

# **CANCER STEM CELL MARKERS**

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 <sup>1</sup>.

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 <sup>2</sup>. 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 <sup>3</sup>.

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 <sup>4</sup>, breast <sup>5</sup>, colon <sup>6</sup>, ovary <sup>7,8</sup>, pancreas <sup>9</sup>, prostate <sup>10,11</sup>, melanoma <sup>12,13</sup>, multiple myeloma <sup>14</sup>, and non-melanoma skin cancer <sup>15,16</sup>.

The term CSCs itself was, however, only coined in 2001 <sup>17</sup>.

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<sup>18</sup>. 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<sup>19</sup>. In brain tumors, such as glioma and glioblastoma, CSCs have instead been identified using cell surface markers including SSEA-1 <sup>20</sup>, EGFR <sup>21</sup>, and CD44<sup>22</sup>.

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 <sup>23</sup>.

Using CD133 (PROM1) as a positive marker for colon CSCs also generated conflicting results <sup>24</sup>.

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) <sup>25</sup>.

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.*

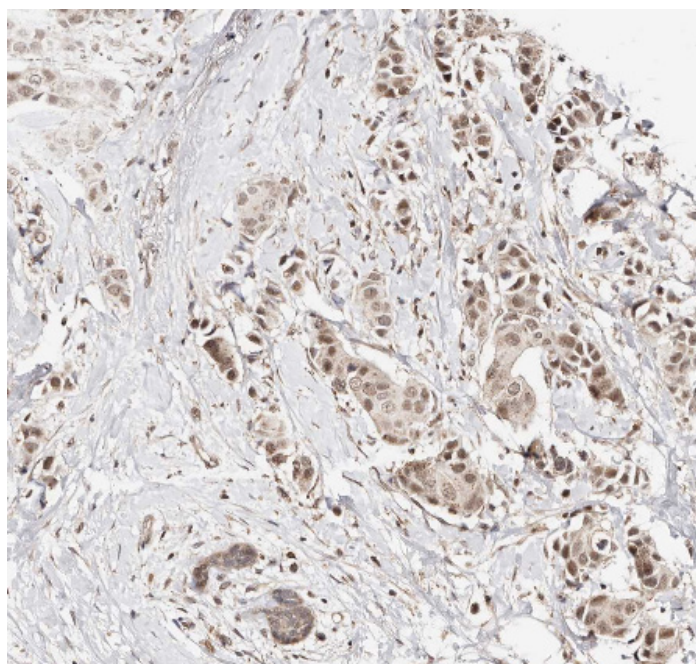
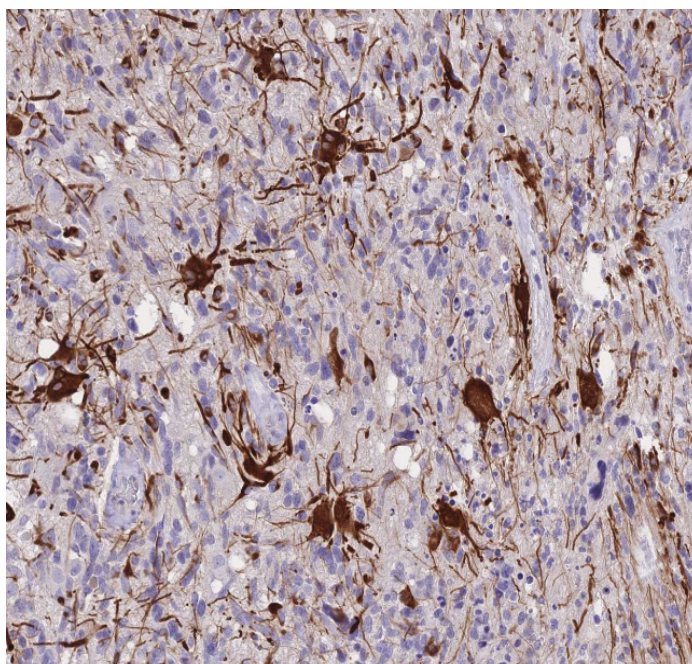
Table 1. CSC antibody markers for solid tumors.

| 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                                  |           |
| 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-CTNBL1              | 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                                       |
|---------------------|--------------------------|----------------------|---|
| <b>Breast</b>       | 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-CTNBL1          | 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 |   |
| <b>Glioblastoma</b> | 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   |
| <b>Prostate</b>     | 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                                  |





**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-CTNNB1 polyclonal antibody (HPA027907) shows a moderate cytoplasmic/membranous and nuclear staining, in brown.

**Table 2. CSC antibody markers for 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-CTNNB1              | HPA027907   |
|                          | Intracellular            | Anti-TET2                | AMAb91439   |
|                          | AML leukemia             | Extracellular/Surface/CD | Anti-CD33   |
| 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     |   |

## 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<sup>26</sup> and TET2<sup>27</sup>, 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<sup>28,29</sup>.

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.

