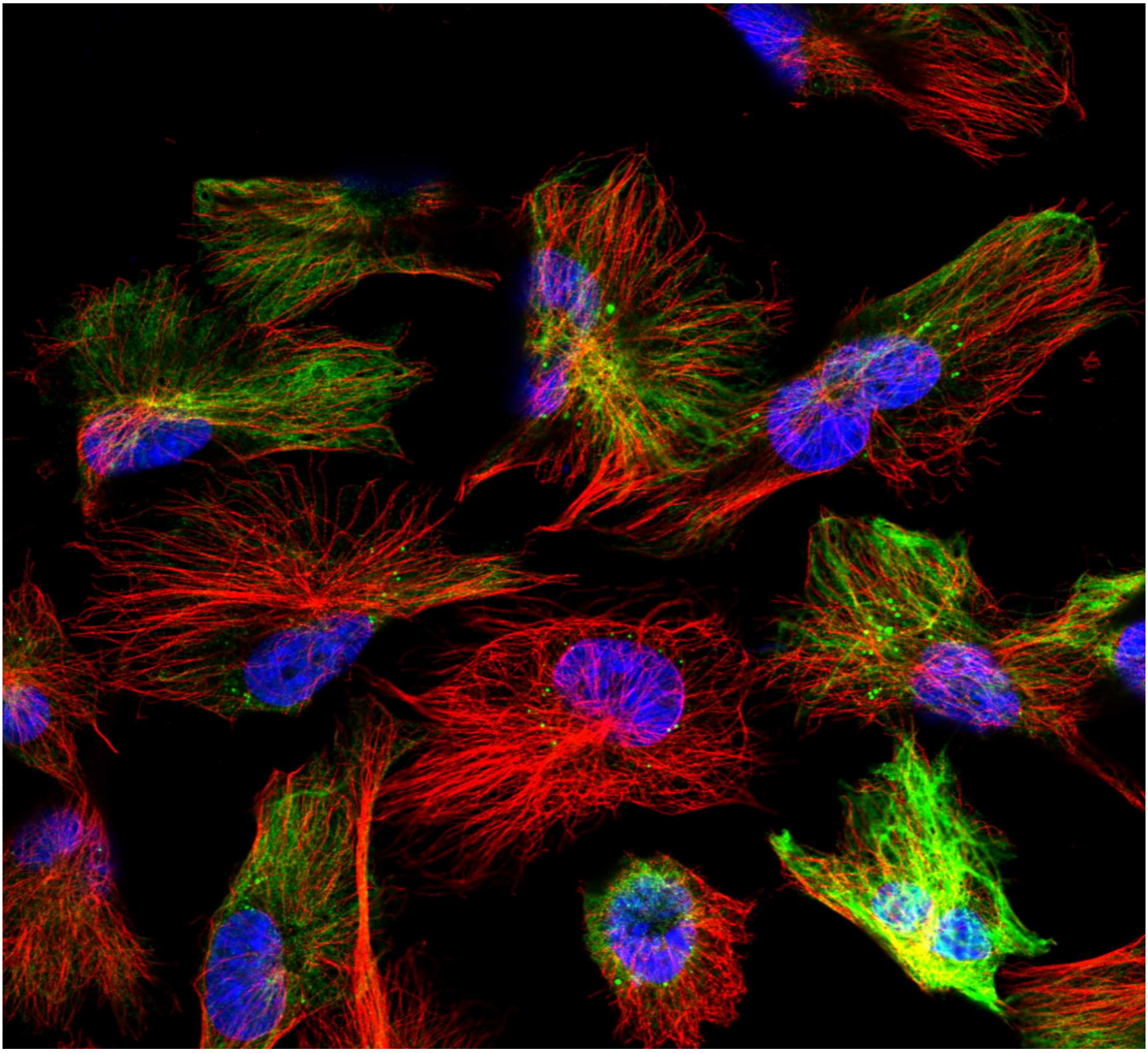
PRIMARY ANTIBODIES FOR CANCER RESEARCH



CANCER STEM CELLS MARKERS

ATLAS ANTIBODIES

PRIMARY ANTIBODIES TARGETING CANCER STEM CELLS

ATLAS ANTIBODIES

There is a high demand to identify biomarkers specific to this disease for screening for early detection, as well as new therapeutic targets. The capacity of these biomarkers to predict the existence, stages, and associated therapeutic efficacy of human cancers would enable improvements in the early diagnosis and survival of cancer patients.

We must expand our knowledge as a step toward the design of practical and safe treatments. Therefore, the identification of molecular biomarkers is unquestionably essential and urgent for an accurate prognosis and development of critical therapeutic targets.

NEEDS

- Specific and effective biomarkers able to identify early stages of the disease and reliable prognostic markers for predicting clinical responses as well as defining the divergent molecular pathways underlying the development of the disease.
- Protein-related data such as citations, application-specific validation and sequence information, and homology, are paramount in the buying process and the single biggest driver for antibody choice.
- A trusted source of data in order to feel confident in the purchase of new antibodies.

WHY ATLAS ANTIBODIES?

Atlas Antibodies continues searching for better early detection markers and new therapeutic targets.

- Over 12,000 product citations worldwide
- Application-specific Enhanced Validation
- Strong roots in the Human Protein Atlas
- Transparency & Open Access Data

Cancer stem cells (CSCs) are a small number of cells, usually 1% to 3% of all cells in a tumor, that drive the tumor's initiation, growth and metastasis, and may cause relapse. Due to their importance, several biomarkers that characterize CSCs have been identified, allowing diagnostic, therapeutic, and prognostic predictions. Thus, selectively targeting CSCs with various agents holds hope for improvement of cancer patients' survival and is a promising therapeutic strategy against cancer. This white paper provides an overview of the most prominent CSC markers, focusing on solid cancers (lung, stomach, liver, breast, and colorectal cancers) and hematological cancers (acute and chronic myeloid leukemias).

Among all cancerous cells, a few acts as stem cells that reproduce and sustain the tumor, much like stem cells normally renew and sustain our organs and tissues. Cancer stem cells (CSCs) are generated by combination of DNA mutations, epigenetic events and tissue microenvironment factors from normal stem cells or precursor/progenitor cells, to which they are closely related and share many of the behaviors and features [1].

