

## CD Markers

### Background

CD: cluster designation of monoclonal antibodies (clusters of differentiation)

Designated at the 1st to 7th Workshops on International Human Leukocyte Differentiation Antigens

Interpretation should be based on cellular distribution of staining, proportion of positively stained cells, staining intensity and cutoff levels.

### CD1

Family of non-polymorphic MHC class I-like glycoproteins

Also member of immunoglobulin superfamily

On chromosome 1q22-23 (not MHC linked)

Has 5 different subsets, all noncovalently associated with 12 kd beta 2 microglobulin

**Function:** restrict T cell responses to certain antigens; may mediate thymic T cell development

**Positive staining (normal):** cortical thymocytes (70%), activated T cells, Langerhans cells, interdigitating dendritic cells

**Positive staining (disease):** pre T ALL with cortical thymocyte phenotype; Langerhans cell histiocytosis

**Negative staining:** mature peripheral T cells

### CD1a

**Positive staining (normal):** Dendritic cells in dermis/epidermis of benign inflammatory skin disorders

**Positive staining (disease):** Langerhans cell histiocytosis (fairly specific), myeloid leukemias, some B cell malignancies; dendritic cells in most peripheral cutaneous T cell lymphomas, [AJCP 2001;116:72](#)

**Negative staining:** normal B cells, most cutaneous peripheral B cell lymphomas (? reflects replacement of reactive pattern containing dendritic cells with a neoplastic pattern of B cells)

### CD1b

**Positive staining (disease):** myeloid leukemias and some B cell malignancies

**Negative staining:** normal B cells

### CD1c

**Positive staining (normal):** subset of normal peripheral B cells

**Positive staining (disease):** myeloid leukemias and some B cell malignancies

**Negative staining:** normal B cells

### CD1d

**Positive staining (normal):** thymus (low levels), bowel

### CD1e

### CD2

Aka E rosette receptor, LFA-2 (leukocyte function antigen)

**Function:** binds CD58 / LFA-3 on antigen-presenting cells, and induces costimulatory signals in T cells

Also regulates T and NK-mediated cytotoxicity, inhibits apoptosis of activated peripheral T cells, mediates T cell cytokine production, regulates T cell anergy

**Positive staining (normal):** thymocytes (95%), mature peripheral T cells (almost all), NK cells (80-90%), thymic B cells (50%)

### CD2R

CD2 epitopes restricted to activated T cells

**Positive staining:** activated T cells, ? NK cells

### CD3

Aka OKT3

**Function:** complex (5 chains) of integral membrane glycoproteins assembled as a complex; has long cytoplasmic tail with antigen recognition activation motif; complex is then down regulated

Also subdivided into delta, epsilon, gamma subtypes

Cytoplasmic expression at early T cell differentiation, then membranous expression

Most specific T cell antibody

**Positive staining (normal):** thymocytes, peripheral T cells, NK cells; also Purkinje cells of cerebellum

**Positive staining (disease):** 80% of T cell lymphomas

**Negative staining:** gamma delta T cell receptors, most B cell lymphomas

### CD4

Aka OKT4, T helper/inducer

On chromosome #12p

Nonpolymorphous glycoproteins belonging to immunoglobulin superfamily

Serves as HIV receptor on T cells (as do chemokine receptors CCR5 and CXCR4), macrophages, brain

CD4+ T cells are killed by HIV

Coreceptor in MHC class II-restricted antigen induced T cell activation

Binds to nonpolymorphic region of class I molecules; may increase avidity of cell-cell interactions

**Positive staining (normal):** thymocytes (80-90%), mature T cells (65%, T helper and CD4/CD8+ thymocytes), macrophages, Langerhans cells, dendritic cells, granulocytes

### CD5

Belongs to ancient scavenger receptor family

Is physically and functionally coupled with T cell receptor-zeta-CD3 signal transducer complex

CD5+ B cells produce "generalist antibodies" - polyreactive low affinity "natural" antibodies to exogenous antigens (tetanus toxoid, lipopolysaccharide) as well as autoreactive antibodies (ssDNA, thyroglobulin,

Note: sharks only have polyreactive IgM

Note: monoreactive IgG is produced by  $< 0.1\%$  of circulating B cells, from positive selection and somatic point mutation

First line of defense against antigens; have a low activation threshold; are the only line of defense for those who cannot produce specific antibody

Produce antibodies using germ line (non mutated) configuration of gene segments, usually IgM

Production elevated in rheumatoid arthritis (27-52% of circulating B cells vs. 20% normal)

CD5 may serve as a dual receptor, giving either stimulatory or inhibitory signals depending both on the cell type and the development stage

**Positive staining (normal):** B cells of mantle zone of spleen and lymph nodes; B cells in peritoneal and pleural cavities; almost all T cells;

In fetus, most B cells in spleen and cord blood are CD5 positive

**Positive staining (disease):** B cell CLL/SLL, mantle cell lymphoma, most T malignancies, thymic carcinomas (70%)

**Negative staining:** spindle cell thymomas, MALT lymphoma, follicular lymphoma

## CD6

Adhesion molecule mediating the binding of developing thymocytes with thymic epithelial cells

May be involved in autoimmunity and graft vs. host disease (GVHD)

Antibodies to CD6 are used to deplete T cells from bone marrow transplants to prevent GVHD

**Positive staining (normal):** low levels on immature thymocytes, high levels on mature thymocytes

## CD7

Membrane glycoprotein and Fc receptor for IgM

Homologous to TCR gamma, Ig kappa

Membrane expression early during T ontogeny, before TCR rearrangement, persists until terminal stages of T cell development

Lower expression in memory T cells vs. naive T cells

**Positive staining (normal):** mature peripheral T cells (85%), post-thymic T cells (majority), NK cells (majority), some myeloid cells

**Positive staining (disease):** T cell ALL; AML (especially M4/M5), chronic myelogenous leukemia, blasts in transient myeloproliferative disorder

**Negative expression:** B cell ALL, Sezary syndrome, adult T cell leukemia/lymphoma

## CD8

Aka OKT8, T cell suppressor/cytotoxic cells

On chromosome #2

MHC class I restricted receptor; binds to nonpolymorphic region of class I molecules; may increase avidity of cell-cell interactions

Associated with lymphoepithelioma-like carcinoma of lung ([AJSP 2002;26:715](#))

**Positive staining (normal):** T cells (25-35% of mature peripheral T cells, most cytotoxic T cells, CD4/CD8+ thymocytes); NK cells (30%-which are also CD3 negative); cortical thymocytes (70-80%), epidermotrophic lymphocytes in mycosis fungoides ([AJSP 2002;26:450](#))

## CD9

May mediate platelet activation and aggregation

Antibodies are used to purge bone marrow prior to peripheral stem cell bone marrow transplant

Viral co-receptor

**Positive staining (normal):** pre B cells, B cell subset, T cells, macrophages, platelets, eosinophils, basophils, megakaryocytes, endothelial cells, brain, peripheral nerve, vascular smooth muscle, cardiac muscle, epithelia

## CD10

Aka Common Acute Lymphoblastic Leukemia Antigen (CALLA), neutral endopeptidase 24.11, neprilysin, enkephalinase

Cell membrane metallopeptidase, characteristic marker of follicular center cells and follicular lymphoma, but also widely distributed in normal tissue and neoplasms; also localized to brush border in small bowel mucosa

Inactivates bioactive peptides

Uses:

**Acute lymphoblastic leukemia:** one of first markers to identify leukemic cells in children (hence its name)

**Burkitt lymphoma:** confirm diagnosis

**Colonic carcinogenesis:** increase in stromal cells from mild to severe dysplasia to invasive carcinoma,

**Endometriosis:** helpful in identifying areas of endometriosis if sparse glandular tissue

**Follicular lymphoma:** to confirm diagnosis

**Hepatocellular carcinoma vs. nonhepatocellular carcinomas:** 68% sensitive and >95% specific with canalicular pattern, [AJSP 2001;25:1297](#), [AJSP 2002;26:978](#), although another study recommends Hepatocyte, MOC31, and pCEA but not CD10, [Mod Path 2002;15:1279](#)

