Ti (WT31)-Negative, CD3-Positive, Large Granular Lymphocyte Leukemia With Nonspecific Cytotoxicity


A case of WT31-...CD3+ large granular lymphocyte leukemia is reported. On surface marker analysis, the proliferating cells were found to be CD3 +4-8-16+ and WT31 -. By two-color immunofluorescence staining, CD3 +4-8- cells were found to be WT31-, and a small population of WT31+ cells expressed either CD4 or CD8. WT31-...CD3+ cells were also identified in a bulk culture of lymphocytes expanded in vitro. Because WT31 monoclonal antibody (MoAb) reacts with the nonpolymorphic epitope of the disulfide-linked heterodimer of the T cell antigen receptor (Ti), the absence of the WT31-reactive Ti determinant may represent an expression of different CD3-associated polypeptides. The rearrangement of the Ti-β and Ti-γ genes but not the immunoglobulin gene was demonstrated, and the single pattern of rearrangement indicated the monoclonal origin of the lymphocytes. When the lymphocytes were assayed for their cytotoxicity against K562, MOLT-4, Daudi, and Raji tumor cell lines, a broad spectrum of cytotoxicity for these tumor cells was observed, and the lymphocytes also exhibited antibody- and lectin-dependent cellular cytotoxicity and lymphokine-activated killer activity. Treatment with anti-CD2 and anti-CD3 MoAbs inhibited their nonspecific cytotoxicity. The anti-CD3-mediated inhibition of nonspecific cytotoxicity suggested that an as yet unidentified Ti present in association with the CD3 molecule on these lymphocytes serves as a specific receptor for target tumor cell recognition.

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improvement was observed. The administration of cyclophosphamide (100 mg per os daily) was begun, and the anemia improved. Because leukopenia and intractable cellulitis developed, the cyclophosphamide treatment was discontinued. She is presently receiving only occasional transfusions. When the above therapeutic procedures were started, the patient was advised of the procedures and attendant risks, in accordance with institutional guidelines, and gave informed consent.

Surface marker analysis. Peripheral blood mononuclear cells (PBMCs) were obtained by Ficoll-Conray density centrifugation. Single-color and two-color immunofluorescence analysis was done as described previously.

Expansion of lymphocytes in vitro. PBMCs were cultured in a 50-mL flask (Falcon 3013, Becton Dickinson, Oxnard, CA) with a fivefold number of irradiated (50 Gy) Epstein-Barr virus-transformed B cell line FMO22 in RPMI 1640 medium supplemented with 1,000 U/mL recombinant IL-2 (Shionogi Pharmaceutical Co., Ltd., Osaka, Japan), 10% fetal calf serum (FCS), 2 mmol/L L-glutamine, 100 U/mL penicillin, and 10 µg/mL streptomycin. The medium was replaced every four to five days with fresh IL-2-containing medium. Feeder cells were added every 2 to 3 weeks. Although the doubling time was not ascertained, the cells seemed to proliferate rapidly after FMO cells were added, and the proliferation rate gradually declined until the culture was replenished with FMO cells. After 4 months of bulk culture, the cells were harvested, and their surface phenotype was analyzed.

Analysis of gene rearrangements. High-molecular weight DNA prepared from PBMCs was digested with BamHI or EcoRI restriction endonuclease, size-fractioned by agarose-gel electrophoresis, and transferred to nylon filter paper. These blots were hybridized with nick-translated, 32P-labeled DNA probes of the human immunoglobulin (Ig) gene, the human Tia-β gene,24,25 or the Ti-γ gene.26 The blots were visualized on autoradiography. The human Ig gene probe used, which consisted of a 2.4-kilobase germine Sau3A fragment, could recognize rearrangements in BamHI-digested DNA without polymorphism. The Ti-β gene probe was a BglII/EcoRI fragment of the cDNA clone YTT-2 that contained the Cβ region of the Ti-β gene.24,25 The human Ti-γ gene probe was a HindIII/EcoRI fragment of T cell-rearranging gene γ, which could recognize Cγ1 and Cγ2 in BamHI-digested DNA without evidence of polymorphism.26