One important ability of the CSCs is to form tumors already at low cell numbers. Therefore, targeting CSCs is of primary importance. Many new anti-cancer therapies are evaluated based on their ability to shrink tumors. However, if these therapies are not destroying CSCs, the tumor will soon grow back, often with high resistance to treatments [2]. In addition, CSCs might give rise to metastases, acting as a reservoir of cancer cells, causing relapse after the surgery or a treatment has eliminated the visible signs of the cancer.

CSCs were first identified in hematological cancer such as acute myeloid leukemia in late 90's, when scientists isolated a subpopulation of leukemia cells that expressed the surface marker CD34, but not CD38. The authors established that this CD34+/CD38− subpopulation was capable of initiating tumors [3].

The existence of stem cells in hematological tissue prompted research in other tissue cancer types. Since 2003, CSCs have been identified in several solid tumors, including brain [4], breast [5], colon [6], ovary [7,8], pancreas [9], prostate [10,11], melanoma [12,13], multiple myeloma [14], and non-melanoma skin cancer [15,16].

The term CSCs itself was, however, only coined in 2001 [17].

The most frequently used markers for CSCs isolation include cell surface markers, such as CD133 (PROM1), CD44, ALDH1A1, CD34, CD24 and EpCAM (ESA).

In addition, expression of stemness genes/proteins is also used to identify CSCs. For instance, OCT4, SOX2, and NANOG are the transcription factors which are analyzed in most studies. They are commonly expressed in pluripotent embryonic stem cells, germ cells, certain committed progenitors, as well as cancer cells[18]. However, depending on the tissue where the tumor is generated, different markers can be used. CSCs isolated in breast cancer, for example, are enriched in CD44+CD24−, SP and ALDH+ subpopulations[19]. In brain tumors, such as glioma and glioblastoma, CSCs have instead been identified using cell surface markers including SSEA-1 [20], EGFR [21], and CD44[22].

The use of CD133 (PROM1) for the identification of CSCs in glioma is still in question because tumorigenic cells are equally found in both CD133+ and CD133− cells in some gliomas, while some CD133+ brain tumor cells may not possess tumor-initiating capacity [23].

Using CD133 (PROM1) as a positive marker for colon CSCs also generated conflicting results [24].

For lung cancers, CSC markers include CD44 and CD133 (PROM1), but also CD117 (KIT), CD90 (or THY1),CD166, EpCAM for non-small-cell lung carcinoma (NSCLC), and PODXL-1, PTCH and CD87 for small-cell lung carcinoma (SCLC) [25].

In this white paper, we have selected our CSC markers for solid (Table 1) and hematological (Table 2) tumors. You can also find a list of our extracellular CSC/CD markers (Table 3), extracellular CSC/not-CD markers (Table 4), and intracellular CSC markers (Table 5).

Cover image: Immunofluorescence staining of human U-251MG cells derived from a malignant glioblastoma using the polyclonal anti-NES antibody (HPA026111), in green. Microtubule- and nuclear probes are visualized in red and blue, respectively.

Table 1. Antibodies targeting cancer stem cells in solid tumors

Target Cancer	Marker Location/CD	Product Name	Product Numbers
Colorectal	Extracellular/Surface/CD	Anti-CD24	HPA045879
	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-ITGA6/CD49	AMAb91450, HPA012696, HPA027582
	Extracellular/Surface/CD	Anti-THY1/CD90	AMAb90844, AMAb90846, HPA003733
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
	Extracellular/Surface/CD	Anti-ALCAM/CD166	HPA010926
	Extracellular/Surface/CD	Anti-EPCAM/CD326	AMAb91411, AMAb91413, HPA026761, HPA067463
	Extracellular/Surface	Anti-LGR5	HPA012530
	Extracellular/Surface	Anti-EGFR	AMAb90816, AMAb90819, HPA001200, HPA018530
	Intracellular	Anti-ALDH1A1	HPA002123
	Intracellular	Anti-LETM1	HPA011029, HPA011100
	Intracellular	Anti-NANOG	AMAb91391, AMAb91393
	Intracellular	Anti-POU5F1	AMAb91477
	Intracellular	Anti-SALL4	HPA015291, HPA015791
	Intracellular	Anti-SOX2	AMAb91307, HPA045725
Gastric	Extracellular/Surface/CD	Anti-CD24	HPA045879
	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-THY1/CD90	AMAb90844, AMAb90846, HPA003733
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
	Extracellular/Surface/CD	Anti-EPCAM/CD326	AMAb91411, AMAb91413, HPA026761, HPA067463
	Extracellular/Surface	Anti-LGR5	HPA012530
	Extracellular/Surface	Anti-LINGO2	HPA016633
	Intracellular	Anti-ALDH1A1	HPA002123
	Intracellular	Anti-LETM1	HPA011029, HPA011100
	Intracellular	Anti-NANOG	AMAb91391, AMAb91393
	Intracellular	Anti-POU5F1	AMAb91477
	Intracellular	Anti-SOX2	AMAb91307, HPA045725
Liver	Extracellular/Surface/CD	Anti-CD24	HPA045879
	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-THY1/CD90	AMAb90844, AMAb90846, HPA003733
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
	Extracellular/Surface/CD	Anti-EPCAM/CD326	AMAb91411, AMAb91413, HPA026761, HPA067463
	Intracellular	Anti-AFP	AMAb91610, AMAb91611, HPA010607, HPA023600
	Intracellular	Anti-NANOG	AMAb91391, AMAb91393
	Intracellular	Anti-NOTCH1	HPA067168
	Intracellular	Anti-NOTCH2	HPA048743
	Intracellular	Anti-NOTCH3	HPA044392
	Intracellular	Anti-POU5F1	AMAb91477
	Intracellular	Anti-SOX2	AMAb91307, HPA045725
	Intracellular	Anti-CTNNBL1	HPA027907
Pancreatic	Extracellular/Surface/CD	Anti-CD24	HPA045879
	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
Lung	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-PLAUR/CD87	HPA050843
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
	Extracellular/Surface/CD	Anti-ALCAM/CD166	HPA010926
	Extracellular/Surface/CD	Anti-EPCAM/CD326	AMAb91411, AMAb91413, HPA026761, HPA067463
	Extracellular/Surface/CD	Anti-KIT/CD117	AMAb90900, AMAb90901, AMAb90904, HPA004471, HPA073252
	Extracellular/Surface/CD	Anti-THY1/CD90	AMAb90844, AMAb90846, HPA003733
	Extracellular/Surface	Anti-EGFR	AMAb90816, AMAb90819, HPA001200, HPA018530
	Intracellular	Anti-ALDH1A1	HPA002123
	Intracellular	Anti-NANOG	AMAb91391, AMAb91393
	Intracellular	Anti-POU5F1	AMAb91477

