membrane viscosity of the stimulated AM compared with the control favors realization of their higher phagocytic and bactericidal potential.

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PANEL OF MONOCLONAL ANTIBODIES TO ANTIGEN CD38

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Monoclonal antibodies (McAb), an important tool in immunologic methods, have found wide application in the study of the structure and function of cell surface antigens and receptors. Research into differential antigens of human hematopoietic cells is particularly important because it enables the mechanisms of blood cell differentiation and of the generation and regulation of immunity to be understood.

An important marker of proliferating cells of the human lymphoid system is an antigen which was classed at the International Working Conference on differential antigens of human leukocytes with the CD38 cluster [3]. Antigen CD38 is very similar in its structural organization to antigens of the class I human major histocompatibility complex [2], but differs in the character of its distribution on hematopoietic cells [1, 4]. Normally antigen CD38 is represented on all thymocytes, myelocytes, myeloblasts, promyelocytes, and medullary B lymphocytes. In the peripheral blood the antigen is expressed on the majority of null cells, NK cells, and 5% of T cells and weakly on monocytes. Mature peripheral T and B lymphocytes and erythrocytes do not contain this antigen. During activation of T cells by mitogens or alloantigens, expression of CD38 rises sharply [5].

As a result of somatic hybridization of mouse myeloma P3X63A 8.653 cells and spleen cells of BALB/c mice, repeatedly immunized with human thymocytes, the following strains of hybrid cells in culture were obtained in the Clinical-Radioimmunologic Laboratory of the All-Union Oncologic Scientific Center, Academy of Medical Sciences of the USSR: ICO-16, ICO-17, ICO-18, ICO-19, ICO-20, ICO-27, and ICO-28.

The aim of this investigation was to characterize antigen CD38, revealed by the McAb panel thus obtained.

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TABLE 1. Reactivity of McAb of the ICO Series to Antigen CD38 with Blood Cells from Healthy Donors

Cells	Number of antigen-positive cells, %							Note
	ICO-16	ICO-17	ICO-18	ICO-19	ICO-20	ICO-27	ICO-28	
Thymocytes	72,3±2,8	61,0±6,6	59,0±8,7	60,8±6,1	68,7±4,7	65,4±6,2	62,5±4,6	All donors tested were antigen-positive
Mononuclears	4,5±1,5	5,2±1,1	4,0±0,7	5,5±1,3	6,4±1,7	8,6±6,4	5,9±1,6	73% of donors tested were antigen-positive
Granulocytes	0	0	0	0	0	0	0	—
Monocytes	0	0	0	0	0	0	0	—
Bone marrow cells	0	0	0	0	0	0	0	—