**Microvillous inclusion disease:** strong CD10+ cytoplasmic staining vs. linear brush border staining in normals,

**Positive staining (normal):** adrenal cortex, pre-B cells, brain, choroid plexus, cortical thymocytes, endometrial stroma, follicular center cells, granulocytes, kidney microvilli, liver, lymphohematopoietic precursors, male GU epithelium, mesonephric remnants, myoepithelial cells (breast), neutrophils, ovary, placenta (cytotrophoblast, intermediate trophoblast, syncytiotrophoblast), small intestine (linear brush border staining)

**Positive staining (disease):** adenomyosis of endometrium, preB ALL (75%), CML in blast crisis (90%), colonic carcinoma, dermatofibroma, dermatofibrosarcoma, endometrial adenocarcinoma (may be present in desmoplastic stroma), endometrial stromal tumors, follicular center cell lymphomas, gastric carcinoma

glioma, hepatocellular carcinoma (canalicular pattern similar to polyclonal CEA), malignant mixed mullerian tumors, mediastinal germ cell tumors, melanomas, mesonephric tumors, microvillous inclusion disease (strong cytoplasmic staining), mullerian adenocarcinoma, pancreatic adenocarcinoma, pancreatic solid-pseudopapillary tumor, placental site trophoblastic tumor, primary mediastinal B cell lymphomas (some), prostate carcinoma, renal cell carcinoma, renal cell sarcoma, rhabdomyosarcoma and other sarcomas, schwannoma, tumor of wolffian origin of broad ligament and ovary, urothelial carcinoma, uterine carcinoma, uterine cellular leiomyomas (50%), uterine leiomyosarcomas and other uterine sarcomas

**Negative staining:** myeloid and erythroid precursors, other female genital tract tumors (including clear cell carcinomas)

### CD11

CD11a, b and c all have same beta chain (CD18)

Members of integrin receptor family; heterodimers of noncovalently associated alpha and beta subunits

### CD11a

Aka alpha L; LFA-1 (in complex with CD18)

An alpha integrin chain that binds to CD18 and mediates leukocyte adhesion and lymphocyte recirculation through lymph nodes

With CD18, binds to ICAM-1 (CD54, leukocyte adhesion molecule) and ICAM-2 (CD102)

Facilitates lymphocyte blastogenesis, cellular cytotoxicity, lymphocyte-endothelial cell adhesion, and binding to unopsonized bacteria (*E. coli*) and fungi (*Histoplasma capsulatum*)

Note: patients with leukocyte adhesion deficiency (mutations in CD18) have often fatal immunodeficiency early in life

Marker of differentiation in acute promyelocytic leukemia

**Positive staining (normal):** all leukocytes

**Negative staining:** platelets

### CD11b

Aka CR3, iC3b receptor

Mediates phagocytosis of particles opsonized with iC3b

Facilitates neutrophil aggregation, adhesion to substrates by opsonization, chemotaxis

Ligands include fibrinogen, Factor X, ICAM-1, *Saccharomyces cerevisiae*, *Staphylococcus epidermidis*, *Histoplasma capsulatum*,

Note: C3 is common to classical and alternate complement pathway, and serves as an amplification step

C3b (activated C3) can amplify by cleaving more C3 via the alternate complement pathway

**Positive staining (normal):** follicular dendritic cells, granulocytes, macrophages, myeloid cells beginning with promyelocytes, NK cells, some B/T cells

**Positive staining (disease):** AML-M1-M3 (35-70%), M4-M5 (80-90%); hairy cell leukemia (virtually all)

### CD11c

Aka CR4, iC3b receptor

Clears opsonized particles and immune complexes; also binds to fibrinogen and is involved in adhesion of monocytes and neutrophils to endothelium

Member of beta 2 family of integrin receptors

**Prognostic value:** associated with good prognosis in B-CLL

**Positive staining (normal):** 50% of activated CD4/CD8+ T cells; granulocytes, lymphocytes, macrophages, NK cells

**Positive staining (disease):** AML-M4-M5 (50%); hairy cell leukemia (virtually all), B-CLL

### CD12

**Positive staining (normal):** granulocytes, monocytes, NK cells, platelets

**Negative staining:** basophils, bone marrow precursors, AML

### CD13

Aka AminoPeptidase N, APN

Myeloid antigen, although CD33 is more specific

Peptide cleaving enzyme of brush border membranes of small intestine, renal proximal tubules and placenta

Also present on CNS synaptic membranes

Receptor for one strain of human coronavirus that causes many upper respiratory tract infections

Defects appear to cause various leukemias/lymphomas

Serves an important function for early CMV infection

CD13 autoantibodies are strongly associated with chronic graft versus host disease after bone marrow transplantation

**Positive staining (normal):** bile duct canaliculi, central nervous system synapses, endothelial cells, fibroblasts, granulocytes (most), large granular lymphocytes (some), macrophages, osteoclasts, perineurium of peripheral nerves, placenta, renal proximal tubules, small intestine

**Positive staining (disease):** AML M1-M5 (75-95%), M6 (usually), CML (90%); pre B ALL (7-10%), pre T ALL (rare)

### CD14

Aka lipopolysaccharide (LPS) receptor, endotoxin receptor

Binding of LPS to CD14 on macrophages causes their activation and release of cytokines

Involved in the clearance of apoptotic cells

Also regulates IgE levels

**Positive staining (normal):** macrophages/monocytes (90%), granulocytes-weak (30%), Langerhans cells; dendritic cells, B cells

**Positive staining (disease):** B-CLL (90%), follicular center cell lymphoma (80%), diffuse large B cell lymphoma (40%); AML-M4/M5 (50-90%)

**Negative staining:** myeloid progenitors, AML M3, M6, M7, Mo-M2 (usually)

### CD15

Aka LeuM1, Lacto-N-Fucopentose III ceramide

Recognizes Hapten X, a carbohydrate linked to cell membrane proteins of myelomonocytic cells

**Positive staining (normal):** myeloid cells (90%); activated B and T cells (including infectious mononucleosis); eosinophils stain intensely

**Positive staining (disease):** Reed-Sternberg cells, 20% of T cell lymphomas, 5% of B cell lymphomas, 50% of carcinomas

**Negative staining:** erythroid cells, platelets; ALL

### CD15s

Aka Sialyl Lewis X; ligand for CD62P and CD62E

**Positive staining (normal):** granulocytes, macrophages

### CD15u

Aka sulfated CD15

### CD16a

Aka Fc receptor III A

Important for Ab dependent cytotoxicity of foreign cells

If target cell has class I MHC, then NK cell's killer cell inhibitory receptor (KIR) inhibits cytolysis

**Positive staining (normal):** NK cells (10-20%), granulocytes, monocytes (rare), alveolar macrophages (common), T cells (some)

**Negative staining:** Myelodysplastic syndrome

### CD16b

Aka Fc receptor III B

**Positive staining:** neutrophils

### CD17

Aka Lactosylceramide

Binds to bacteria and may function in phagocytosis

**Positive staining (normal):** granulocytes, macrophages/monocytes, platelets, basophils, CD19+ B cells, tonsillar dendritic cells

### CD18

Forms the beta 2 chain of CD11a, b, c (leukocyte adhesion molecule)

Important for adhesion and signaling in the hematopoietic system (see CD11 a-c above)

Leukocyte Adhesion Deficiency (LAD-1) caused by CD18 defect coding for common b2 subunit; patients suffer from recurrent infections

**Positive staining:** leukocytes

### CD19

Response regulator that plays a dominant role in establishing signaling thresholds for antigen receptors and other surface receptors on B cells; also regulates B cell development, activation and differentiation

CD19 antibody inhibits B cell activation from anti-immunoglobulin

Coreceptor with CD21

Earliest B cell antigen in fetal tissue

**Positive staining (normal):** Pre B, B cells; first B cell antigen after HLA-DR, follicular dendritic cells

**Negative staining:** plasma cells

### CD20

Aka L26

33kd phosphoprotein with 3 hydrophobic regions that traverse the cell membrane, creating a structure similar to an ion channel