Table 1. *(cont.)*

Target Cancer	Marker Location/CD	Product Name	Product Numbers
Breast	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-EPCAM/CD326	AMAb91411, AMAb91413, HPA026761, HPA067463
	Extracellular/Surface/CD	Anti-ITGB1/CD29	HPA059297, HPA069003
	Extracellular/Surface/CD	Anti-IL2RA/CD25	HPA054622
	Extracellular/Surface/CD	Anti-ITGA6/CD49	AMAb91450, HPA012696, HPA027582
	Extracellular/Surface/CD	Anti-ITGB3/CD61	AMAb91470, HPA027852
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
	Extracellular/Surface/CD	Anti-THY1/CD90	AMAb90844, AMAb90846, HPA003733
	Extracellular/Surface	Anti-LGR5	HPA012530
	Extracellular/Surface	Anti-PROCR	HPA039461
	Extracellular/Surface	Anti-TSPAN8	HPA044337
	Intracellular	Anti-ALDH1A1	HPA002123
	Intracellular	Anti-BMI1	HPA030471, HPA030472
	Intracellular	Anti-CTNNBL1	HPA027907
	Intracellular	Anti-FOXO3	HPA063104
	Intracellular	Anti-NANOG	AMAb91391, AMAb91393
	Intracellular	Anti-NOTCH1	HPA067168
	Intracellular	Anti-NOTCH2	HPA048743
	Intracellular	Anti-NOTCH3	HPA044392
	Intracellular	Anti-POU5F1	AMAb91477
	Intracellular	Anti-SOX2	AMAb91307, HPA045725
Glioblastoma	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-IL2RA/CD25	HPA054622
	Extracellular/Surface/CD	Anti-FUT4/CD15	AMAb91414, AMAb91416
	Extracellular/Surface/CD	Anti-THY1/CD90	AMAb90844, AMAb90846, HPA003733
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
	Extracellular/Surface	Anti-CHL1	HPA003345, HPA005830
	Intracellular	Anti-ALDH1A1	HPA002123
	Intracellular	Anti-KLF4	AMAb91389, AMAb91388, HPA002926
	Intracellular	Anti-NANOG	AMAb91391, AMAb91393
	Intracellular	Anti-NES	AMAb90556, HPA006286, HPA007007, HPA026111
	Intracellular	Anti-POU5F1	HPA015291, HPA015791
	Intracellular	Anti-SALL4	AMAb91307, HPA045725
	Intracellular	Anti-SOX2	HPA027907
Prostate	Extracellular/Surface/CD	Anti-ALCAM/CD166	HPA010926
	Extracellular/Surface/CD	Anti-CD44	HPA005785
	Extracellular/Surface/CD	Anti-EPCAM/CD326	AMAb91411, AMAb91413, HPA026761, HPA067463
	Extracellular/Surface/CD	Anti-KIT/CD117	AMAb90900, AMAb90901, AMAb90904, HPA004471, HPA073252
	Extracellular/Surface/CD	Anti-PROM1/CD133	AMAb91494, HPA004922, HPA031053
	Extracellular/Surface	Anti-TACSTD2	HPA043104, HPA055067
	Intracellular	Anti-ALDH1A1	HPA002123
	Intracellular	Anti-TGM2	HPA021019, HPA029518

* Products with enhanced validation for indicated application
AMAbxxxxx indicate PrecisA Monoclonals ™
HPAxxxxxx indicate TripleA Polyclonals™

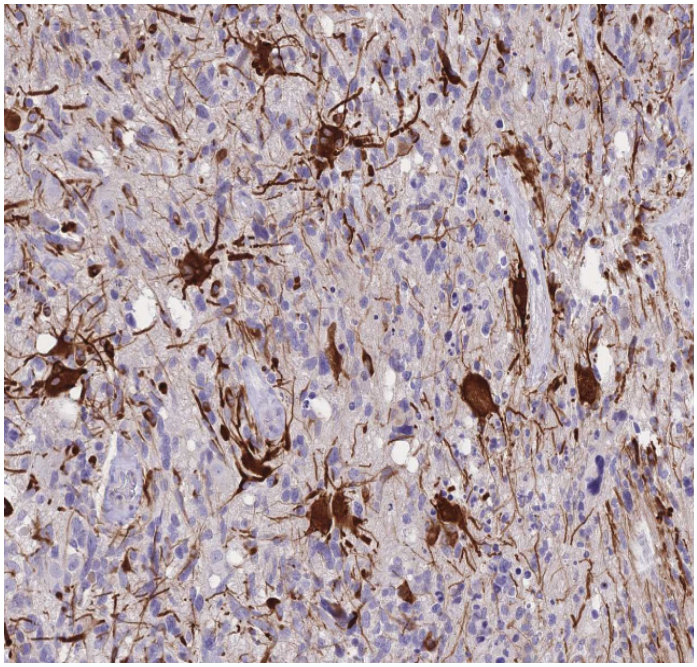


FIGURE 1. Immunohistochemical staining of high grade glioma tissue using the **anti-IL2RA** polyclonal antibody (HPA054622) shows strong cytoplasmic/membranous intensity, in brown.

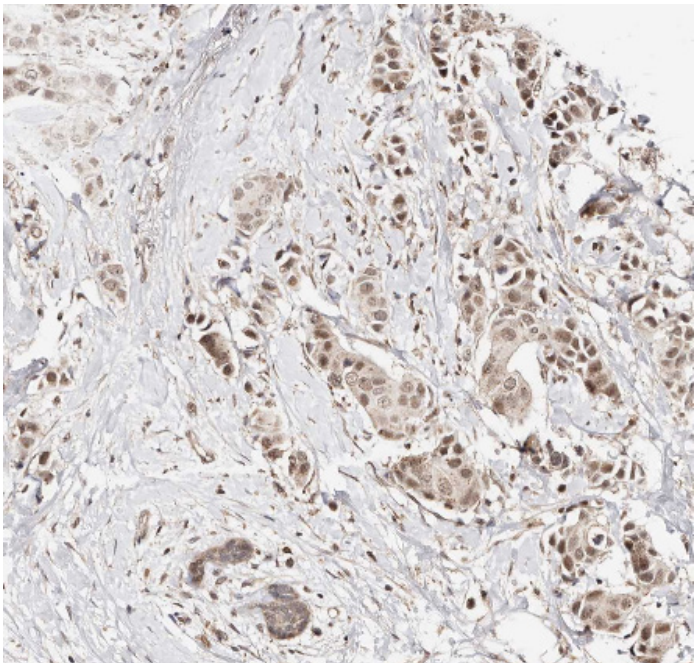


FIGURE 2. Immunohistochemistry on breast duct carcinoma using the **anti-CTNNBL1** polyclonal antibody (HPA027907) shows a moderate cytoplasmic/membranous and nuclear staining, in brown.