Hematopoietic progenitor cell assay. Erythropoiesis was assayed by examining bone marrow erythroid colony-forming units (CFU-E) and burst-forming units–erythroid (BFU-E). Granulo-poiesis was assayed by examining granulocyte-macrophage colony-forming units (CFU-GM). Bone marrow cells were obtained from the patient and healthy volunteers after informed consent. This study was approved by the human experimentation committee of our college. For CFU-E and BFU-E assays, mononuclear cells of the marrow, 2 x 10^5 cells, in 1 mL final volume were plated in tissue culture dishes (Lux tissue culture dish, 35 mm diameter; Lab-Tek Division, Miles Laboratories, Inc., Naperville, IL). To test the effects of the patient’s PBMCs on colony formation, various numbers of PBMCs were mixed with normal donor’s bone marrow mononuclear cells. The cells were then cultured in Iscove’s modified Dulbecco’s minimal essential medium that contained 0.8% methylcellulose, 30% FCS, and 1 U/mL of human recombinant erythropoietin (Toyobo Co., Ltd., Osaka, Japan) in a humidified atmosphere of 95% air and 5% CO2, at 37°C. CFU-E colonies were scored on day 7 and BFU-E on day 14. Colonies consisting of eight or more erythroid cells were defined as CFU-E–derived colonies, and colonies consisting of three or more subcolonies of erythroid cells or a large single accumulation of erythroid cells (300 cells) were defined as BFU-E–derived colonies. For the CFU-GM assay, 2 x 10^5 cells in 1 mL final volume were plated with various numbers of the patient’s PBMCs. The cells were cultured for seven days in McCoy’s 5A medium that contained 0.3% 10% and 10% giant cell tumor–conditioned medium (Life Technologies, Inc., Chagrin Falls, OH) as a source of colony-stimulating factor. Colonies containing 40 or more granulocytes and macrophages were defined as CFU-GM–derived colonies. All cultures were performed in quadruplicate.

Detection of neutrophil-reactive antibodies. To detect neutrophil-reactive antibodies in the sera, the methods described by Verheugt et al27 were modified as follows. In the indirect immunofluorescence test, neutrophils from the patient and ten normal donors were incubated with patient’s serum, labeled with fluorescein isothiocyanate (FITC)-conjugated, F(ab')2, fragment, goat antihuman IgG or IgM antibodies, and then immunofluorescence-positive cells were counted by flow cytometry. In the microagglutination test, neutrophils from the patient and 20 normal donors were incubated with patient’s serum, and neutrophil agglutination was observed by phase-contrast microscopy. Because the patient had anti-HLA antibodies, probably because of pregnancies and/or multiple transfu-
sions, HLA antibodies were absorbed from the serum by incubation with a large quantity of platelets.

**Cytotoxicity assay.** A five-hour $^{51}$Cr release test was used for the assay of non-MHC-restricted cytotoxicity. Natural killer (NK)-sensitive cell lines K562 and MOLT-4, and NK-insensitive cell lines Daudi, Raji, and P815 were used as target tumor cells. Various concentrations of PBMCs were incubated in triplicate with $8 \times 10^5 ^{51}$Cr-labeled target cells. After five hours of incubation, the supernatant fluid was harvested, and the radioactivity was determined with a gamma well counter. The specific $^{51}$Cr release was calculated by the following formula: percent release = (experimental $^{51}$Cr release - spontaneous $^{51}$Cr release) / (maximum $^{51}$Cr release - spontaneous $^{51}$Cr release)] x 100. The results of cytotoxicity were expressed as the mean percent specific $^{51}$Cr release ± SD. The SD of the percent specific $^{51}$Cr release was less than 5% in most of the experiments.

For the assay of antibody-dependent cellular cytotoxicity (ADCC), heat-inactivated rabbit anti-P815 serum was added at a final dilution of 1:900 to $^{51}$Cr-labeled P815 target cells in a cytotoxicity assay. Lectin-dependent cellular cytotoxicity (LDCC) was assayed against $^{51}$Cr-labeled P815 target cells with the addition of 1:9,000-diluted phytohemagglutinin (PHA)-P (GIBCO, Grand Island, NY).

Lymphokine-activated killer (LAK) cells were induced as described elsewhere. PBMCs were cultured for five days with 2,500 U/mL recombinant IL-2. After being washed once, the cells were used as effector cells. The target tumor cells used in the LAK assay were K562, Raji, and patient's autologous PBMC. Freshly isolated blasts (>90% blasts) from patients with T-ALL and acute myelogenous leukemia (AML) were also used as target cells.

