Chronic T Cell Leukemia with a NK Phenotype Reacting with Anti-Myelin-Associated Glycoprotein (MAG) Mouse Monoclonal Antibody

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TANAKA, M., NISHIZAWA, M., INUZUKA, T., BABA, H., SATO, S., MIYATAKE, T., AOKI, S. and SHINADA, S. *Chronic T Cell Leukemia with a NK Phenotype Reacting with Anti-Myelin-Associated Glycoprotein (MAG) Mouse Monoclonal Antibody*. Tohoku J. exp. Med., 1986, **150** (2), 225-226 — We describe a patient demonstrating chronic T cell leukemia with a natural killer (NK) phenotype. The leukemic cells could be stained by OKT 3 (T cells), anti-Leu-7 and anti-myelin-associated glycoprotein (MAG) (NK cells) but not anti-Leu-11 monoclonal mouse antibody (activated NK cells). Fresh mononuclear cells showed a very low NK activity, although this activity returned to normal levels after 18 days incubation with interleukin-2 and some stimulants. It was not known why the NK activity of fresh mononuclear cells was low. This report is the first on leukemia characterized by anti-MAG monoclonal antibody. — myelin; myelin-associated glycoprotein; natural killer; monoclonal antibody; leukemia

The authors (Sato et al. 1983; Tanaka et al. 1984) and McGarry et al. (1983) have demonstrated a shared antigenic determinant between myelin-associated glycoprotein (MAG) and Leu-7 (HNK-1), a surface marker of human natural killer cells reported by Abo and Balch (1981). We found that about nine percent of the mononuclear cells in the peripheral blood was stained by anti-MAG rabbit antisera (MAG⁺ cells) (Tanaka et al. 1985a). In a two-color immunofluorescence study, more than 95% of MAG-positive human mononuclear cells were also stained with anti-Leu-7, but only 50-90% of Leu-7 positive cells were stained with anti-MAG antisera (Tanaka et al. 1984). Eighty percent of MAG-positive cells were stained with anti-Leu-11, a monoclonal antibody against the IgG Fc receptor of human activated NK cells reported by Phillips and Babcock (1983) (Tanaka et al. 1985a). It may be possible that MAG-positive cells are closely related to activated NK cells and that "MAG" is a useful marker of human NK cells, since some patients with multiple sclerosis showed a normal number of Leu-7-positive cells but a reduced number of MAG-positive cells (Tanaka et al. 1985a).

Several patients demonstrating chronic lymphocytic leukemia or lymphocytosis with NK phenotype have been reported (Itoh et al. 1983; Reynolds and Foon 1984). We described a 56-year-old female patient with chronic T cell leukemia. Detailed clinical

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findings will be reported (Aoki, in preparation). The peripheral blood showed 14,000 leukocytes with 86% lymphocytes. Her lymphocytes were analyzed by Spectrum III (Ortho). Most (97.0%) were stained by OKT 3 (T cell marker) and anti-Leu-7 (NK cells) (84.3%). However, B7⁺ (B cells) and Leu-11⁺ cells (activated NK cells) were 2.0% and 1.3%, respectively. Normal values obtained from 20 healthy young adults are as follows: T3⁺ (71.2±5.9%); Leu-7⁺ (15.4±6.4%); B7⁺ (11.5±3.6%) and Leu-11⁺ cells (17.0±6.5%). These leukemic cells resembled large granular lymphocytes which could not be distinguished from mature human NK cells. The anti-MAG monoclonal mouse antibody reacting with a carbohydrate moiety of MAG could stain 92.2% of the mononuclear cells by fluorescence microscopy. Since the NK activity of healthy individuals was reduced by treatment with the anti-MAG monoclonal mouse IgM antibody and complement, MAG⁺ cells could show NK activity (Tanaka et al. 1985b). However, fresh mononuclear cells from this patient showed only 9.6 percent NK activity by ⁵¹Cr release assay when NK activity was examined using K-562 cells as target cells at 20:1 as the effector/target ratio for four hours incubation (Tanaka et al. 1985b). The patient's mononuclear cells were cultured in RPMI 1640 containing 15% FCS, 20% crude interleukin-2 (Lymphocult-T, Biotest) and 1×10⁻⁵ M 2-Mercaptoethanol. They were incubated under three different stimulants such as PHA-P diluted to 1:100, 20 ng/ml of Phorbol 12-Myristate 13-Acetate (TPA) or both for the first two days. After 18 days, the NK activity increased to 33.3% (PHA-P), 52.7% (TPA) and 52.1% (PHA-P+TPA). A case of chronic T cell leukemia with NK (leu-7) phenotype but lacking any NK activity has been reported previously (Itoh et al. 1983). It was not known why the NK activity of freshly isolated mononuclear cells in our patient should be so low.

Further investigations on cell lineages of human NK cells including MAG⁺ and Leu-7⁺ cells and on their functional profiles may enable us to classify chronic T cell leukemia.

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