Table 2. Antibodies targeting cancer stem cells in hematological tumors

Target Cancer	Marker Location/CD	Product Name	Product Numbers
CML leukemia	Extracellular/Surface/CD	Anti-IL2RA/CD25	HPA054622
	Extracellular/Surface/CD	Anti-CD33	HPA035832
	Extracellular/Surface/CD	Anti-CD34	HPA036722, HPA036723
	Extracellular/Surface/CD	Anti-CD36	HPA071026, HPA002018
	Extracellular/Surface/CD	Anti-KIT/CD117	AMAb90900, AMAb90901, AMAb90904, HPA004471, HPA073252
	Extracellular/Surface/CD	Anti-IL3RA/CD123	HPA003539
	Extracellular/Surface	Anti-IL1RAP	HPA035293
	Intracellular	Anti-FOXO1	HPA001252
	Intracellular	Anti-FOXO3	HPA063104
	Intracellular	Anti-FOXO4	HPA039560, HPA040232
	Intracellular	Anti-GLI2	HPA074275
	Intracellular	Anti-CTNNBL1	HPA027907
	Intracellular	Anti-TET2	AMAb91439
AML leukemia	Extracellular/Surface/CD	Anti-CD33	HPA035832
	Extracellular/Surface/CD	Anti-CD34	HPA036722, HPA036723
	Extracellular/Surface/CD	Anti-IL3RA/CD123	HPA003539
	Intracellular	Anti-ALDH1A1	HPA002123
	Intracellular	Anti-DNMT3A	HPA026588
	Intracellular	Anti-KRAS	HPA049830
	Intracellular	Anti-LDHB	HPA019007
	Intracellular	Anti-LDHC	HPA045442
	Intracellular	Anti-LDHD	HPA041766
	Intracellular	Anti-NANOG	AMAb91391, AMAb91393
	Intracellular	Anti-NPM1	HPA011384
	Intracellular	Anti-POU5F1	AMAb91477
	Intracellular	Anti-SOX2	AMAb91307, HPA045725

* Products with enhanced validation for indicated application
AMAbxxxxx indicate PrecisA Monoclonals ™
HPAxxxxxx indicate TripleA Polyclonals™

TUMORS OF THE HEMATOPOIETIC AND LYMPHOID TISSUES

Hematological cancers (blood cancers) arise in the blood-forming tissues, such as bone marrow, lymph nodes and lymphatic system. Examples of hematologic cancer include leukemia, lymphoma, and multiple myeloma.

Since these tissues are all intimately connected through both the circulatory and the immune system, a disease affecting one system will often affect the other as well, making myeloproliferation (leukemias) and lymphoproliferation (lymphomas) closely related and often overlapping conditions.

The more aggressive forms of hematopoietic and lymphoid tissue diseases require treatment with chemotherapy, radiotherapy, immunotherapy and, in some cases, a bone marrow transplant.

Acute (AML) and chronic (CML) myeloid leukemia, are cancer of the myeloid line of blood cells, characterized by the rapid growth of abnormal cells that build up in the bone marrow and blood and interfere with normal blood cell production. AML progresses rapidly into CML becoming fatal within weeks or months if left untreated.

CSC markers in leukemia

Unlike solid tumors, a common cause of hematological cancers are chromosomal translocations. Interestingly, studies show that there is a sequential order for the acquisition of mutations during leukemogenesis: a) somatic mutations in epigenetic modifiers that regulate cytosine methylation, such as DNMT3A, IDH1/2[26] and TET2[27], occur early in pre-leukemic hematopoietic stem cells; b) mutations in signaling pathways that drive proliferation, such as NPM1, FLT3-ITD, and KRAS/NRAS, are later events in AML transformation [28,29].

A combinatorial approach is often used when determining which markers to select for leukemia. Common CSCs markers in leukemia include CD34, CD38, CD123, TIM3, CD25, CD32 and CD96.

CSC markers in lymphomas

Lymphomas are a heterogeneous group of lymphoid malignancies with varied clinical behavior and responses to treatment. The two main categories of lymphomas are the non-Hodgkin lymphoma and Hodgkin lymphoma. Non-Hodgkin lymphoma (about 90% of cases) is further subdivided in different subtypes, some examples are: mantle cell lymphoma and diffuse large B cell lymphoma.

Mantle cell lymphoma (MCL) is a rare but unique subtype of B-cell non-Hodgkin lymphoma. The presence of CD45+/CD19- cell population was first demonstrated in 2014 in bone marrow aspirates of patients with MCL. These CD45+/CD19- cells, resistance to treatment, might also be associated with treatment failure [30,31].

Diffuse large B cell lymphoma (DLBCL) accounts for about 40% of non-Hodgkin's lymphoma (NHL) cases. Since CD45+CD19- is a marker of CSCs in MCL, a recent study explored the possibility of CD45+CD19- as a potential marker of DLBCL CSCs in vivo and in vitro. However, the results show that in DLBCL, CSCs are not enriched in the CD45+CD19- but ALDH high cells [32].