Delivers early signal in B cell activation, allowing resting B cells to respond to later antigens

Rituximab is a chimeric murine-human anti-CD20 antibody used for treatment of B cell lymphomas

**Uses:** commonly used marker for B cells

**Positive staining (normal):** Most B cells (after CD19 and CD10 expression, before CD21/22 expression and surface immunoglobulin expression), retained on mature B cells until plasma cell development; also follicular dendritic cells

**Positive staining (disease):** 90% of B cell lymphomas, 40% of pre B ALL/LBL; 80% of lymphocyte predominant Hodgkin's lymphoma, dimly expressed in T cells (benign and neoplastic), spindle cell thymomas

**Negative staining:** non-hematopoietic cells, most T cells, plasma cells

### CD21

Aka CR2, C3d receptor, EBV receptor

Binds to Epstein Barr virus and breakdown products of complement component C3

Forms a signaling complex with CD19, CD81 and CD225

Both CD21 and CD23 are dendritic cell markers

Hodgkin's lymphoma demonstrates disruption of follicular dendritic cell-germinal cell clusters (evaluated by CD21 and CD23)

**Positive staining (normal):** Mature B cells, follicular dendritic cells

### CD22



Aka B lymphocyte cell adhesion molecule (BL-CAM)

May localize B cells in lymphoid tissues; binds CD45

**Positive staining (normal):** B cells, B-ALL

**Negative staining:** plasma cells

CD23

Aka low affinity IgE receptor

Regulates IgE synthesis by negative feedback

Triggers monokine release (TNF, IL-1, IL-6, GM-CSF) by monocytes

After physiologic germinal cell development, the follicular dendritic cell meshwork expands and follicular dendritic cells in the light zone of the germinal center become CD23 positive

CD23 also acts as B cell growth factor, promoting differentiation into plasma cells

Both CD21 and CD23 are dendritic cell markers

**Positive staining (normal):** Activated mature B cells expressing IgM or IgD, monocytes/macrophages, T cell subsets, platelets, eosinophils, Langerhans cells, follicular dendritic cells

**Positive staining (disease):** B-cell CLL/SLL

**Negative staining:** other B cells; mantle cell lymphoma

CD24

Promotes antigen dependent proliferation of B cells; prevents differentiation into plasma cells

Expressed at high levels in small cell lung carcinoma

**Positive staining (normal):** all B cells, granulocytes, kidney cells, epithelial cells

**Positive staining (disease):** carcinomas, most pre-B ALL/LBL, virtually all B cell lymphomas

**Negative staining:** plasma cells, multiple myeloma, T cells, monocytes, red blood cells, platelets

CD25

Aka IL-2 receptor alpha chain, exists in at least 3 forms

Limited expression may safeguard against catastrophic T-cell proliferation by immunogenic stimulus.

**Positive staining:** Activated B, T, macrophages

**Positive staining (disease):** hairy cell leukemia

CD26

Aka dipeptidylpeptidase IV, adenosine deaminase complexing protein 2

Costimulatory molecule in T cell activation

Cofactor with CD4 for HIV entry into cells

**Positive staining (normal):** Activated T, B cells, NK cells, macrophages, renal proximal tubular epithelial cells, small intestinal epithelium, biliary canaliculae, splenic sinus lining cells

Negative/dim staining: T cells in peripheral blood of mycosis fungoides patients, [AJCP 2001;115:885](#)

### CD27

Marker of T cell activation

CD27/CD70 interactions also regulate B cell proliferation and T cell differentiation

**Positive staining:** T cells, memory B cells

### CD28

Cell adhesion molecule; co-receptor for B cell-T cell cooperation

Promotes T cell activation

Receptor for CD80 (B7) & CD86 (BB1), found on activated B cells

Constitutive, high abundance, low affinity receptor; opposite signals are mediated by CTLA4 (CD152)

Result of T cell antigen stimulation depends on sum of effects of T cell receptor, CD28 and its ligand, CTLA4 and its ligand

CD8+, CD28+ T cells mediate antigen specific cytotoxic T cells (class I restricted) (90% of CD8+ T cells)

CD8+, CD28- T cells mediate suppressor T cells (10% of CD8+ T cells)

**Positive staining (normal):** CD4+ T cells (95%), CD8+ T cells (50%); activated B cells, plasma cells

### CD29

Aka platelet GPIIa, beta-1 integrin, fibronectin receptor

**Positive staining (normal):** fibroblasts, platelets, T cells

### CD30

Aka Ki-1, Ber-H2

Lymphocyte activation antigen, related to tumor necrosis factor

Doesn't work well with B5 fixed tissue

May be involved in negative T cell selection in thymus

**Interpretation:** membranous staining

**Positive staining (normal):** granulocytes, plasma cells, activated B, T and NK cells

**Positive staining (disease):** infectious mononucleosis, lymphocytes infected with HIV, HTLV-1, EBV, HHV8 or hepatitis B; Reed-Sternberg cells, 90% of anaplastic large cell lymphomas, lymphomatoid papulosis, peripheral T-cell lymphomas, embryonal carcinoma of testis, primary effusion lymphoma

### CD31

Aka platelet endothelial cell adhesion molecule, PECAM-1

Encoded on #17

Most sensitive and specific endothelial marker in paraffin sections

Important role in diapedesis step of leukocyte emigration in inflammation; also angiogenesis

**Note:** don't confuse CD31+ macrophages (granular, membranous expression) with a vascular tumor, [AJSP 2001;25:1167](#)

Sensitive for malignant vascular tumors; may be less sensitive for benign lesions

**Interpretation:** membranous stain (not cytoplasmic); endothelium is a positive internal control

**Positive staining (normal):** endothelium, platelets, macrophages and Kupffer cells, granulocytes, T / NK cells, lymphocytes, megakaryocytes, fibroblasts, osteoclasts, neutrophils

**Positive staining (tumors):** epithelioid hemangioendothelioma; epithelioid sarcoma-like hemangioendothelioma ([AJSP 2003;27:48](#)); other vascular tumors, histiocytic malignancies, plasmacytomas; rare carcinomas and sarcomas

### CD32

Aka Fc gamma RII

Low affinity receptor that binds to the Fc region of IgG immune complexes

If B cells are stimulated so that surface immunoglobulin receptors are coclustered with CD32 receptors, B cells do NOT proliferate and may undergo apoptosis instead of proliferation

**Positive staining:** macrophages, granulocytes, B cells, eosinophils, basophils, platelets

### CD33

Myeloid cell antigen (also CD113); a sialoadhesin that may mediate cell-to-cell adhesion, acts as a receptor that inhibits the proliferation of normal and leukemic myeloid cells

**Positive staining (normal):** Precursor myeloid cells; most monocytic cells, epidermal Langerhans cells (variable)

**Positive staining (disease):** AML M1-M5 (75-85%), M7 (variable), CML (90%); blasts (all), some ALL

**Negative staining:** granulocytes, mature bone marrow cells, non-myeloid cells

### CD34

Cell-cell adhesion molecule and cell surface glycoprotein

May mediate attachment of stem cells to bone marrow extracellular matrix or directly to stromal cells

Antibodies are used to quantify and purify lymphohematopoietic stem cell / progenitor cells for research and for clinical bone marrow transplantation; however, counting CD34+ mononuclear cells may overestimate myeloid blasts in bone marrow smears due to hematogones and CD34+ megakaryocytes,

**Interpretation:** membranous stain; endothelium acts as a positive internal control

**Uses:** possibly confirm chronic intestinal pseudo-obstruction, [AJSP 2003;27:228](#)

**Positive staining (normal):** hematopoietic progenitor cells, vascular endothelial cells (these cells are TdT+, HLA-DR+)