To determine the effects of MoAbs on non-MHC-restricted cytotoxicity, a final concentration of 1 µg/mL of MoAb OKT1 (anti-CD5), OKT3 (anti-CD3), OKT4 (anti-CD4), OKT8 (anti-CD8), and OKT11 (anti-CD2), provided by Dr. G. Goldstein, and a final concentration of 10 µg/mL of MoAb WT31 (Sanbio BV-Biological Products, Uden, The Netherlands) were added to effector lymphocytes one hour before a $^{51}$Cr release assay. MoAbs at these concentrations did not affect spontaneous $^{51}$Cr release from target tumor cells.

**Isolation of lymphocyte subsets.** To examine the possibility that some of the normal T lymphocytes mediate cytotoxicity, subsets of lymphocytes were isolated, and their non-MHC-restricted cytotoxicity was assayed. For isolation, half of the PBMCs were stained with saturating concentrations of anti-CD4 and anti-CD8 MoAbs simultaneously and the other half with WT31 MoAb. After labeling MoAb-stained cells with FITC-conjugated, antimouse immunoglobulin antibodies, the cells were isolated by a cell sorter (FACS 440, Becton Dickinson Immunocytometry Systems, Mountain View, CA). CD4-8- cells, CD4+ or -8+ cells, WT31- cells, and WT31+ cells were isolated and assayed for their non-MHC-restricted cytotoxicity. The isolated cells were reanalyzed for their purity, and the purity of each fraction was more than 95%. Because of the probable inhibition of non-MHC-restricted cytotoxicity by anti-CD3 MoAb treatment as is described in Results, anti-CD3 MoAb was not used for the isolation of lymphocytes.

**RESULTS**

PBMCs isolated from the patient exhibited a CD3 + 4 - 8-, WT31- phenotype (Table 1). By using two-color immunofluorescence staining, a small population of WT31+ cells was seen to be CD4+ or CD8+ cells, and the CD3 + 4-8- cells were found to lack WT31-reactive Ti antigen (Fig 3A), which suggests that the WT31+ cells were normal T cells expressing either CD4 or CD8 antigen and the leukemia cells were CD3 + 4-8-, WT31-. The presence of CD16 antigen was detected by CLB FcR gran 1 (VD2) MoAb,29 but not detected by Leu-11a or Leu-11c MoAb, which reacts with different epitopes of the IgGFc receptor expressed on NK cells and neutrophils.30

Lymphocytes were expanded in bulk culture for 4 months. The cells harvested thereafter contained ~25% CD3+, WT31- cells (Fig 3B), which indicates that CD3+, WT31- cells could be expanded in vitro, although it should be clarified whether these expanded cells correspond to the leukemic cell population. The cloning of CD3+, WT31- cells is in progress.

The possible rearrangement of the Ti-β, Ti-γ and Ig genes was examined (Fig 4). Both Ti-β and Ti-γ genes were rearranged, but the Ig gene was not rearranged. Rearrangement of the Ti-β gene was observed in one allele, and that of the Ti-γ gene was observed in both alleles. The single pattern of rearrangements indicated the monoclonal origin of these lymphocytes. In control studies, cells from a patient with adult T cell leukemia showed rearranged Ti-β and Ti-γ genes, and those from a patient with B cell ALL (B-ALL) showed rearranged Ig genes. Human placental cells were in a germline configuration. Northern blot analysis was not done because of the limited number of available leukemic cells.

To study the mechanism(s) of anemia and neutropenia, a hematopoietic progenitor cell assay was performed. No CFU-E or BFU-E colonies were formed with the patient's marrow cells. CFU-E and BFU-E colony formation of normal bone marrow cells was inhibited by the patient's PBMCs, whereas CFU-GM was not (Fig 5), which suggests that lymphocytes infiltrating into the bone marrow inhibited the proliferation and differentiation of erythroid but not myeloid progenitor cells. Because the patient's marrow was hypercellular in neutrophil granulocytes, the possibility that neutropenia was caused by autoantibodies directed against the neutrophils was investigated. The patient's serum, however, was negative for antineutrophil antibodies against autologous and allogeneic normal donors' neutrophils by the indirect immunofluorescence test and microagglutination test.