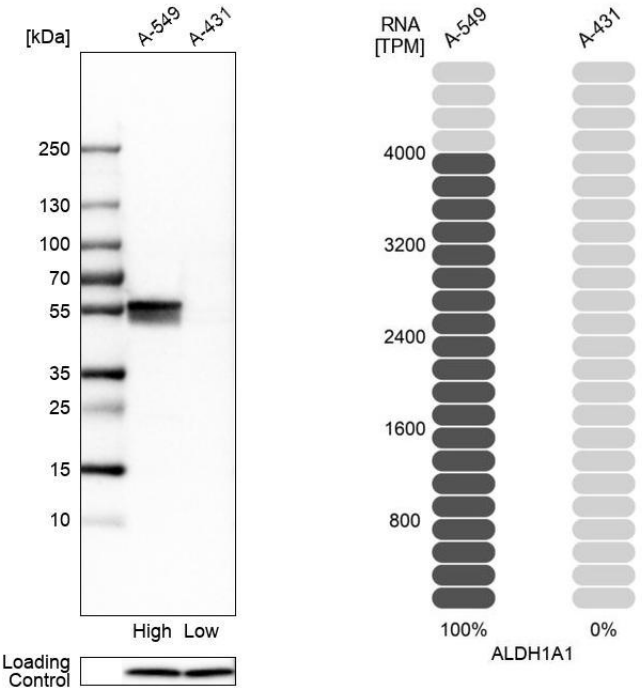


FIGURE 3.
Left: Western blot analysis in human cell lines A-549 and A-431 using the **anti-ALDH1A1** antibody (HPA002123). Loading control: Anti-PPIB.
Right: orthogonal validation of protein expression by comparison to RNA-seq data of corresponding ALDH1A1 RNA-seq data for the same cell lines.

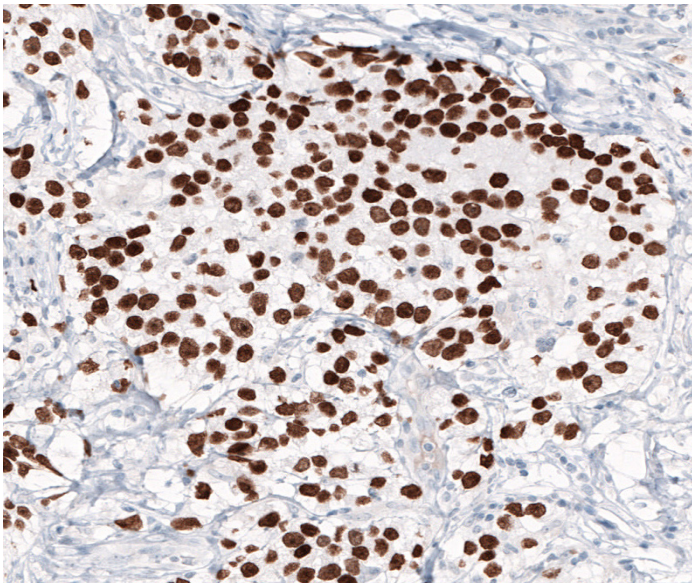


FIGURE 4. Immunohistochemical staining of human testis cancer with the intracellular marker **anti-NANOG** (monoclonal antibody, AMAb91393) shows strong nuclear immunoreactivity in tumor cells, in brown.

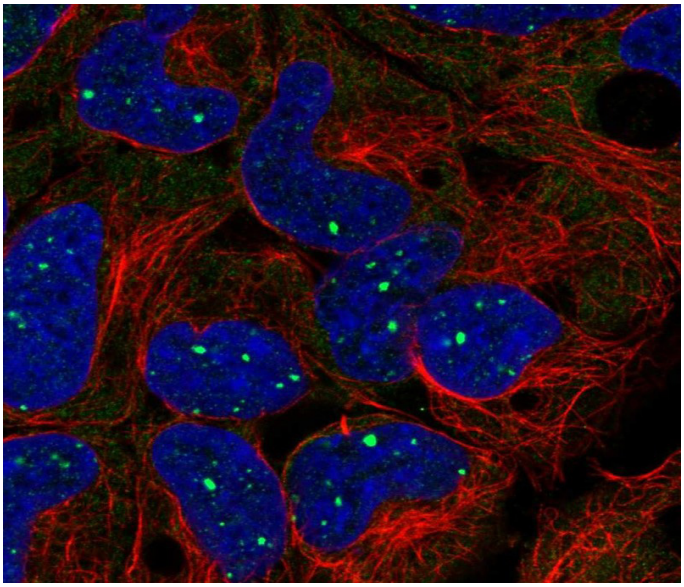


FIGURE 5. Immunofluorescent staining of human cell line HEK 293 using the intracellular marker **anti-BMI1** (polyclonal antibody, HPA030471) shows strong localization to nuclear bodies, in green. Microtubule- and nuclear probes are visualized in red and blue, respectively.

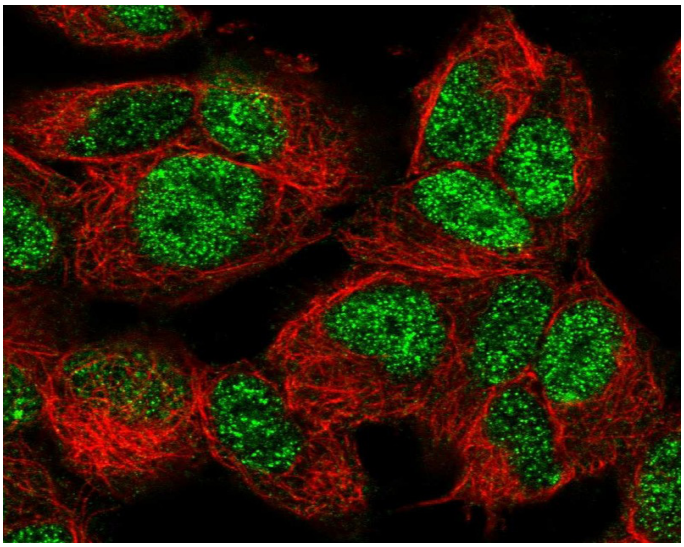


FIGURE 6. Immunofluorescent staining of human cell line SH-SY5Y (derived from neuroblastoma) with the intracellular marker **anti-FOXO3** (polyclonal antibody, HPA063104) shows localization to nucleoplasm, in green. Microtubules are shown in red.