**Positive staining (disease):** alveolar soft part sarcoma, preB-ALL (75%), AML (40%), AML-M7 (most), chordoid gliomas, dendritic fibromyxolipoma, dermatofibrosarcoma protuberans, epithelioid sarcomas, gastrointestinal stromal tumors, giant cell fibroblastoma, granulocytic sarcoma, hamartomatous tumors of

([Hum Path 2002;33:307](#)), Kaposi's sarcoma (strong, diffuse in spindle cells), liposarcomas (myxoid, pleomorphic), MFH, malignant peripheral nerve sheath tumors, meningeal hemangiopericytomas, meningiomas (some), metanephric adenocarcinoma of kidney (stroma only), myelodysplastic syndrome (myeloid blasts), myofibroblastoma of breast, neurofibromas, nuchal fibromas (also CD99+), papillary thyroid carcinoma, paratesticular leiomyosarcoma (30%), pleomorphic hyalinizing angiectatic tumor, pseudoangiomatous stromal hyperplasia of breast, schwannomas (usually), sclerosing liposarcoma (spindle and atypical cells), solitary fibrous tumors, synovial sarcoma (focal in 6% of monophasic tumors), blasts in transient myeloproliferative disorder

**Negative staining:** Ewing's sarcoma/PNET, myofibrosarcoma of breast, inflammatory myofibroblastic tumors of stomach

### CD35

Aka CR1, C3b and C4b receptor

Mediates adherence of immune complexes coated with C4b/C3b and their transport to the fixed phagocyte systems of the spleen and liver

Cofactor for specific proteolytic cleavage of C3b and C4b by plasma serine protease factor I, which limits complement activation and produces ligands for other complement receptors

The Knops, McCoy, Swain-Langley, and York blood group antigens are located on CD35

**Positive staining:** granulocytes, macrophages, B cells, T cells (10%), NK cell subset, erythrocytes, follicular dendritic cells, eosinophils, glomerular podocytes, some astrocytes

### CD36

Aka platelet GPIV or GPIIb; thrombospondin receptor

Scavenger receptor for 50% of oxidized LDL and shed photoreceptor outer segments

Cell adhesion molecule in platelet adhesion and aggregation, platelet-monocyte and platelet-tumor cell interaction

Site of cytoadherence of Plasmodium falciparum infected erythrocytes to microvascular endothelial cells

CD36 deficiency frequent in sub-Saharan Africa, Asia; associated surprisingly with susceptibility to severe cerebral malaria

Development of anti-CD36 antibodies can cause serious complications in multiply transfused patients (sickle cell disease)

**Positive staining (normal):** platelets, macrophages, endothelial cells, early erythroid cells, megakaryocytes

**Positive staining (disease):** AML M4-M7

**Negative staining:** AML M0-M2 (usually), M3

### CD37

Possibly involved in signal transduction, belongs to tetraspanin family

**Positive staining (normal):** B cells, B cell lymphomas, low levels on T cells, neutrophils, granulocytes, monocytes

**Positive staining (disease):** hairy cell leukemia

### CD38

Novel enzyme capable of catalyzing multiple reactions; two enzyme products are calcium messengers

Positive and negative regulator of cell activation and proliferation, depending on the cellular environment

Involved in adhesion between human lymphocytes and endothelial cells

Important for leukemia phenotyping and classification, targeting of immunotoxin antibody in myeloma treatment

Increases with HIV seroconversion; coexpression with CD8 associated with progression (indicates persistent viral stimulation)

**Positive staining (normal):** plasma cells (strong), lymphoid progenitor cells, NK cells, B and T cells, monocytes, erythroid and myeloid precursors, thymocytes, blasts, brain, muscle, kidney, liver, ovary, pancreas, placenta, testis

**Positive staining (disease):** lymphoma, neuroblastoma

### CD39

Aka vascular ATP diphosphohydrolase

Plasma membrane-bound enzyme that hydrolyzes extracellular ATP and ADP to AMP

Important inhibitor of platelet activation

**Positive staining (normal):** B, T and NK cells, endothelial cells, placenta

### CD40

Plays a central role in regulating cell-mediated immunity and antibody mediated immunity

May mediate inflammatory component of atherogenesis

**Positive staining (normal):** B cells, macrophages, dendritic cells, endothelial cells, fibroblasts, keratinocytes

**Positive staining (disease):** carcinomas, most B cell lymphomas, B-ALL (some)

**Negative staining:** plasma cells

### CD41

Aka platelet GPIIb

Receptor for fibrinogenin, von Willebrand factor and fibronectin

Mutations cause thrombasthenia

**Positive staining (normal):** platelets, megakaryocytes

**Positive staining (disease):** AML M7, blasts in transient myeloproliferative disorder

### CD42a

Aka platelet GPIX

CD42a-d complex is receptor for von Willebrand factor and thrombin

Actual binding site of vWf and thrombin is on CD42b

This complex mediates adhesion of platelets to subendothelial matrices exposed upon damage to endothelium and amplifies platelet response to thrombin

Absence of CD42 complex (mutations in CD42 a-c) causes Bernard-Soulier syndrome (BSS), a bleeding disorder with thrombocytopenia and giant platelets

**Positive staining (normal):** platelets and megakaryocytes

#### CD42b

Aka platelet GPIb alpha

CD42a-d complex is receptor for von Willebrand factor and thrombin

Actual binding site of vWf and thrombin is on CD42b

**Positive staining (normal):** platelets and megakaryocytes

**Positive staining (disease):** blasts in transient myeloproliferative disorder

#### CD42c

Aka platelet GPIb beta

**Positive staining (normal):** platelets and megakaryocytes

#### CD42d

Aka platelet GP V

CD42d mouse monoclonal antibodies are used to detect auto- and allo-anti-platelet antibodies

Co-expression studies suggest that CD42d may be essential to form the high affinity thrombin receptor

**Positive staining (normal):** platelets and megakaryocytes

#### CD43

Aka leukosialin, sialophorin

Appears to be an anti-adhesive molecule mediating repulsion between leukocytes and other cells, although it may act as an adhesion molecule under other circumstances

Expression defective in Wiskott-Aldrich syndrome, although secondary to X linked genetic defect; causes defects in cytotoxic and helper T cell functions

**Positive staining (normal):** Most T cells, activated B cells, NK cells, granulocytes, monocytes, megakaryocytes, brain

**Positive staining (disease):** 80% of T cell lymphomas; coexpressed with CD20 in SLL but not benign lesions; granulocytic sarcomas, AML, most ALL's, plasmacytomas; mast cell disease (also positive for tryptase, CD68, CD117)

#### CD44

Family of cell surface glycoproteins with isoforms generated by alternate splicing of mRNA

Important in epithelial cell adhesion to hyaluronate in basement membranes and maintaining polar orientation of cells; also binds laminin, collagen and fibronectin

May help lymphomas disseminate by binding to high endothelial venules

Involved in leukocyte attachment and rolling on endothelial cells, homing to peripheral lymphoid organs and sites of inflammation and leukocyte aggregation

Uses: reactive urothelium has diffuse full thickness staining vs. carcinoma in situ, [AJSP 2001;25:1074](#)

**Prognostic significance:**

**Colon carcinoma:** overexpression of CD44v predicts an aggressive course

**Endometrial carcinoma:** loss of CD44 related to invasion

**Lung carcinoma:** loss of CD44 related to invasion

**Lymphomas - diffuse large cell and B-CLL:** expression associated with poor prognosis

**Neuroblastoma:** loss of CD44 related to invasion

**Prostate cancer:** loss associated with poor outcome

**Urothelial neoplasms, papillary:** loss of CD44 immunoreactivity (restricted to basal cell layer in normal urothelium) associated with increasing tumor grade and stage in pTa and pT1 patients, [Mod Path 2000;13:1315](#)

**Positive staining (normal):** white blood cells, red blood cells, breast, colon, stomach, uterus, most tissue; urothelial basal cells; reactive urothelium has diffuse full thickness staining ([AJSP 2001;25:1074](#))

**Positive staining (tumors):** 80% of colorectal carcinomas; tumors or mucosa with well-developed squamous differentiation [Archives 2000;124\(2\):212](#)

