with carcioembryonic antigen (CEA) and maintained in DMEM/F12 (1:1) supplemented with 10% FCS, penicillin (100 units/mL)/streptomycin (100 μg/mL), and geneticin (0.8 mg/mL), and, for production batch, in DMEM/F12 (1:1) supplemented with penicillin (100 units/mL)/streptomycin (100 μg/mL) without FCS or geneticin. Recombinant soluble MICA-hFc fusion protein was purified from the culture supernatant by affinity chromatography on a HiTrap Protein G column (Amersham Pharmacia Biotech AB, Uppsala, Sweden) and then by gel filtration on a Superdex 200 column (Amersham Pharmacia Biotech).

Monoclonal antibodies and Fab’ fragments. Anti-CEA mAb 35A7 is a murine IgG1 specific for CEA that does not bind to cross-reacting antigens expressed by granulocytes (31). Trastuzumab (Herceptin; Genentech, Inc., San Francisco, CA) is a recombinant humanized mAb of human IgG1κ isotype specific for HER2 extracellular domain (32). Rituximab (Rituxan; IDEC Pharmaceuticals Corporation, San Diego, CA) is a chimeric murine/human mAb of human IgG1κ isotype directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes (33). The F(ab’)2 fragments from these mAbs were prepared by pepsin digestion (Sigma Chemical Co., St. Louis, MO) at 3:100 (w/w) ratio of pepsin/IgG in 0.2 mol/L sodium acetate buffer (pH 4.0) for 14 hours for mAb 35A7, 4 hours for trastuzumab, and 3 hours for rituximab, followed by gel filtration on a Superdex 200 column. Fab’ fragments were obtained by mild reduction of the F(ab’)2 with 10 mmol/L cysteamine (Fluka, Buchs, Switzerland) in PBS with...
on SDS-PAGE. The amount of protein in each fraction was determined by the Bradford method (Bio-Rad, Hercules, CA).

**SDS-PAGE analysis and Western blotting.** The antitumor Fab-rMICA conjugate and rMICA were analyzed by Western blotting. After electrophoresis on a 6% SDS-PAGE gel under nonreducing conditions, the proteins were transferred to a nitrocellulose membrane. The membrane was saturated for 2 hours in PBS-0.1% Tween 20 containing 5% nonfat dry milk at room temperature under agitation and then, after washing, incubated with a polyclonal rabbit anti-MICA serum specific for the α2 domain of the MICA molecule (kindly provided by Prof. A. Toubert, Laboratoire d’Immunologie et d’Histocompatibilité, Institut National de la Santé et de la Recherche Medicale Unit 396, Institut Universitaire d’HématoLOGie, Hôpital Saint-Louis, AP-HP, Paris, France; ref. 34), and revealed by a horseradish peroxidase–conjugated goat anti-rabbit IgG whole molecule (Sigma-Aldrich), or the membrane was incubated directly with a horseradish peroxidase–conjugated antimouse IgG whole molecule (Chemicon, Hampshire, United Kingdom). After washing, both membranes were revealed using the ECL Western Blotting System (Amersham Pharmacia Biotech).