The patient's PBMCs exhibited strong nonspecific cyto-
Fig 3. Two-color immunofluorescence staining of PBMCs. (A) Freshly isolated PBMCs of the patient. (B) IL-2-expanded cells of the patient. (C) Freshly isolated PBMCs of a normal donor.
Fig 4. Analysis of the rearrangement of Ti-β, Ti-γ, and Ig genes. (A) BamHI-digested DNAs hybridized with Ti-β gene. (B) EcoRI-digested DNAs hybridized with Ti-β gene. (C) BamHI-digested DNAs hybridized with the Ti-γ gene. (D) BamHI-digested DNAs hybridized with the Ig gene. Lanes a, e, i, and m: the patient. Lanes b, f, j, and n: human placenta. Lanes c, g, k, and o: adult T cell leukemia case. Lanes d, h, l, and p: B-ALL case.

Toxicity for K562 target cells, and the cytotoxicity was further enhanced by a one-day incubation in culture medium (Fig 6). The level of cytotoxicity was significantly higher than that of two normal donors. Because K562 lacks cell surface expression of both class I and II MHC antigens, these results show that the patient's lymphocytes recognized and lysed tumor cell targets without MHC restriction. When the lymphocytes were incubated for one day with medium

Fig 5. Effects of patient's PBMCs on normal donor's CFU-E, BFU-E, and CFU-GM. PBMCs from the patient (O-O) and a normal donor (△-△) were added to bone marrow cells of a normal donor, and colonies derived from CFU-E (A), BFU-E (B), and CFU-GM (C) were assayed.

Fig 6. Cytotoxic functions of PBMCs from the patient (O-O) and two normal individuals (O-O, △-△). (A) Non-MHC-restricted cytotoxicity of fresh PBMCs. (B) One day-cultured PBMCs. (C) One day-cultured PBMCs with 500 U/ml IL-2. (D) One day-cultured PBMCs with 500 U/ml IFN-α against K562 target cells. (E) ADCC function of fresh PBMCs and one day-cultured PBMCs (F). (G) LDCC function of fresh PBMCs and one day-cultured PBMCs (H).
containing 500 U/mL recombinant IL-2 or 500 U/mL recombinant interferon-α (IFN-α), their non–MHC-restricted cytotoxicity was further enhanced, and the level of cytotoxicity was significantly higher than that of normal controls. ADCC and LDCC functions for P815 target cells were also observed. Although the ADCC level of freshly isolated patient PBMCs was slightly but significantly lower than that of normal controls at an effector-to-target (E:T) ratio of 20:1, the level attained the normal range after one day of incubation. The LDCC level of freshly isolated patient PBMCs was significantly higher than that of normal controls at an E:T ratio of 20:1, and that of one day–incubated patient PBMCs was significantly higher at E:T ratios of 20:1 and 5:1. Cytotoxicity for P815 was not detected in the absence of anti-P815 serum or PHA (data not shown). Because of the possibility that some of the normal T cells could account for the functional tests, CD4+ or -8+ cells, CD4-/8- cells, WT31+ cells, and WT31– cells were isolated by a cell sorter, and non–MHC-restricted cytotoxicity of each fraction was assayed. As shown in Fig 7. CD4–8– cells and WT31– cells exhibited much higher cytotoxicity than their antigen-positive counterparts. Because ADCC and LDCC activities of the sorted cells were not studied, the possibility that these cytotoxicities were mediated by some normal cells could not be ruled out. Figure 8 shows that LAK activity was induced against NK-resistant Raji cells and that leukemic blasts isolated from patients with T-ALL and AML were also lysed by the patient’s LAK cells; LAK activity for T-ALL cells was higher than that of one normal donor but similar to that of another normal donor, with LAK activity for AML cells being significantly lower than that of the two normal donors. The patient’s PBMCs were not lysed by the patient’s autologous and normal donors’ allogeneic LAK cells.

The effects of T cell antigen–reactive MoAbs on non–MHC-restricted cytotoxicity were examined. As shown in Fig 9, non–MHC-restricted cytotoxicity of the patient’s lymphocytes was significantly inhibited by the addition of anti-CD2 and anti-CD3 MoAbs. Anti-CD4, -5, -8 and WT31 MoAbs did not affect the cytotoxicity.

**DISCUSSION**

We have described a case of LGL leukemia whose proliferating cells exhibited a CD3+, WT31– phenotype and a
strong non-MHC-restricted cytotoxicity. To our knowledge, this is the first case of CD3+, WT31– LGL leukemia in which CD3+, WT31– cells exhibited non-MHC-restricted cytotoxicity.