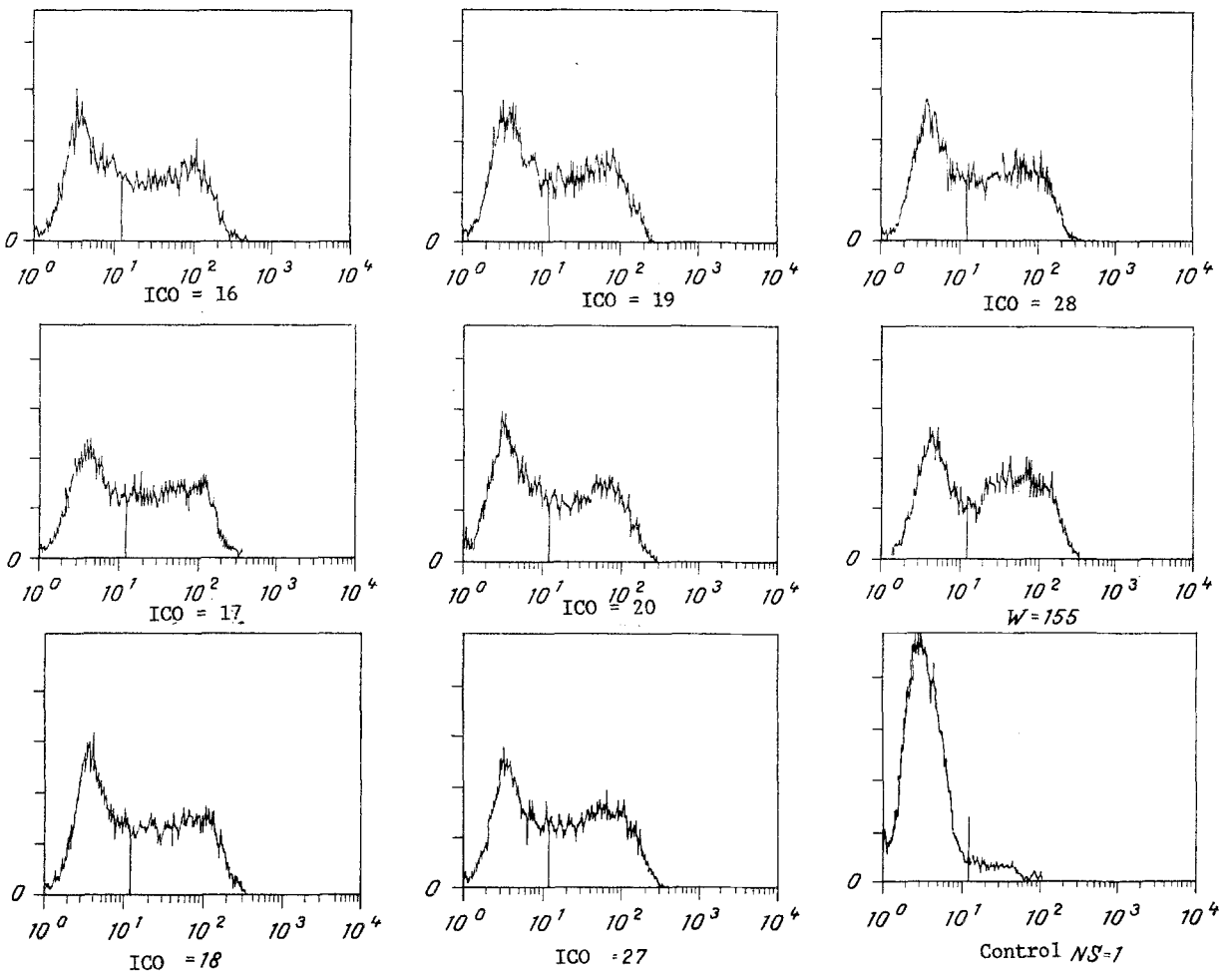

Fig. 1. Reactivity of McAb with lymphocytes from healthy blood donors. Abscissa, intensity of immunofluorescence; ordinate, number of cells.

All the hybridomas obtained produce under stable conditions McAb of the IgG_{2a} isotype. In the indirect surface immunofluorescence test (IFT) the McAb reacted ("Leitz" luminescence microscope) with thymocytes of all donors tested and with the peripheral blood mononuclear cells of some healthy blood donors (Table 1). The antibodies did not react with monocytes, granulocytes, and bone marrow cells. By the use of flow cytometry on the FACStar instrument, expression of an antigen detected by the McAb thus obtained was found on 100% of thymocytes, 43-53% of lymphocytes, and 32-46% of peripheral blood monocytes. The antigen was not found on granulocytes. Direct comparison of histograms of immunofluorescence of the McAb we had obtained with antibodies OKT10 and W-155, directed against CD38, showed them to be identical (Fig. 1). Competitive binding of ^{125}I-labeled McAb with unlabeled McAb on human thymocytes, fixed with glutaraldehyde, was carried out (Table 2). It was found that ICO-16-28 McAb mutually block one another. In the complement-dependent cytotoxic test, our McAb lysed 60.8 ± 4.2% of thymocytes and 10.5 ± 3.5% of blood mononuclear cells. Treatment of normal bone mar-

TABLE 2. Competitive Binding of ^{125}I-McAb and Unlabeled McAb with Human Thymocytes Fixed by Glutaraldehyde

McAb	^{125}I-labeled McAB						
	ICO-16	ICO-17	ICO-18	ICO-19	ICO-20	ICO-27	ICO-28
ICO-16	134	221	94	241	106	116	96
ICO-17	120	203	94	181	91	79	91
ICO-18	143	230	86	176	100	94	101
ICO-19	117	213	92	189	97	64	39
ICO-20	124	252	109	184	109	77	90
ICO-21	150	225	120	207	112	79	110
ICO-22	118	201	101	184	111	68	100
	271	392	203	503	260	271	255

Legend. Number of counts indicated.

TABLE 3. Reactivity of McAb of the ICO Series to Antigen CD38 in IFT with Cells from Patients with Leukemias

Leukemia	ICO-16	ICO-17	ICO-18	ICO-19	ICO-20	ICO-27	ICO-28
ALL in gen.	1/8	2/12	1/10	0/10	1/17	1/2	0/2
Ia-ALL	0/2	0/3	0/4	1/3	0/6	0/1	0/1
T_1-ALL	1/3	1/5	2/4	1/4	1/3	1/3	2/3
T_2-ALL	3/4	4/5	4/5	4/5	4/4	4/5	4/5
T_3-ALL	Н. Д.	3/3	2/2	3/3	4/5	n.d.	n.d.
Pre-B-ALL	0/4	0/5	1/5	1/5	1/8	1/3	0/3
B-ALL	0/1	0/1	1/2	0/2	1/2	0/2	0/2
CLL	0/10	0/5	0/5	0/5	0/10	0/4	0/5
ANL	2/8	6/16	8/13	5/13	6/12	2/8	1/8

Legend. Numerator gives number of positive cases, denominator gives number of patients tested. n.d.) No data; ALL) acute lymphoblastic leukemia; CLL) chronic lymphatic leukemia; ANL) acute nonlymphoblastic leukemia.