Flow cytometry. MICA expression on tumor cell lines was assessed by flow cytometry with supernatant of the BAM 195 hybridoma, secreting an anti-MICA MICA IgG1 mAb, kindly provided by Prof. D. Pende (IST, Genova, Italy; ref. 17). Expression of NGK2D on NKL and NK-92 was assessed using a mouse anti-human NGK2D IgG (R&D Systems, Minneapolis, MN). An FcR blocking reagent (Miltenyi Biotec, Auburn, CA) was used as recommended by the manufacturer (20 µL per 1 × 10^6 cells for 15 minutes at 4°C) in flow cytometry experiments and in reverse antibody-dependent, cell-mediated cytotoxicity lysis assays (see below) for blocking rMICA binding to the FcRs on the THP-1 cells. Specificity of each of the different Fab-rMICA conjugates for the targeted tumor-associated antigens (TAA) was assessed as follows: Tumor cells (5 × 10^5) were first incubated with each of the different antitumor Fab-rMICA conjugates for 1 hour at 4°C, washed, then incubated with murine anti-MICA mAb BAM 195 for 1 hour at 4°C washed, and finally incubated with a goat anti-mouse IgG Fc-specific FITC-conjugated mAb (Sigma-Aldrich) for 45 minutes at 4°C. Washed cells were finally analyzed on a FACScan (Becton Dickinson, San Jose, CA). As controls, cells were first incubated with parental intact mAbs or BAM 195 antibody, washed, and then incubated with goat anti-mouse IgG Fc-specific or goat anti-human IgG Fc-specific (Sigma-Aldrich) FITC-conjugated antibodies or the cells were incubated with the different secondary antibodies. To evaluate NGK2D expression at the NK cell surface, NKL and NK-92 cells (5 × 10^5) were first incubated with mouse anti-hNGK2D IgG, washed, and then incubated with a goat anti-mouse IgG Fc-specific FITC-conjugated mAb. To evaluate the specific FcR coating of rMICA at the THP-1 cells surface, THP-1 cells (5 × 10^5) were incubated with rMICA, washed, incubated with the BAM 195 antibody, washed, and finally incubated with a goat anti-mouse IgG Fc-specific FITC-conjugated mAb, or preincubated as recommended by the manufacturer with the FcR blocking reagent before incubation with rMICA.

**Chromium release assay.** NK cell–mediated cytotoxicity was measured by the chromium release assay. Tumor target cells (2 × 10^5 in 100 µL) were coincubated for 1 hour at 37°C with 100 µCl of ^51^Cr and 5 µg of the relevant antitumor Fab-rMICA conjugate at the same time. After washing, the labeled tumor target cells were plated in 96-well plates (2,000 per well) and incubated with the NK-92 cell line at different effector-to-target cell ratios. After incubation for 4 hours at 37°C, 100 µL of supernatant was taken to measure the amount of ^51^Cr released by target cells, reflecting the number of target cells killed by the NK cells. Spontaneous release of ^51^Cr was determined by incubating the target cells with medium alone. Maximum release was determined by adding 0.1 mol/L HCl. The percentage of specific lysis was calculated as 100 × [(experimental – spontaneous release) / (total – spontaneous release)] (6). In control experiments, ^51^Cr-labeled tumor target cells were preincubated without any conjugate, with 5 µg of irrelevant conjugates, or with 5 µg of rMICA, and tested with NK cells preincubated or not for 30 minutes at room temperature with mouse anti-human NGK2D IgG

**Fig. 2.** Fab-rMICA conjugate characterization by gel filtration chromatography, SDS-PAGE, and Western blotting. A, a typical elution chromatography profile of the chemical Fab-rMICA conjugate (peak a) separated from F(α2)V (peak b) and uncoupled Fab (peak c). Fraction 18 (hatched zone) was used in all of our experiments because it did not contain rMICA, as shown by the superimposed profile of purified rMICA (dotted peak). B, SDS-PAGE analysis of fraction 18 confirmed that the Fab-rMICA conjugate was free from any contamination by unconjugated rMICA, as showed by the Western blot using rabbit polyclonal anti-MICA (C, left membrane). C, the right membrane, incubated with antismurine immunoglobulin (Ig), shows that our purified conjugate preparation contained between one and three Fab fragments per rMICA.
used at 20 μg/mL. In a reverse antibody-dependent cell-mediated cytotoxicity lysis assay, THP-1 cells were incubated with 100 μCi of 51Cr and 5 μg rMICA, without or with preincubation with the FcR blocking reagent, followed by incubation with the NKL cell line.