**Negative staining:** platelets, hepatocytes, cardiac muscle, kidney tubular epithelium, testis, normal glandular type epithelium, well differentiated adenocarcinomas, urothelial carcinoma

**CD44h**

Aka CD44s

Principal receptor for hyaluronic acid

Theoretical utility in differentiating mesothelioma since it produces abundant hyaluronic acid, but not actually useful because CD44H is reactive in 1/3 to 1/2 of adenocarcinomas, [Hum Path 2002;33:953](#)

**CD44r**

May be involved in leukocyte attachment and rolling on endothelial cells, homing to peripheral lymphoid organs and to sites of inflammation

Heterogeneous group of CD44 variant isoforms expressed constitutively in epithelial cells and monocyte lineage cells; upregulated in activated leukocytes

**CD45**

Aka leukocyte common antigen (LCA); a tyrosine phosphatase

Critical requirement for T and B cell antigen receptor-mediated activation

Target of immunosuppressive antibody treatment

Major component of glycocalyx

Negative in patients with severe combined immunodeficiency, characterized by a defect in function or B and T cell development, lymphopenia, and deficiency in humoral and cell-mediated immunity.

Different subsets of hematopoietic cells express different isoforms, which can change in response to cytokines:

CD45RA - naive/resting T cells, medullary thymocytes

CD45RO - memory/activated T cells, cortical thymocytes

**Positive staining (normal):** all hematopoietic cells, stronger in lymphocytes (10% of surface area)

**Negative staining:** red blood cells, non-hematopoietic cells, lymphoplasmacytic lymphoma, lymphoblastic lymphoma, anaplastic lymphoma, multiple myeloma, Reed-Sternberg cells

CD45RO

Aka UCHL-1

**Positive staining (normal):** memory and activated T cells, some B cells, granulocytes (weak), macrophages (weak), cortical thymocytes

**Positive staining (disease):** 75% of T cell non-Hodgkin's lymphomas, variable T cell ALL/LBL, 25% of AML

**Negative staining:** Most B cell non-Hodgkin's lymphomas, carcinomas

CD46

Aka membrane cofactor protein (MCP)

Cofactor for Factor I proteolytic cleavage of C3b and C4b; prevents inappropriate complement activation, especially via alternative pathway, by limiting formation and function of C3 convertases

Receptor for measles virus and HHV-6

Has multiple isoforms

Acrosomal CD46 is exposed on sperm head at capacitation; may help fuse spermatozoa and oocyte

**Positive staining (normal):** all cells except erythrocytes

CD47

Aka integrin associated protein (IAP); one of many thrombospondin receptors

Similar to Rh-antigen

May interact with integrins and mediate intracellular calcium increase during cell adhesion

May help macrophages distinguish self from foreign substances

May have role in giant cell creation from macrophage fusion

**Positive staining (normal):** hematopoietic cells, epithelial cells, endothelial cells, fibroblasts, mesenchymal cells

**Positive staining (disease):** tumor cell lines

CD47R

Aka Rh related antigen

Similar to Rh-antigen; may interact with integrins

Previously CDw149

CD48

Mediates adhesion via its receptor, CD2



CD48-positive lymphocytes decreased in paroxysmal nocturnal hemoglobinuria

**Positive staining (normal):** most leukocytes, activated lymphocytes

**Negative staining:** neutrophils, platelets

### CD49a

Aka very late antigen (VLA) alpha 1 chain, integrin alpha 1 chain

Integrins are integral cell-surface proteins composed of an alpha chain and a beta chain. A given chain may combine with multiple partners resulting in different integrins.

Very late activation proteins (VLA) are a family of integrins originally identified on activated human T cells, later on fibroblasts, platelets, others. Six forms, VLA<sub>1</sub> to VLA<sub>6</sub>, have been identified, each with distinct alpha chain (numbered alpha-1 to alpha-6) associated with a common beta chain.

CD49a - Laminin and collagen receptor

**Positive staining (normal):** activated B and T cells, monocytes

### CD49b

Aka very late antigen (VLA) alpha 2 chain - on T cells

Aka GPIa/IIa when expressed on platelets

Receptor for laminin, collagen, fibronectin, e-cadherin

Responsible for platelet adhesion to collagen (blood clotting), role in angiogenesis

**Positive staining (normal):** platelets, activated B & T cells

### CD49c

Aka very late antigen (VLA) alpha 3 chain

Receptor for laminin, collagen, fibronectin, thrombospondin

**Positive staining (normal):** nonhematopoietic cells

### CD49d

Aka very late antigen (VLA) alpha 4 chain

Receptor for fibronectin, thrombospondin, VCAM-1

Role in cell-cell interactions and cell adhesion to the extracellular matrix

Promotes (a) lymphocyte migration into tissue by strengthening lymphocyte adhesion to endothelial cells, (b) rolling of T cells in vascular lumen on VCAM-1 of endothelium, (c) homing of T cell subsets to Peyer's patches, (d) differentiation of hematopoietic precursor cells by adhesion to bone marrow stromal cells

Relevant to tumor progression and metastasis

**Positive staining (normal):** macrophages, T and B cells, thymocytes, eosinophils, basophils, NK cells, dendritic cells, myeloid cells, erythrocyte precursors

**Positive staining (disease):** melanoma cells

**Negative staining:** erythrocytes, platelets, neutrophils

### CD49e

Aka very late antigen (VLA) alpha 5 chain

**Positive staining (normal):** platelets, monocytes, neutrophils

### CD49f

Aka very late antigen (VLA) alpha 6 chain

Laminin receptor

Important for formation of hemidesmosomes of stratified squamous and transitional epithelia

**Positive staining (normal):** epithelial cells

### CD50

Aka ICAM-3; ligand for LFA-1 (CD54)

Provides adhesion signals important in B-T cell interactions

Important in MHC restricted interaction between T cells and target cells

Regulates leukocyte morphology

**Positive staining (normal):** leukocytes, epidermal Langerhans cells, endothelial cells

**Negative staining:** non-hematopoietic cells

### CD51

Aka vitronectin receptor-alpha chain; beta chain of vitronectin receptor is CD61

**Positive staining (normal):** platelets, endothelial cells, megakaryocytes

### CD52

Aka Campath-1

CD52 antibodies are lytic for target cells, both with human complement and via antibody dependent cellular cytotoxicity

CD52 antibodies used for long-term depletion of lymphocytes in vivo, in trials for CLL and as immunosuppressant; patients have higher risk for opportunistic infections

**Positive staining (normal):** thymocytes, lymphocytes, monocytes/macrophages, eosinophils, epithelial cells lining the male reproductive tract

**Positive staining (disease):** most lymphoid malignancies (variable levels),

**Negative staining:** lymphocytes from patients with PNH, neutrophils (weaker than eosinophils)

### CD53

Most specific and reliable pan-leukocyte marker

May transduce CD2-generated signals in T cells and natural killer cells

**Positive staining (normal):** leukocytes

**Negative staining:** platelets, red blood cells, non-hematopoietic cells

### CD54

Aka ICAM-1 (intercellular adhesion molecule 1); ligand for LFA-1 (CD50)

Receptor for rhinovirus, malaria infected erythrocytes

Involved in adhesion of neutrophils to endothelium at site of inflammation

Reacts with CD11a / CD18 or CD11b / CD18 resulting in immune reaction or inflammation

**Positive staining (normal):** broad, B and T cells, monocytes, endothelial cells, epithelial cells (various)

**Positive staining (tumors):** keratoacanthoma (more in fully developed lesions with inflammatory infiltrate), cutaneous squamous cell carcinoma

## CD55

Aka decay accelerating factor

Binds C3bBb (alternative pathway convertase) and C4b2a (classical pathway convertase) to accelerate decay of the C3 convertases; protects against inappropriate complement activation

Receptor for CD97

Receptor for echovirus and Coxsackie B virus

Deficient in red blood cells from patients with paroxysmal nocturnal hemoglobinuria