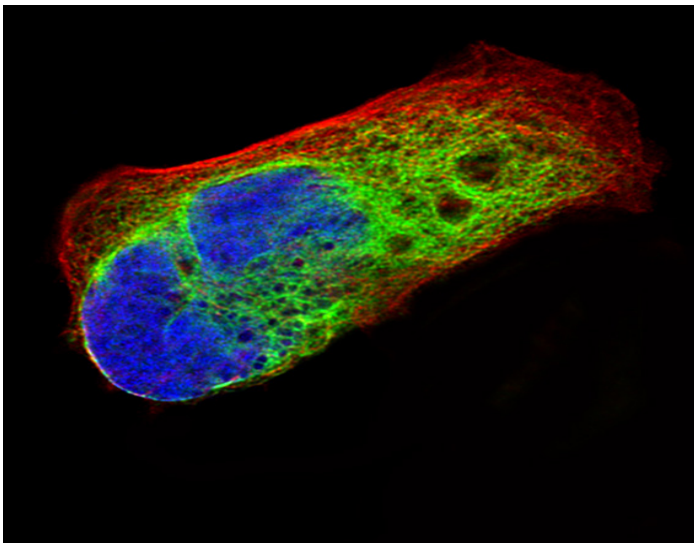
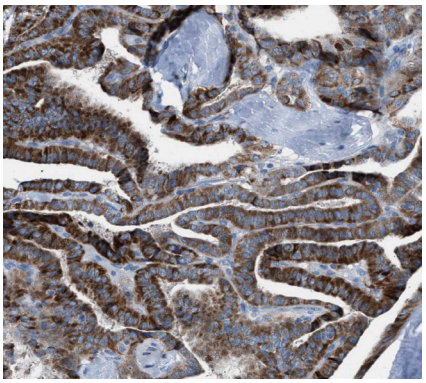


FIGURE 7. Immunofluorescence staining of RH-30 cells (derived from rhabdomyosarcoma) with the intracellular marker **anti-NES** (monoclonal antibody, AMAb90556), showing specific staining in intermediate filaments in green. Microtubule- and nuclear probes are visualized in red and blue, respectively.

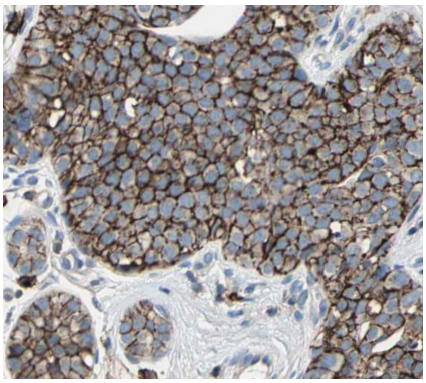
Table 3. Extracellular cancer stem cells markers (clusters of differentiation, CD)

Product Name	Alternative Gene Names	Product Number	Clonality	Validated Applications	Antigen sequence identity to mouse / rat
Anti-ALCAM	CD166, MEMD	HPA010926	Polyclonal	IHC*	94% / 93%
Anti-CD24	CD24A	HPA045879	Polyclonal	ICC-IF	49% / 45%
Anti-CD33	FLJ00391, p67, SIGLEC-3, SIGLEC3	HPA035832	Polyclonal	IHC	36% / 35%
Anti-CD36	FAT, GP3B, GP4, GPIV, SCARB3	HPA071026	Polyclonal	ICC-IF	86% / 91%
Anti-CD36	FAT, GP3B, GP4, GPIV, SCARB3	HPA002018	Polyclonal	IHC*, ICC-IF	84% / 84%
Anti-CD44	CD44R, CSPG8, MDU2, MDU3, MIC4	HPA005785	Polyclonal	IHC*, WB*, ICC-IF	51% / 47%
Anti-EPCAM	CD326, CO-17A, EGP-2, EGP34, EGP40	AMAb91411	Monoclonal	IHC*, WB*	n.d.
Anti-EPCAM	CD326, CO-17A, EGP-2, EGP34, EGP40	AMAb91413	Monoclonal	IHC*, WB	n.d.
Anti-EPCAM	CD326, CO-17A, EGP-2, EGP34, EGP40	HPA026761	Polyclonal	IHC*, WB*	83% / 82%
Anti-EPCAM	CD326, CO-17A, EGP-2, EGP34, EGP40	HPA067463	Polyclonal	ICC-IF	71% / 72%
Anti-FUT4	CD15, ELFT, FCT3A, FUC-TIV	AMAb91414	Monoclonal	WB	n.d.
Anti-FUT4	CD15, ELFT, FCT3A, FUC-TIV	AMAb91416	Monoclonal	WB	n.d.
Anti-IL2RA	CD25, IDDM10, IL2R	HPA054622	Polyclonal	IHC*	57% / 57%
Anti-IL3RA	CD123	HPA003539	Polyclonal	IHC	32% / 35%
Anti-ITGA6	CD49f	AMAb91450	Monoclonal	IHC*	88% / 86%
Anti-ITGA6	CD49f	HPA012696	Polyclonal	IHC*, WB*	88% / 86%
Anti-ITGA6	CD49f	HPA027582	Polyclonal	IHC*	85% / 86%
Anti-ITGB1	CD29, FNRB, GPIIA, MDF2, MSK12	HPA059297	Polyclonal	IHC*, WB	91% / 91%
Anti-ITGB1	CD29, FNRB, GPIIA, MDF2, MSK12	HPA069003	Polyclonal	IHC*	90% / 88%
Anti-ITGB3	CD61, GP3A, GPIIIa	AMAb91470	Monoclonal	IHC*, WB	92% / 90%
Anti-ITGB3	CD61, GP3A, GPIIIa	HPA027852	Polyclonal	IHC	92% / 90%
Anti-L1CAM	CD171, HSAS1, MASA, MIC5, S10, SPG1	HPA005830	Polyclonal	IHC*	75% / 75%
Anti-KIT	C-Kit, CD117, PBT, SCFR	AMAb90900	Monoclonal	WB	66% / 72%
Anti-KIT	C-Kit, CD117, PBT, SCFR	AMAb90901	Monoclonal	IHC, WB	66% / 72%
Anti-KIT	C-Kit, CD117, PBT, SCFR	AMAb90904	Monoclonal	IHC, WB	66% / 72%
Anti-KIT	C-Kit, CD117, PBT, SCFR	HPA004471	Polyclonal	IHC	66% / 72%
Anti-KIT	C-Kit, CD117, PBT, SCFR	HPA073252	Polyclonal	ICC-IF	88% / 89%
Anti-PLAUR	CD87, UPAR, URKR	HPA050843	Polyclonal	IHC	54% / 56%
Anti-PROCR	CCD41, CD201, EPCR	HPA039461	Polyclonal	IHC	65% / 63%
Anti-PROM1	AC133, CD133, CORD12, PROML1	AMAb91494	Monoclonal	IHC, WB	57% / 60%
Anti-PROM1	AC133, CD133, CORD12, PROML1	HPA004922	Polyclonal	IHC*, WB*	57% / 60%
Anti-PROM1	AC133, CD133, CORD12, PROML1	HPA031053	Polyclonal	IHC*, WB	55% / 55%
Anti-THY1	CD90	AMAb90844	Monoclonal	IHC, WB	64% / 68%
Anti-THY1	CD90	AMAb90846	Monoclonal	IHC, WB	64% / 68%
Anti-THY1	CD90	HPA003733	Polyclonal	IHC*, ICC-IF	64% / 68%
Anti-TSPAN8	CO-029, TM4SF3	HPA044337	Polyclonal	IHC, ICC-IF	60% / 59%