Results

Induction of natural killer cell–mediated cytotoxicity by recombinant MICA-hFc fusion protein. Purified recombinant dimeric MICA-hFc fusion protein was tested for its capacity to coat the FcRs expressing monocyte leukemia THP-1 cells, which do not express MICA (Fig. 1A), and to induce their lysis by NK cells through the NKG2D receptor. Flow cytometry showed that purified rMICA binds to THP-1 cells and that this binding is FcR dependent because it is specifically inhibited by an FcR blocking reagent (Fig. 1B). The NKG2D receptor expressing NKL cells (Fig. 1C) were used in the chromium release assay as effectors. Preincubation of THP-1 cells with rMICA induced a 2-fold increase in target cell lysis by NKL cells (Fig. 1D). The fact that the target cell lysis was reduced to background level by the FcR blocking reagent (Fig. 1D, hatched column) shows that the specific cytotoxicity was due to the addition of purified soluble rMICA and, thus, to the presence of MICA at the THP-1 cell surface membrane. On the basis of these results, rMICA was coupled to anti-TAA fragments to target MICA on various tumor cell lines.

Production and characterization of antitumor Fab-rMICA conjugates. rMICA-hFc fusion protein was chemically coupled to Fab’ fragments of mAbs directed against TAA, such as CEA (35), HER2 (ErbB-2; ref. 32), and CD20 (33). Purified rMICA molecules were derivatized with the succinimidyl-maleimide cross-linker. Then, the Fab’ fragments from the different mAbs were coupled by creating a thioether bond between their reduced COOH-terminal cysteine residues and the maleimide groups, randomly distributed on lysine residues on the derivatized rMICA. Purification of the conjugate by fast protein liquid chromatography on a Superdex 200 column (Fig. 2A) allowed separation of the antitumor Fab-rMICA conjugate (peak a) from F(ab’)2 fragments (peak b, fraction 23) and uncoupled Fab’ fragments (peak c, fraction 27). The superimposed peak of rMICA purified on the same column (Fig. 2A, dotted peak) did not overlap with fraction 18 (hatched zone), containing antitumor Fab-rMICA conjugate selected for all the further experiments. SDS-PAGE (Fig. 2B) and Western blotting (Fig. 2C, left membrane) confirmed that fraction 18 was not contaminated with uncoupled soluble dimeric rMICA and that this fraction contained conjugate molecules with one to three antitumor Fab fragments per rMICA molecule (Fig. 2C, right membrane).

Binding of antitumor Fab-rMICA conjugates to tumor cell lines. Four tumor cell lines that express different TAAs (Fig. 3, column 1) were tested for their capacity to bind our conjugates. Flow cytometry analysis showed that the anti-CEA Fab-rMICA conjugate specifically bound to the CEA-transfected cell line, a murine colon carcinoma cell line, C15.4.3AP (Fig. 3, column 3). Similarly, only the CD20+ B-cell lymphoma Raji cells bound the anti-CD20 Fab-rMICA conjugate (Fig. 3, column 5), and only the HER2+ cell lines, the breast SK-BR-3, and ovarian SK-OV-3 carcinoma cells showed staining with the anti-HER2 Fab-rMICA conjugate (Fig. 3, column 4). These results clearly show the capacity of our conjugates to coat tumor cell lines expressing the relevant TAA with MICA.

Sensitization of tumor cells to natural killer cell lysis. The above tumor cell lines, not expressing or expressing only low levels of MICA (Fig. 3, column 2), were tested for their susceptibility to lysis by NK cells after incubation with the