**Positive staining (normal):** all hematopoietic cells and all cell types in intimate contact with complement proteins; also epithelial cells lining extracellular compartments, body fluids, extracellular matrix

## CD56

Aka N-CAM (neural cell adhesion molecule), at #11q23

Regulates homophilic (like-like) interactions between neurons and between neurons and muscle

Also associates with fibroblast growth factor receptor and stimulates tyrosine kinase activity of receptor to induce neurite outgrowth

When neural crest cells stop making N-CAM and N-cadherin and start displaying integrin receptors, cells separate and migrate

Contributes to cell-cell or cell-matrix adhesion during development

Lymphocyte activated killer phenomenon mediated by IL-2 activated CD56+, CD3-, NK cells

Prototypic marker of NK cells, also present on subset of CD4+ and CD8+ T cells

**Positive staining (normal):** NK cells (80-90%), activated T cells; cerebellum and brain at neuromuscular junctions, also normal neuroendocrine tissues

**Positive staining (tumors):** myeloma, myeloid leukemia, neuroendocrine tumors, Wilm's tumor, adult neuroblastoma, NK/T cell lymphomas, pancreatic acinar cell carcinoma, pheochromocytoma, small cell lung carcinoma

**Negative staining:** PNET/Ewing's sarcoma

## CD57

Aka Leu7

Glycoprotein with cell adhesion functions

NK cell marker and neuroendocrine marker

Subset of NK cells (note: NK cells have no TCR membrane expression or gene rearrangement)

CD16+, CD57-: substantial NK activity

CD16-, CD57-: no NK activity

CD16-, CD57+: weak NK activity

CD16+, CD57+: variable NK activity

Associated with poor prognosis in nasal lymphomas

**Positive staining (normal):** NK subset, T cell subset (CD2,3,5), neuroectodermal tissue, brain, prostate, proximal tubules of kidney

**Positive staining (tumors):** neuroectodermal tumors, small cell lung cancer (some), prostatic adenocarcinoma, nerve sheath origin lesions, metanephric adenoma, renal carcinoid tumors, some clear cell renal cell carcinomas, spindle cell thymomas ([AJSP 2001;25:111](#)), lymphomas (some)

CD58

Aka LFA-3 (lymphocyte function associated antigen); ligand for CD2

Mediates adhesion between NK and target cells, antigen presenting cells and T cells, thymocytes and thymic epithelial cells

**Positive staining (normal):** leukocytes, erythrocytes, endothelial cells, epithelial cells, fibroblasts

CD59

Aka protectin

Regulates complement mediated cell lysis by inhibiting formation of membrane attack complex (MAC)

Genetic defects that cause a reduction or loss of both CD59 and CD55 on erythrocytes produce paroxysmal nocturnal hemoglobinuria (PNH)

Incorporated into HIV envelope, protects virus and HIV infected cells against complement deposition

Expression on erythrocytes important for their survival

**Positive staining (normal):** most cells

CDw60

Antibodies provide costimulatory/comitogenic signals for T cells

Expressed on most T cells in autoimmune lesions

**Positive staining (normal):** platelets, T subset, thymic epithelium, activated keratinocytes, synovial fibroblasts, glomeruli, smooth muscle cells, astrocytes

CD60a

GD3 - carbohydrate structure

CD60b

9-O-acetyl-GD3 - carbohydrate structure

CD60c

## 7-O-acetyl-GD<sub>3</sub> - carbohydrate structure

### CD61

Aka platelet glycoprotein IIb/IIIa

Receptor for fibrinogen, fibronectin, prothrombin, thrombospondin, vitronectin, plasminogen

Mediates platelet aggregation by binding soluble fibrinogen, forming platelet plug

Defects cause Glanzmann thrombasthenia, an autosomal recessive disorder and the most common inherited platelet disease

**Positive staining (normal):** platelets, megakaryocytes, myeloid progenitor cells, endothelial cells

**Positive staining (disease):** AML M7, AML M6 (some), blasts in transient myeloproliferative disorder

**Negative staining:** AML M0-M5, M6 (most)

### CD62E

Aka E selectin; endothelial leukocyte adhesion molecule-1 (ELAM-1)

Ligand for sialyl-Lewis X

Mediates leukocyte rolling on activated endothelium at inflammatory sites, atherosclerosis, tumor cell adhesion during hematogenous metastasis

Patients with Leukocyte Adhesion Deficiency 2 syndrome, who lack sialyl Lewis X component of selectin counter-receptors, suffer recurrent pyogenic infections

**Positive staining (normal):** endothelial cells (after cytokine stimulation)

### CD62L

Aka L selectin; LECAM-1

Mediates lymphocyte homing to high endothelial venules of peripheral lymphoid tissue, leukocyte rolling on activated endothelium at inflammatory sites

**Positive staining (normal):** B, T, NK cells, monocytes, neutrophils, eosinophils, precursors

### CD62P

Aka P selectin; PADGEM

Interaction with CD162 mediates tethering and rolling of leukocytes on the surface of activated endothelial cells, the first step in leukocyte extravasation and migration

Mediates rolling of platelets on endothelial cells, platelet-mediated delivery of lymphocytes to high endothelial venules

Constitutive expression in inflammation may contribute to tissue destruction, atherogenesis and thrombosis

May be reduced in gray platelet syndrome, [139090](#)

Redistributes to the plasma membrane during platelet activation and degranulation.

**Positive staining (normal):** platelets, megakaryocytes, activated endothelial cells

### CD63

Aka lysosomal-membrane-associated glycoprotein 3, LAMP-3, melanoma associated antigen, NKI-C3

Intracellular lysosomal/endosomal/granule protein, in Weibel-Palade bodies of vascular endothelium

Marker of platelet activation (transported to surface after activation)

Associated with early stages of melanoma progression

**Positive staining (normal):** activated platelets, macrophages, fibroblasts, osteoclasts, endothelium, smooth muscle, neural tissue (brain white matter and peripheral nerves), synovial lining cells

**Positive staining (tumors):** melanoma

## CD64

Aka Fc gamma RI

High affinity receptor binds to Fc region of IgG

Important in phagocytosis via receptor-mediated endocytosis of IgG-antigen complexes

Mediates antigen capture for presentation to T cells, antibody-dependent cellular cytotoxicity, release of cytokines and reactive oxygen intermediates

**Positive staining (normal):** Macrophages/monocytes, activated granulocytes, dendritic cells, early myeloid cells

**Positive staining (disease):** AML M0-M2 (variable); M3 (usually); M4, M5

**Negative staining:** AML M7

## CD65

Aka VIM2, ceramide-dodecasaccharide

Adhesive molecule that appears to be significant risk factor for extravascular AML infiltration

**Positive staining (normal):** myeloid cells, monocytes

## CD65s

Widely used for acute leukemia cell typing and to identify a subset of pre-pre-B ALL

Aka sialylated-CD65

May inhibit phagocytosis

**Positive staining (normal):** granulocytes, monocytes

**Positive staining (disease):** myeloid leukemia cells

## CD66a

Aka CEACAM1, biliary glycoprotein, BGP, C-CAM

Primordial protein of carcinoembryonic antigen (CEA) family

Cell adhesion molecule capable of activating neutrophils; may regulate CD11/CD18 activity

Receptor for Neisseria gonorrhoea and N. meningitidis

Downregulated in colorectal, endometrial and hepatocellular carcinomas; supplementation may cause tumor regression in vitro or in rodents

Downregulated in Gleason grade 4/5 prostate carcinoma, [Hum Path 2002;33:290](#)

**Positive staining (normal):** granulocytes, epithelial cells, prostate glands and ducts (dense), bile canaliculi between liver cells

**Positive staining (disease):** low grade prostatic carcinoma

**Negative staining:** prostate carcinoma, Gleason grade 4/5

#### CD66b

Aka CEA gene member 6; formerly CD67

Capable of activating neutrophils; may regulate CD11/CD18 adhesion activity

**Positive staining (normal):** granulocytes

**Positive staining (disease):** chronic myelogenous leukemia

#### CD66c

Aka noncross reactive antigen (NCA)

Capable of activating neutrophils; may regulate CD11/CD18 adhesion activity

**Positive staining (normal):** granulocytes

#### CD66d

Capable of activating neutrophils and functions as a receptor for Neisseria gonorrhoea and N. meningitidis

May play a signaling role and regulate adhesion activity of CD11/CD18 in neutrophils

**Positive staining (normal):** granulocytes

#### CD66e

Aka CEA, carcinoembryonic antigen

May play a role in the process of metastasis of cancer cells

Serum marker of tumor burden, relapse

Removed by hepatic Kupffer cells via a specific receptor.