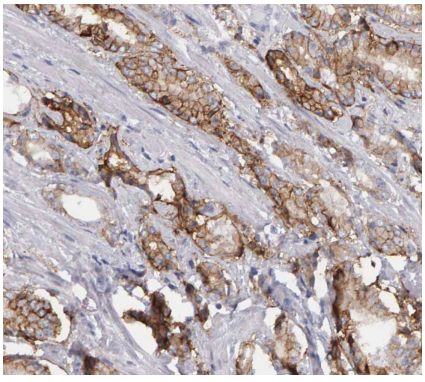
FIGURE 8. Examples of IHC staining of human cancerous tissues using CD markers from Atlas Antibodies.



CD1B - Thyroid Cancer (Papillary Adenocarcinoma)
Anti-CD1B (HPA021824)
Strong cytoplasmic/membranous staining in tumor cells, in brown.



CD44 - Breast Cancer (Lobular carcinoma)
Anti-CD44 (HPA005785)
Strong membranous staining in tumor cells, in brown.



CD38 - Prostate Cancer (Adenocarcinoma, Low grade)
Anti-CD38 (HPA022132)
Moderate cytoplasmic/membranous staining in tumor cells, in brown.

Table 4. Extracellular cancer stem cells markers

Product Name	Alternative Gene Names	Product Number	Clonality	Validated Applications	Antigen sequence identity to mouse / rat
Anti-CHL1	CALL, FLJ44930, L1CAM2, MGC132578	HPA003345	Polyclonal	IHC	79% / 74%
Anti-EGFR	ERBB, ERBB1	AMAb90816	Monoclonal	IHC, WB	90% / 91%
Anti-EGFR	ERBB, ERBB1	AMAb90819	Monoclonal	WB	90% / 91%
Anti-EGFR	ERBB, ERBB1	HPA001200	Polyclonal	IHC*	90% / 91%
Anti-EGFR	ERBB, ERBB1	HPA018530	Polyclonal	IHC*, WB, ICC-IF	84% / 82%
Anti-IL1RAP	C3orf13, IL-1RAcP, IL1R3	HPA035293	Polyclonal	IHC	85% / 85%
Anti-LGR5	FEX, GPR49, GPR67, HG38	HPA012530	Polyclonal	IHC	88% / 87%
Anti-LINGO2	LERN3, LRRN6C	HPA016633	Polyclonal	IHC	98% / 98%

Table 5. Intracellular cancer stem cells markers

Product Name	Alternative Gene Names	Product Number	Clonality	Validated Applications	Antigen sequence identity to mouse / rat
Anti-AFP	FETA, HPAFP	AMAb91610	Monoclonal	IHC, WB	59% / 57%
Anti-AFP	FETA, HPAFP	AMAb91611	Monoclonal	IHC, WB	59% / 57%
Anti-AFP	FETA, HPAFP	HPA010607	Polyclonal	IHC, WB*	59% / 57%
Anti-AFP	FETA, HPAFP	HPA023600	Polyclonal	IHC, WB	66% / 69%
Anti-ALDH1A1	ALDH1, PUMB1, RALDH1	HPA002123	Polyclonal	IHC, WB*, ICC-IF	91% / 90%
Anti-BMI1	PCGF4, RNF51	HPA030472	Polyclonal	IHC, WB*	95% / 95%
Anti-BMI1	PCGF4, RNF51	HPA030471	Polyclonal	ICC-IF	94% / 86%
Anti-CTNNBL1	C20orf33, FLJ21108, NAP	HPA027907	Polyclonal	IHC, WB	99% / 99%
Anti-DNMT3A	-	HPA026588	Polyclonal	IHC, ICC-IF	91% / 91%
Anti-FOXO1	FKH1, FKHR, FOXO1A	HPA001252	Polyclonal	IHC, WB*	91% / 90%
Anti-FOXO3	AF6q21, FKHRL1, FOXO2	HPA063104	Polyclonal	ICC-IF	95% / 95%
Anti-FOXO4	AFX1, MLLT7	HPA039560	Polyclonal	WB, ICC-IF	87% / 85%
Anti-FOXO4	AFX1, MLLT7	HPA040232	Polyclonal	IHC	84% / 85%
Anti-GLI2	HPE9, THP1, THP2	HPA074275	Polyclonal	ICC-IF	90% / 95%
Anti-KLF4	EZF, GKLF	AMAb91389	Monoclonal	IHC, WB, ICC-IF	n.d.
Anti-KLF4	EZF, GKLF	AMAb91388	Monoclonal	IHC, WB, ICC-IF	n.d.
Anti-KLF4	EZF, GKLF	HPA002926	Polyclonal	IHC*, WB*, ICC-IF	89% / 89%
Anti-LETM1	SLC55A1	HPA011029	Polyclonal	IHC*, WB, ICC-IF	78% / 79%
Anti-LETM1	SLC55A1	HPA011100	Polyclonal	IHC*	56% / 53%
Anti-LDHB	-	HPA019007	Polyclonal	IHC, WB, ICC-IF	98% / 98%
Anti-LDHC	CT32	HPA045442	Polyclonal	IHC*	66% / 66%
Anti-LDHD	-	HPA041766	Polyclonal	IHC*, WB	78% / 79%
Anti-NANOG	FLJ12581, FLJ40451	AMAb91393	Monoclonal	IHC, WB, ICC-IF	n.d.
Anti-NANOG	FLJ12581, FLJ40451	AMAb91391	Monoclonal	IHC, ICC-IF	n.d.
Anti-NES	FLJ21841	AMAb90556	Monoclonal	IHC, WB*, ICC-IF	47% / 42%
Anti-NES	FLJ21841	HPA006286	Polyclonal	ICC-IF	47% / 42%
Anti-NES	FLJ21841	HPA007007	Polyclonal	IHC*, WB*	47% / 42%
Anti-NES	FLJ21841	HPA026111	Polyclonal	IHC*, WB, ICC-IF	49% / 55%
Anti-NOTCH1	TAN1	HPA067168	Polyclonal	ICC-IF	75% / 75%
Anti-NOTCH2	-	HPA048743	Polyclonal	IHC, ICC-IF	87% / 86%
Anti-NOTCH3	CADASIL, CASIL	HPA044392	Polyclonal	ICC-IF	83% / 83%
Anti-POU5F1	MGC22487, OCT3, OCT4, OTF3	AMAb91477	Monoclonal	WB, ICC-IF	n.d.
Anti-SALL4	dJ1112F19.1, ZNF797	HPA015291	Polyclonal	IHC*, WB*, ICC-IF	72% / 71%
Anti-SOX2	SRY	AMAb91307	Monoclonal	IHC, WB*, ICC-IF	99% / 99%
Anti-SOX2	SRY	HPA045725	Polyclonal	WB*, ICC-IF	99% / 99%
Anti-TET2	FLJ20032, KIAA1546	AMAb91439	Monoclonal	IHC*, WB, ICC-IF	n.d.