Fig. 3. Flow cytometry analysis of different tumor cell lines. First column, each cell line was tested for expression of different tumor associated antigens. Second column, endogenous MICA expression (black-filled peak) on each tumor cell line was evaluated. Columns 3 to 5, each tumor cell line was first incubated with each of the different Fab-rMICA conjugates produced, and next, tested for MICA expression at the cell surface membrane. Conjugate-mediated increase of MICA expression at the cell surface (black-filled peak) was found to be highly specific for the targeted antigen.
Preincubation of tumor cells with the appropriate anti-TAA Fab-rMICA conjugate induced a significant lysis of all tumor targets by the NK-92 cells (Fig. 4, A). For instance, the anti-HER2 Fab-rMICA conjugate induced efficient lysis of the HER2+ SK-BR-3 and SK-OV-3 cell lines (Fig. 4A and B, respectively), whereas the irrelevant anti-CD20 Fab-rMICA was not effective (a). Titration of the anti-HER2 Fab-rMICA conjugate showed that it was still able to significantly enhance the NK92-mediated lysis of tumor cells at a concentration of 3 μg/mL. Anti-CD20 Fab-rMICA and anti-CEA Fab-rMICA sensitized the CD20+ B-cell lymphoma Raji and CEA+ murine colon C15.4.3.AP carcinoma tumor cells, respectively, to lysis by the NK cells (Fig. 4C and D, respectively). The addition of an anti-NKG2D antibody prevented the specific lysis induced by the conjugate (a), demonstrating that NK cell-mediated lysis is the result of MICA engagement by the NKG2D-activating receptor present on NK cells. Two additional controls were included: (a) preincubation of tumor cells with uncoupled rMICA did not induce their susceptibility to NK cell-mediated lysis and (b) the addition of FcR blocking reagent did not inhibit the induction of NK cell-mediated tumor cell lysis by the antibody-MICA conjugates (data not shown). Finally, we observed that preincubation of NK cells for 1 hour at 37°C with soluble rMICA-hFc, up to 10 μg/mL, did not significantly inhibit the subsequent induction of tumor cell lysis by the pretreated NK cells.

**Discussion**

We have evaluated the possibility of rendering tumor cells susceptible to NK cell-mediated lysis. To this end, we developed conjugates consisting of anti-TAA mAb fragments, as the tumor-targeting device, linked to the human MICA as the effector portion. The latter triggers the NK cells by its binding to the NKG2D-activating receptor. We first showed that the anti-TAA Fab-rMICA conjugates could specifically coat tumor cells expressing the relevant TAA with the rMICA molecules. We then showed in vitro that tumor cells resistant to NK cell-mediated lysis became susceptible to lysis upon addition of the appropriate anti-TAA Fab-rMICA conjugate.

Friese et al. (19) have recently shown that the transfection of human glioma cells with MICA induced NK cell-mediated lysis. This occurred despite the high expression on these tumor cells of MHC class I, which inhibits NK cell activation. These results provide important information concerning the role of MICA-type molecules and/or other NKG2D ligands in tumor rejection. However, the translation of these results into a form of tumor immunotherapy would require a gene therapy approach that is presently not available. In contrast, the proposed strategy of antibody-mediated tumor targeting of MICA molecules, illustrated by the in vitro results presented here, has more of a chance to be translated into a practical form of tumor immunotherapy. Indeed, it has been shown that radiolabeled anti-TAA mAbs and antitumor Fab-MHC class I/peptide conjugates can specifically target tumor cells in vivo (8). Furthermore, unconjugated mAbs directed against CD20 and HER2 are accepted as therapeutic agents against chemotherapy-resistant B-cell lymphoma and breast carcinoma, respectively (32, 33). However, the low percentage of complete remission observed, especially when mAbs are used as single modality therapy, indicates a need to improve the efficacy of unconjugated mAbs to kill cancer cells.
Friese et al. (19) reported relatively low specific NK cell–mediated lysis of MICA-transfected tumor cells in vitro compared with the results we report here. They did, however, show a significant growth inhibition of glioma cells grafted in nude mice when the cells were MICA transfected, suggesting that the antitumor cell effect was indeed mediated by the NK cells. Immunotargeting using MICA, as described here, is reminiscent of the strategy of antibody-mediated targeting of antigenic MHC class I/peptide complexes on tumor cells capable of inducing CD8⁺ T cell–mediated cytolysis (4–7). We recently showed this as an approach that could prevent growth and induce regression of a syngeneic tumor in immunocompetent mice in vivo (8).