**Uses:** 85% sensitive, 96% specific for lung adenocarcinomas vs. mesotheliomas; diffuse cytoplasmic staining with membrane enhancement

**Positive staining (normal):** biliary tract, colon (fetal), epithelial cells (apical surfaces), GI adenocarcinomas (endodermally derived), granulocytes, small intestinal crypts; small intestinal goblet cell mucin (not intracytoplasmic)

**Positive staining (tumors):** colonic and lung adenocarcinoma, medullary thyroid carcinoma

**Variable staining:** breast carcinoma, endometrial carcinoma, neuroendocrine carcinoma, urothelial carcinoma

**Negative staining:** hepatocellular carcinoma, mesothelioma, ovarian carcinoma, prostate adenocarcinoma, renal cell carcinoma, thyroid carcinoma other than medullary

#### CD66f

Aka pregnancy-specific glycoprotein

May be involved in immune regulation, protection of fetus from maternal immune system

Low levels in maternal blood predict spontaneous abortion

## CD67

Recognizes non-specific cross-reactive antigens present on granulocytes

May have role in neutrophil activation

## CD68

Aka KP-1

May have role in macrophage phagocytic activities

Specific to lysosomes, not cell lineage

**Positive staining (normal):** macrophage/monocytes, basophils, dendritic cells, mast cells, myeloid cells, CD34+ progenitor cells, neutrophils, osteoclasts, activated platelets, B and T cells

**Positive staining (tumors):** AML-M4/M5, angiosarcoma (granular cell type), B cell lymphoma (some), giant cell angioblastoma, granular cell tumors, hairy cell leukemia, histiocytic sarcoma, interdigitating dendritic cell sarcoma ([AJSP 2002;26:530](#)), Langerhans cell histiocytosis, mastocytosis, mast cell disease (also positive for tryptase, CD43, CD117), melanoma (some)

## CD69

Aka activation inducer molecule (AIM), early activation antigen (EA-1)

Earliest inducible cell surface glycoprotein acquired during lymphoid activation

Involved in early events of T cell, NK cell, monocyte and platelet activation

Associated with Th-1 T cell differentiation and associated cytokines (IL-2, TNF-alpha, interferon-gamma), [Hum Path 2002;33:330](#)

Highly expressed on T cells from inflammatory infiltrates of rheumatoid arthritis, viral hepatitis, autoimmune thyroid disorders;

**Positive staining (normal):** activated T cells, B cells, NK cells, neutrophils, eosinophils, epidermal Langerhans cells

**Positive staining (disease):** T cell lymphomas (angioimmunoblastic, Lennert's, mycosis fungoides/Sezary syndrome)

**Negative staining:** anaplastic large cell lymphoma

## CD70

Aka CD27 ligand

Role in T cell activation; induces T cell proliferation and enhances generation of cytolytic T cells

**Positive staining (normal):** activated B, T cells

**Positive staining (disease):** Reed-Sternberg cells

## CD71

Aka transferrin receptor



Present on actively proliferating cells; essential for iron transport into proliferating cells (benign and malignant)

Ferrotransferrin binds CD71 at neutral pH, is internalized to an acidic endosomal compartment

Iron-free apotransferrin remains bound to CD71 at pH 5, is returned to cell surface, where pH rises to 7.4.

At neutral pH, apotransferrin loses affinity for receptor, is released into circulation, allowing a new cycle to begin

**Positive staining (normal):** all proliferating cells plus iron requiring cells: reticulocytes, erythroid precursors, capillary endothelium in brain

**Positive staining (disease):** AML M6, primary effusion lymphoma

### CD72

Cell surface protein expressed exclusively on B cells; may control B cell proliferation

Associated with CD5

**Positive staining (normal):** B cells

**Positive staining (disease):** hairy cell leukemia

### CD73

Aka ecto-5'-nucleotidase, PI-linked

Catalyses dephosphorylation of purine and pyrimidine ribo- and deoxyribonucleoside monophosphates to their corresponding nucleosides

Mediates costimulatory signals in T cell activation, lymphocyte adhesion to endothelium

May be lymphocyte maturation marker

High levels are poor prognostic factors in leukemia/lymphomas

**Positive staining (normal):** B and T cell subset; endothelial cells, on follicular dendritic cells, epithelial cells

**Positive staining (disease):** acute T cell leukemia, CLL, ALL

### CD74

Gamma chain antigen associated with MHC class II antigen

In synthesis of class II antigens of MHC, newly synthesized alpha and beta chains form stable complex with gamma chains in the endoplasmic reticulum; then transported to Golgi, where gamma chain dissociates

**Positive staining (normal):** B-cells, activated T-cells, macrophages, activated endothelial and epithelial cells

### CD75

Aka lactosamines; LN-1

Ligand for CD22

Involved in cell adhesion

**Positive staining (normal):** B cells, T cells, endothelial cells

**Positive staining (disease):** “popcorn cells” of lymphocyte predominance Hodgkin disease

CD75s

Alpha-2,6-sialylated lactosamines (formerly CDw75 and CDw76)

CDw76

Deleted at 7th HLDA Workshop; see new CD75s

CD77

Aka globotriaosylceramide, pK blood group

Binds to Shiga toxin (produced by *Shigella dysenteriae*), verotoxin 1 (produced by *E. coli*), CD19

**Positive staining (normal):** B cells

**Positive staining (disease):** Burkitt's lymphoma

CDw78

Deleted at 7th HLDA Workshop

CD79a

Encodes the Ig-alpha protein of the B-cell antigen receptor; receptor also includes Ig-beta protein, surface immunoglobulin

Expressed early in B-cell differentiation (often positive when mature B-cell markers are negative); also expressed in plasma cells

**Uses:** positive in acute lymphoblastic leukemia, small B cell lymphoproliferative disorders when CD20 may be negative; more consistently preserved in infarcted lymphomas than CD20, [Archives 2003;127:60](#)

**Positive staining:** B cell lymphomas, lymphocyte-predominant Hodgkin lymphoma, classic Hodgkin lymphoma

CD79b

Encodes the Ig-beta protein of the B-cell antigen receptor; receptor also includes Ig-alpha protein, surface immunoglobulin

CD80

Aka B7-1, BB1

Ligand for T cell marker CD28 or CTLA4 (CD152)

Co-regulator of T cell activation with CD86

Has critical role in autoimmune, humoral, and transplant responses

**Positive staining (normal):** activated B cells, T cells, macrophages, dendritic cells

CD81

### Aka Target of an Anti-Proliferative Antibody (TAPA1)

Antibodies against TAPA1 induce homotypic aggregation of cells and can inhibit their growth

Member of CD19/CD21/Leu-13 signal transduction complex; regulates cell growth in unknown manner

May be site of binding of Hepatitis C virus

**Positive staining (normal):** lymphocytes, endothelial cells, epithelial cells

**Negative staining:** erythrocytes, platelets, neutrophils

### CD82

Aka prostate cancer antimetastasis gene KAI1, 'kang ai' (Chinese for anticancer).

Metastasis suppressor gene; downregulated in tumor progression of cancers

Expression correlates with p53 expression

Associates with CD4 or CD8 and delivers costimulatory signals for T cell receptor pathway

Activation antigen for T cells

**Positive staining (normal):** activated/differentiated hematopoietic cells

**Negative staining:** erythrocytes

### CD83

**Summary:** Marker for dendritic cells

May assist in antigen presentation or cellular interactions that follow lymphocyte activation.