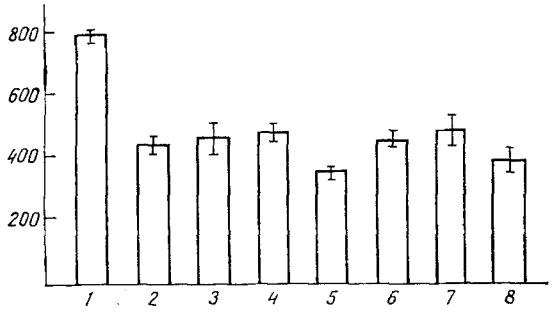

Fig. 2. Inhibition of NK-cell activity of human peripheral blood mononuclears by McAb of the ICO series to antigen CD38. 1) Control, 2) ICO-16 McAb + complement, 3) ICO-17 McAb + complement, 4) ICO-18 McAb + complement, 5) ICO-19 McAb + complement, 6) ICO-20 McAb + complement, 7) ICO-27 McAb + complement, 8) ICO-28 McAb + complement, K-562 cells were used as target cells.

row with antibodies and complement inhibited the formation of colonies of the granulocytic-macrophagal series, evidence that the antigen is present on colony-forming bone marrow cells. Treatment of mononuclear cells with ICO-16-28 McAb and complement inhibited NK-cell activity against K-562 target cells, indicating that the antigen is present on NK cells (Fig. 2). ICO-16-28 McAb did not affect the blast-transformation of lymphocytes reaction to phytohemagglutinin.

A protein with mol. wt. of 45 kD was immunoprecipitated from I^{125}-labeled human thymocytes by ICO-16-28 McAb. Antigen CD38 has this molecular weight.

Different variants of human hemoblastoses are considered to be a true reflection of the consecutive stages of differentiation of hematopoietic cells under normal conditions. The reactivity of our McAb panel to antigen CD38 was studied with blood cells from patients with different immunologic subvariants of leukemias (Table 3). Antigen CD38 is represented on T-cell subvariants of acute lymphoblastic leukemia, and its expression is increased on more highly differentiated cells. Antigen CD38 is not expressed in "general" and Ia-like subvariants of acute lymphoblastic leukemia and it is absent in chronic lymphatic leukemia.

Investigation of frozen sections in the IFT revealed reactivity of our McAb with the majority of lymphoid cells in the tunica propria of the gastric mucosa in normal subjects and patients with peptic ulcer and adenocarcinomas.

Antigen CD38 thus is widespread and is not limited to a particular line, but characterizes proliferating cells.

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MONOCLONAL AUTOANTIBODIES TO EPITHELIAL STRUCTURES OF THE THYMUS OBTAINED BY IMMUNIZATION WITH GROUP A STREPTOCOCCAL ANTIGENS

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The epithelial tissue of the thymus constitutes a microenvironment in which T lymphocytes undergo maturation and differentiation. Direct contact between lymphocytes and epithelium and synthesis of hormones and other soluble factors are important [10]. It has been shown with the aid of monoclonal antibodies (MCA) that the epithelium of the thymus is heterogeneous, and different microenvironments are found in the human thymus [9]. This may probably have an important role in maturation of different T-lymphocyte subpopulations.

It was shown previously that the polysaccharide of group A streptococcus (A-PSC) is a cross-reacting antigen. Antibodies to A-PSC are autoantibodies and react with the epithelium of the stratum basale of the skin and with epithelium of the cortical and medullary zones of the thymus [14]. These data have been confirmed by the obtaining of MCA to A-PSC [5]. Autoantibodies to the same epithelial structures of the thymus and skin have been found in rheumatic fever and other autoimmune processes in man [7, 13] and also in the early stage of the autoimmune process in New Zealand mice [6].

It has been shown with the aid of MCA to various keratins that antibodies reacting with the basal epithelium of the skin are directed toward the endocrine epithelium of the thymus [10]. On the basis of the data given above it has been suggested that the main cause of immunoregulatory disturbances during autoimmune processes is damage to the endocrine epithelium of the thymus by autoantibodies [4]. In some immunopathological processes autoantibodies have been found to other epithelial structures of the thymus [10].

It is accordingly interesting to look for autoantibodies to epithelial structures of the thymus in connection with immunization by various microbial antigens.

As a result of immunization of BALB/c mice with nontype-specific (NTS) protein cell wall antigens of group A streptococcus, MCA reacting with various epithelial structures of the skin were obtained previously [1]. It was shown that the MCA are autoantibodies arising as a result of polyclonal activation of lymphocytes by NTS streptococcal antigens and they do not interact with antigens of group A streptococcus [1].

The greater part of the epithelium of the thymus consists of cells of epidermal genesis [10]. However, no clear evidence has yet been obtained to show against which epithelial struc-

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