A group of disorders termed LGL leukemia, LGL lymphoproliferation, or Tγ-lymphoproliferative disease are characterized by the proliferation of large lymphocytes with azurophilic granules in the cytoplasm. In contrast to LGLs isolated from normal peripheral blood, LGLs in these disorders have a tendency to exhibit fewer and smaller granules. Expanded LGLs are largely CD3+4–8+, whereas normal LGLs of CD3+4+8–, CD3+4–8–, or CD3–16+ (Leu-11+) are less often expanded. Indeed, of the ten LGL lymphocytosis patients we have recently observed, five had CD3+4–8+; one CD3+4–8– (this case); one CD3+4+8–; and three CD3–16+ (unpublished observation).

In contrast to the demonstration of ADCC function in the patient’s PBMCs (Fig 6), the percentage of Tγ cells, ie, T cells with an IgG Fc receptor, detected by the double rosetting of sheep erythrocytes and ox erythrocytes coated with rabbit anti ox erythrocyte IgG was low. This could be explained by a low affinity of the IgG Fc portion of rabbit antibody to LGLs because the presence of this receptor was identified by CCL FCr gran 1 (VD2) MoAb2 (Table 1). CD16 antigen was thus detected by CCL FCr gran 1 MoAb, but not by Leu-11a or Leu-11c MoAbs. Similar findings were observed in our other six cases of CD3+ LGL lymphocytosis (unpublished observation) and by others.

In patients with LGL lymphocytosis, Ti-β gene rearrangement was observed in patients with CD3+ LGL lymphocytosis, whereas it was not found in patients with CD3– LGL lymphocytosis. In this patient, proliferating LGLs exhibited Ti-β and Ti-γ gene rearrangements, and the single pattern of rearrangements confirmed the monoclonal origin of these LGLs. Thus, the term LGL leukemia could be applied to the present case.

Approximately half of the patients with LGL lymphocytosis are anemic. The mechanism(s) by which this anemia occurs is not clear. In several cases, direct suppression of erythropoiesis by LGLs was shown by the in vitro inhibition of CFU-E or BFU-E. In our patient, there were no signs of bleeding, hemolysis, or other disorders that could explain the severe anemia, and the patient’s PBMCs inhibited CFU-E and BFU-E colony formation of normal marrow cells (Fig 5). Furthermore, the supernatant from a mixture of the patient’s PBMCs and K562 cells exhibited a suppressive effect on CFU-E (Takahashi M, manuscript in preparation). Thus, the anemia and the hypopcellularity of erythroid cells in the patient’s marrow may reflect a suppression of the development of erythroid progenitor cells by infiltrating LGLs. Because the patient’s PBMCs inhibited colony formation of CFU-E and BFU-E but not BFU-GM of allogeneic normal marrow cells, it seems unlikely that reactivity of PBMCs was directed against alloantigens on hematopoietic progenitor cells.

Neutropenia is seen in more than half of the patients with LGL lymphocytosis. The mechanism underlying this neutropenia is not clear. Insufficient neutrophil granulocytepoiesis, a reduced release of neutrophils from the bone marrow, and a shortened life span of the circulating peripheral blood neutrophils as well as excessive margination of these cells may cause neutropenia. In the present case, the neutrophils in the patient’s marrow were hypercellular, and the development of CFU-GM-derived colonies was not inhibited by patient’s PBMCs, which suggests that neutrophil granulopoiesis was normal. Failure to detect circulating antineutrophil antibodies excludes the possibility of antineutrophil autoantibody-mediated neutropenia. Furthermore, the CIq-binding assay did not reveal the presence of circulating immune complexes, thus making the possibility unlikely of immune complex-mediated sequestration of neutrophils in the vascular bed. Further studies are required to clarify the mechanism of neutropenia.