**Positive staining (normal):** dendritic cells, Langerhans cells, lymphocytes

**Positive staining (disease):** Churg-Strauss syndrome myocarditis in inflammatory infiltrates,

### CD84

**Summary:** Homophilic adhesion molecule that enhances IFN-gamma secretion

**Positive staining (normal):** B cells, thymocytes, T cell subset, monocytes/macrophages, platelets

### CD85

**Summary:** Marker of plasma cells and hairy cell leukemia

Aka LILRB1

ILT/LIR family

Inhibitory MHC class I receptor prevents killing by NK and T cells

Also inhibits B cells activated by antigen receptor and myelomonocytic cells activated by HLA-DR

**Positive staining (normal):** plasma cells (strong), mantle zone, germinal center B cells, T cell subset, NK cell subset; dendritic cells

**Positive staining (disease):** hairy cell leukemia (strong)

CD85a-ILT5/LIR3

CD85b-ILT8

CD85c-LIR8

CD85d-ILT4/LIR2, MIR10

CD85e-ILT6/LIR4

CD85f-ILT11

CD85g-ILT7

CD85h-ILT1/LIR7

CD85i-LIR6

CD85j-ILT2/LIR1, MIR7

CD85k-ILT3/LIR5

CD85l-ILT9

CD85m-ILT10

**CD86**

**Summary:** Costimulates IL-2 production and T cell proliferation

Aka B7-2

Ligand for CD28 (CD80 also binds CD28), CD152 (CTLA4)

Induction of an immune response requires T cells to receive 2 sets of signals from antigen presenting cells. The first is delivered through the T-cell receptor complex, while the second is provided by the B-cell activation antigens B7-1, or CD80 and B7-2, or CD86 by interaction with the T-cell surface molecules CD28 and CTLA4

**Positive staining (normal):** interdigitating dendritic cells in T zones of secondary lymphoid organs, Langerhans cells, peripheral blood dendritic cells, memory B cells, germinal center B cells, monocytes (higher levels after g-IFN), endothelial cells, activated T cells

**CD87**

**Summary:** Receptor for urokinase plasminogen activator (uPA), which converts plasminogen to plasmin

Subject to negative feedback regulation by uPA, which cleaves it into an inactive form

Implicated in metastasis - receptors for uPA and plasmin are found at leading edge of tumor cells; plasmin causes hydrolysis of extra-cellular matrix proteins in the path of cellular invasion

May have adherence and chemotaxis functions

**Positive staining (normal):** T-cells, NK cells, monocytes, neutrophils (higher after activation), endothelial cells, fibroblasts, smooth muscle cells, keratinocytes, placental trophoblasts, hepatocytes

**Positive staining (tumors):** carcinomas of breast, colon and prostate; melanoma

**CD88**

**Summary:** receptor for C5a, the chemotactic and inflammatory peptide anaphylatoxin

Stimulates chemotaxis, granule enzyme release and superoxide anion production

Reduced levels in HIV patients

**Positive staining (normal):** granulocytes, macrophages/monocytes, dendritic cells, astrocytes, microglia

### CD89

**Summary:** IgA Fc receptor, binds IgA and eliminates IgA coated targets

Induces phagocytosis, degranulation, respiratory burst and killing of microorganisms

**Positive staining (normal):** granulocyte lineage, monocyte lineage, activated eosinophils, alveolar and splenic macrophages

### CD90

**Summary:** May mediate differentiation of hematopoietic stem cells and synaptogenesis in the CNS

Aka Thy-1

CD34+CD90+ cells include hematopoietic stem cells that serve as autologous grafts to replace the bone marrow in patients with malignancies

**Positive staining (normal):** hematopoietic stem cells, neurons, connective tissue

### CD91

**Summary:** low density lipoprotein receptor-related protein 1; aka alpha-2-macroglobulin receptor

Binds to apoE-containing lipoproteins and mediates chylomicron remnant clearance from the plasma

Also a cell surface receptor for heat shock proteins, [Archives 2003;127:178](#)

**Positive staining (normal):** fibroblasts, dendritic cells, macrophages; liver, brain, lung

### CDw92

May regulate dendritic cell function

**Positive staining (normal):** leukocytes, endothelial cells

### CD93

**Positive staining (normal):** granulocytes, monocytes, endothelial cells

**Positive staining (disease):** AML blasts

### CD94

Inhibits NK cell function

**Positive staining (normal):** NK cells, gamma/delta and alpha/beta T cells

### CD95

**Summary:** activates apoptosis when bound by Fas ligand (FasL, CD178)

## Aka FAS, APO-1

Receptor for FasL; when activated, FADD (Fas-associated death domain, a separate protein from Fas) recruits caspase-8 to the receptor; resulting “death-inducing signaling complex” performs caspase-8 proteolytic activation; activated caspase-8 initiates a subsequent cascade of caspases mediating apoptosis

Fas-FasL system mediates extra-thymic self-tolerance (FasL+ cells induce apoptosis in infiltrating Fas+ lymphocytes), T cell mediated cytotoxicity, halting of immune response

Mutations cause loss of regulation of B lymphocytes, predisposing to systemic autoimmunity (SLE); Fas mutant mice develop lymphadenopathy and systemic autoimmune disease

Downregulation may cause reduction in CD4+ T cells in HIV, [Archives 2002;126:28](#)

**Positive staining (normal):** activated B cells, activated T cells (initially extra but nonfunctional Fas), resting T cells (low levels), breast, vaginal, endometrial and ovarian epithelium

**Positive staining (disease):** thyroid epithelial cells in Hashimoto’s thyroiditis, Reed-Sternberg cells in classic Hodgkin’s lymphoma, [AJSP 2001;25:388](#), Barrett’s esophagus, esophageal adenocarcinoma

**Negative staining:** normal gastric mucosa

## CD96

Aka T cell activated increased late expression (TACTILE)

May be involved in adhesion of activated T and NK cells late in immune response

**Positive staining (normal):** activated T cells

## CD97

Binds to CD55 and G protein-coupled receptors

May be involved in cell adhesion and signaling processes early after leukocyte activation

Highly expressed at sites of inflammation in skin, lung and rheumatoid arthritis.

**Positive staining (normal):** activated T > B cells, monocytes/macrophages, dendritic cells, granulocytes

**Positive staining (tumors):** thyroid carcinomas, GI adenocarcinomas

**Negative staining:** microglia

## CD98

Amino acid transporter, aka SLC3A2

Associated with function of pancreatic islet cells, thyroid C cells and parathyroid cells

Also involved in normal and neoplastic cell growth

Upregulated on leukocytes in inflammatory lesions, strongly expressed by neoplastic cells.

**Positive staining (normal):** broad

**Positive staining (tumors):** transformed cells

## CD99

Aka MIC2, O13

Associated with EWS-FLI1 fusion transcript, t(11;22)(q24;q12), causing FLI-1 protein overexpression

**Interpretation:** distinct membranous staining for Ewings/PNET; cytoplasmic for other tumors

**Positive staining (normal):** ovarian granulosa cells, pancreatic islets, infant thymus, Sertoli cells

**Positive staining (tumors):** T cell acute lymphoblastic lymphoma, calcifying aponeurotic fibroma, Ewing's sarcoma/PNET (95% sensitive), gastrointestinal stromal tumor, intraabdominal desmoplastic small round cell tumor (23-35%), leukemia cutis, nuchal fibromas, perineuroma (myxoid sclerosing type), rhabdomyosarcoma (membranous staining, [AJSP 2002;26:1175](#)), sinonasal undifferentiated carcinoma (rare, [AJSP 2001;25:156](#)), small cell carcinomas of lung (rare), solitary fibrous tumor, synovial sarcoma (poorly differentiated, monophasic and myxoid types), Wilm's tumors (some), endometrial stromal tumors with sex cord differentiation

**Negative staining:** adult neuroblastoma

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