* Products with enhanced validation for indicated application
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REFERENCES

1. Lia Walcher et al, (2020) Cancer Stem Cells-Origins and Biomarkers: Perspectives for Targeted Personalized Therapies. Review - eCollection Frontiers Immunology

2. Arnold CR, et al, (2020) The Role of Cancer Stem Cells in Radiation Resistance. Front Oncol. 10:164

3. Bonnet D, Dick JE (1997) "Human acute myeloid leukemia is organized as a hierarchy that originates from a primitive hematopoietic cell". Nature Medicine. 3 (7): 730–7

4. Singh SK, et al, (2003) "Identification of a cancer stem cell in human brain tumors". Cancer Research. 63 (18): 5821–8

5. Al-Hajj M, et al, (2003) "Prospective identification of tumorigenic breast cancer cells". PNAS USA 100 (7): 3983–8

6. O'Brien CA, et al, (2007) "A human colon cancer cell capable of initiating tumour growth in immunodeficient mice". Nature. 445 (7123) 106–10

7. Zhang S, et al, (2008) "Identification and characterization of ovaria cancer-initiating cells from primary human tumors". Cancer Research. 68 (11): 4311–20

8. Alvero AB, et al, (2009) "Molecular phenotyping of human ovarian cancer stem cells unravels the mechanisms for repair and chemoresistance". Cell Cycle. 8 (1): 158–66

9. Li C, et al.,(2007). "Identification of pancreatic cancer stem cells" Cancer Research. 67 (3): 1030–7

10. Maitland NJ, Collins AT (2008) "Prostate cancer stem cells: a new target for therapy". Journal of Clinical Oncology. 26 (17): 2862–70

11. Lang SH,et al, (2009) "Prostate cancer stem cells". The Journal of Pathology. 217 (2): 299–306

12. Schatton T, et al, (2008) "Identification of cells initiating human melanomas". Nature. 451 (7176): 345–9

13. Schmidt P, et al, (2011) "Eradication of melanomas by targeted elimination of a minor subset of tumor cells". PNAS USA 108 (6): 2474–9

14. Matsui W, et al,(2004) "Characterization of clonogenic multiple myeloma cells". Blood. 103 (6): 2332–6

15. Colmont CS, et al,(2013) "CD200-expressing human basal cell carcinoma cells initiate tumor growth". PNAS USA 110 (4): 1434–9

16. Patel GK, et al, (2012) "Identification and characterization of tumor initiating cells in human primary cutaneous squamous cell carcinoma". The Journal of Investigative Dermatology. 132 (2): 401–9

17. Reya T, et al, (2001) "Stem cells, cancer, and cancer stem cells". Nature. 414 (6859): 105–11

18. Kim YS, et al, (2017) "Cancer stem cell molecular markers verified in vivo". Biochem. Moscow Suppl. Ser. B. 11 (1): 43–54.

19. Pece S, et al, (2010) "Biological and molecular heterogeneity of breast cancers correlates with their cancer stem cell content". Cell. 140 (1): 62–73

20. Son MJ, et al, (2009) "SSEA-1 is an enrichment marker for tumor-initiating cells in human glioblastoma". Cell Stem Cell. 4 (5): 440–52

21. Mazzoleni S, et al, (2010) "Epidermal growth factor receptor expres-sion identifies functionally and molecularly distinct tumor-initiating cell in human glioblastoma multiforme and is required for gliomagenesis". Cancer Research. 70 (19): 7500–13

22. Anido J, et al, (2010). "TGF-β Receptor Inhibitors Target the CD44(high)/Id1(high) Glioma-Initiating Cell Population in Human Glioblastoma". Cancer Cell. 18 (6): 655–68

23. Singh SK, et al, (2004) "Identification of human brain tumour initiating cells". Nature. 432 (7015): 396–401

24. Dalerba P, et al., (2007) "Phenotypic characterization of human colorectal cancer stem cells". PNAS USA 104 (24): 10158–63

25. Hardavella G. et al, (2016) "Lung cancer stem cells—characteristics, phenotype". Transl Lung Cancer Res. 2016 Jun; 5(3): 272–279

26. AP Im et al, (2014) "DNMT3A and IDH mutations in acute myeloid leukemia and other myeloid malignancies: associations with prognosis and potential treatment strategies". Leukemia 28, 1774–1783

27. Ting-Juan Zhang et al, (2018) "TET2 expression is a potential prognostic and predictive biomarker in cytogenetically normal acute myeloid leukemia". J Cell Physiol. 233(8):5838-5846

28. Welch JS, et al, (2012) "The origin and evolution of mutations in acute myeloid leukemia". Cell. 150:264–78

29. Corces-Zimmerman MR, et al, (2014) "Preleukemic mutations in human acute myeloid leukemia affect epigenetic regulators and persist in remission". PNAS U S A. 111:2548–53

30. Sung Min Kim, et al, (2014) "Clinical Relevance of CD45+/CD19- Stem-like Tumor Cells in Patients with Mantle Cell Lymphoma: A Single Center Experience". Blood 124 (21): 1622

31. Kim SM, et al, (2015) "A subset of CD45+/CD19 - cells in bone marrow may be associated with clinical outcomes of patients with mantle cell lymphoma". Leuk Lymphoma. 56(11):3052-7

32. Song S. et al, (2020) "Cancer Stem Cells of Diffuse Large B Cell Lymphoma Are Not Enriched in the CD45+CD19- cells but in the ALDH-high Cells". J Cancer. 11(1): 142–152

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