The targeting of MICA-type molecules described here differs significantly in that it induces the engagement of NK effector cells, which are more abundant than specific CD8⁺ T cells. At the same time, this may actually improve CD8⁺ T-cell responses, with NKG2D functioning this time as a costimulatory receptor to augment T-cell antigen receptor–dependent responses, with NKG2D functioning this time as a costimulatory receptor to augment T-cell antigen receptor–dependent CD8⁺ T-cell cytolytic responses (20). Furthermore, the fact that MICA is a single polypeptide should greatly facilitate the large-scale production and its clinical use in tumor immunotherapy.

The anti-TAA Fab-rMICA conjugates have some functional similarity with the bispecific anti-TAA/anti-CD16 antibody, which is able to direct NK cells to tumor cells (36). However, bispecific antibodies differ in several aspects from the bifunctional conjugates described here. First, the anti-NK cell arm of the published bispecific antibodies is directed against CD16 (FcγRIII), which might not be the optimal activating receptor, compared with NKG2D that specifically binds MICA. Second, the anti-CD16 mAbs fragments, used as Fab in the bispecific antibody, are generally of high affinity. Thus, when used in vivo, the injected bispecific antibodies might bind directly to the NK cells encountered in the circulation. This would lead to activation of circulating NK cells and preclude their localization in the region of the tumor. In the conjugates described here, we used a natural ligand, MICA, known to bind the NKG2D receptor with low affinity (37). Using flow cytometry, even in the dimeric form as soluble rMICA-hFc, we were not able to show any staining of either NK cell line tested (data not shown). Furthermore, preincubation of NK cells with soluble rMICA-hFc did not inhibit their capacity to lyse MICA conjugate–coated tumor cells. On the basis of these results, we hypothesize that circulating NK cells would not bind to the free conjugate but only to target cell–coated Fab-rMICA. Indeed, when coated and oligomerized on a tumor cell, the conjugate should allow the cooperative binding of multiple NKG2D receptors and lead to the activation of NK cells. Indeed, it is logical to assume that the natural ligand of an activating receptor coated on tumor cells would be the optimal form to induce activation of effector cells.

A potential limitation of the novel immunotherapy proposed here is that MICA might be shed from the tumor, leading to a down-regulation of NKG2D receptors on NK cells (24, 38, 39). However, although most of these reports showed a correlation between the presence of soluble MIC molecules and the down-regulation of NKG2D on NK cells, the causality between the two observations was difficult to prove. Due to the low affinity of soluble monomeric MIC molecules for the NKG2D receptor and the negative flow cytometry staining of NK cells by dimeric rMICA-hFc we observed, we have some doubts that it can efficiently bind to circulating NK cells and down-regulate the receptor. However, this possibility should be kept in mind. NKG2D triggering of tumor-bound ligand provides a relatively powerful antitumor reaction so our approach should be particularly effective for tumors that do not express NKG2D ligands and/or have lost them. Interestingly, Wu et al. (39) provided in vitro evidence that the down-regulation of NKG2D receptor could be overcome by interleukin-2 and interleukin-15 treatment.

Another observation made by Wu et al. was that the progressive decrease of MIC expression by cancer cells correlated with the degree of cancer invasion. Vetter et al. (25) observed the same correlation but rather suggested a phenomenon of MIC-negative clone selection during cancer progression and metastatic development.

Finally, we underline that the antibody-mediated targeting of MIC molecules on tumor cells, proposed here, could compensate for their down-regulation observed on invading cancer cells and activate not only NK cells but also γδ T cells. Furthermore, the presence of additional MIC molecules on tumor cells could act as costimulatory molecules for classic tumor-specific CD8 CTLs (20). Recently, Hanna et al. (40) described the novel antigen-presenting–like properties of human NK cells, which, after recognition and killing of tumor cells, could present antigen in the context of MHC class II and so bridge innate to adaptive immunity.

References


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MHC Class I–Related Chain A Conjugated to Antitumor Antibodies Can Sensitize Tumor Cells to Specific Lysis by Natural Killer Cells

Claire Germain, Christel Larbouret, Valérie Cesson, et al.


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