We have recently studied seven cases of CD3+ LGL lymphocytosis, and except for the present case, all six had LGLs expressing WT31-reactive Ti antigen (unpublished observation). Thus, the incidence of CD3+, WT31– LGL lymphocytosis seems to be low. CD3+, WT31– T lymphocytes have recently been identified in low frequencies in normal peripheral blood and the thymus. These lymphocytes in normal peripheral blood express neither CD4 nor CD8 antigen. Thus, CD3+4–8–, WT31– LGL leukemia cells of the present patient seemed to be derived from the normal counterpart of the aforementioned; however, normally present CD3+4–8– T cells are different in a few ways from those of the patient. More than 90% of normal CD3+4–8– cells did not contain azurophilic granules and did not exhibit non-MHC-restricted cytotoxicity. When these cells were cultured in medium containing IL-2, they exhibited LGL morphology, NKH-1 antigen, and non-MHC-restricted cytotoxicity. LGLs of our patient differ also from these cells because our patient’s LGLs did not express NKH-1 antigen and their non-MHC-restricted cytotoxicity was inhibited by anti-CD3 MoAb, as opposed to IL-2–cultured cells whose non-MHC-restricted cytotoxicity was enhanced by anti-CD3.

Although the LGL leukemia cells were found to have a rearranged Ti-β gene, the Ti-αβ structure was not detected by WT31 MoAb. Of the CD3+, WT31– cell lines reported, some expressed full-length Ti-β mRNA. Thus, checking for the presence or absence of full-length Ti-β mRNA would be helpful for understanding the expression of the Ti-αβ structure; however, Northern blot analysis was not performed because of the limited number of available leukemic cells. Because the rearrangement of the Ti-γ gene was observed in the patient’s PBMCs, the absence of a WT31-reactive Ti determinant may represent the presence of mutually present CD3-associated polypeptides Ti-γγ or Ti-γδ. Recently, a case of T-ALL has been reported in which the leukemic cells exhibited CD3+, WT31– phenotype, a rearranged Ti-γ gene, and a putative Ti-γ protein. The cells, however, did not have LGL morphology.

Our patient’s lymphocytes expressed non-MHC-restricted cytotoxicity, which was inhibited by anti-CD2 and anti-CD3 treatment. Anti-CD2 MoAb probably inhibits antigen-independent conjugate formation between the CD2 antigen on the effector lymphocytes and the lymphocyte function-associated antigen-3 on target tumor cells. The mechanism of the anti-CD3–mediated suppression of the
cytotoxicity must be explained differently. Moingeon et al19,20 have recently reported that CD3+, WT31 — lymphocyte clones expressed Ti-γγ chains, and a MoAb that was generated against the clonotypic structure of Ti-γγ chains as well as an anti-CD3 MoAb blocked non-MHC-restricted cytotoxicity of the clones. Borst et al21 and Brenner et al13 have also reported CD3+, WT31 — cell lines with a CD3/Ti-γγ or CD3/Ti-γδ complex whose non-MHC-restricted cytotoxicity was inhibited by anti-CD3. Hercend et al22 detected CD3+, WT31+, CD8+, NKH-1+ cell lines whose non-MHC-restricted cytotoxicity was blocked by the anti-CD3 MoAb and a MoAb that was generated against clonotypic determinants of the clones. Based on the finding that, in antigen-specific cytotoxic T lymphocyte clones, antigen-specific cytotoxicity is blocked by MoAbs directed at Ti clonotypic structures and MoAbs directed at CD3,4,23 the aforementioned findings suggest that clonotypic structures of Ti-γγ and Ti-γδ chains are directly involved in non-MHC-restricted cytotoxicity and act as a specific receptor for target tumor cell recognition. Accordingly, anti-CD3-mediated inhibition of non-MHC-restricted cytotoxicity in our patient also indicates the same possibility, ie, that a putative Ti present on the LGL leukemia cells serves as a specific receptor for target tumor cell recognition, though the possibility cannot be ruled out that the activity of an anti-CD3 MoAb in this situation is unrelated to its ability to block the relevant receptor on the leukemic cells.

Cloning of in vitro—expanded CD3+, WT31 — cells, generation of a MoAb directed at their clonotypic structure, and immunoprecipitation of Ti with CD3 antigen will delineate the biologic significance of the CD3/Ti complex putatively present on these CD3+, WT31 — LGL leukemia cells.

NOTE ADDED IN PROOF

We have recently analyzed the expression of Ti-γA chains in the patient’s PBMCs. Anti-Ti-γA MoAb did not react with the cells, while anti-TCR-δ1 MoAb reacted with them. Furthermore, anti-TCR-δ1 MoAb treatment inhibited their non-MHC-restricted cytotoxicity, thus suggesting that the CD3/Ti complex is a receptor for target tumor cells.

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