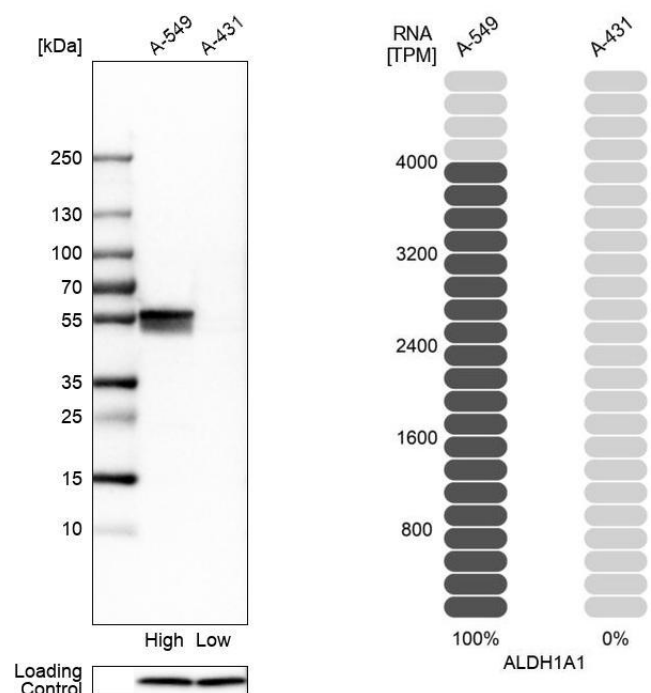
A combinatorial approach is often used when determining which markers to select for leukemia. Common CSCs markers in leukemia include CD34, CD38, CD123, TIM3, CD25, CD32 and CD96.

### CSC markers in lymphomas

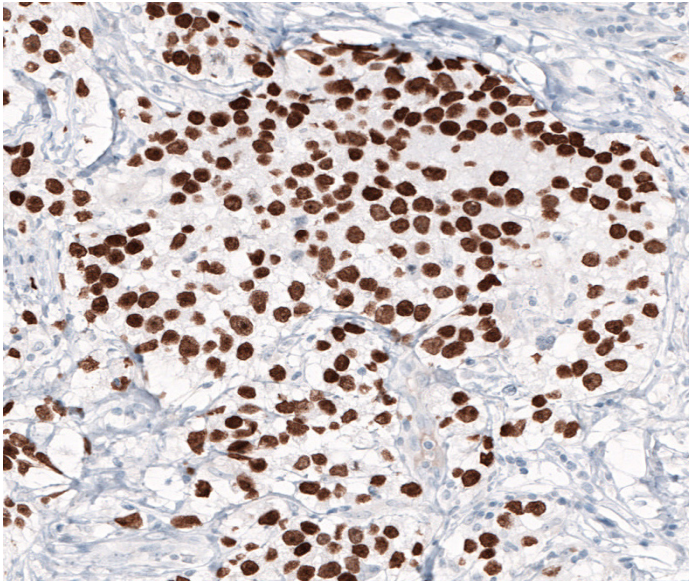
Lymphomas are a heterogeneous group of lymphoid malignancies with varied clinical behavior and responses to treatment. The two main categories of lymphomas are the non-Hodgkin lymphoma and Hodgkin lymphoma. Non-Hodgkin lymphoma (about 90% of cases) is further subdivided in different subtypes, some examples 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<sup>30,31</sup>.

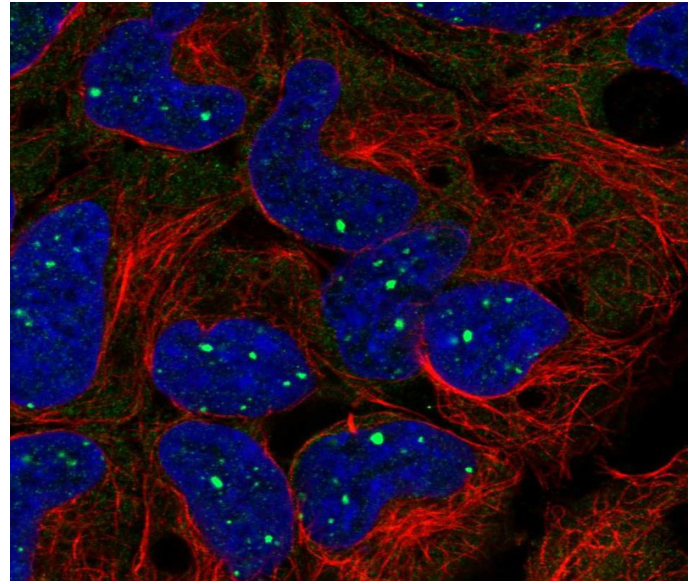
Diffuse large B cell lymphoma (DLBCL) accounts for about 40% of non-Hodgkin's lymphoma (NHL) cases. Since CD45+CD19- is a marker of CSCs in MCL, a recent study explored the possibility of CD45+CD19- as a potential marker of DLBCL CSCs in vivo and in vitro. However, the results show that in DLBCL, CSCs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



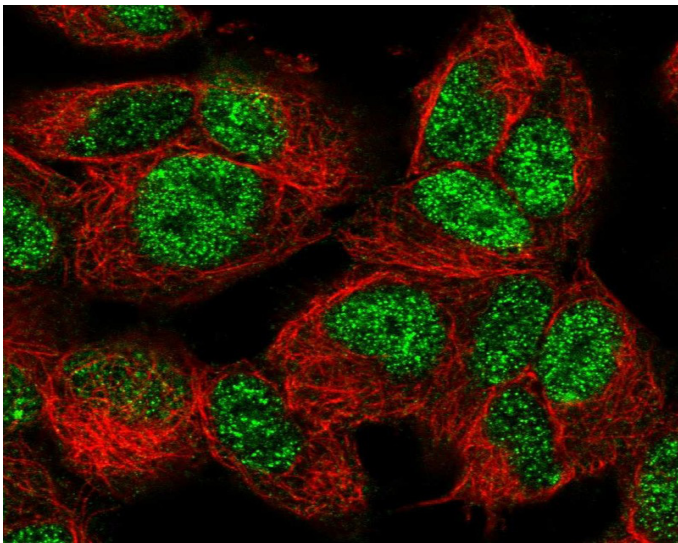




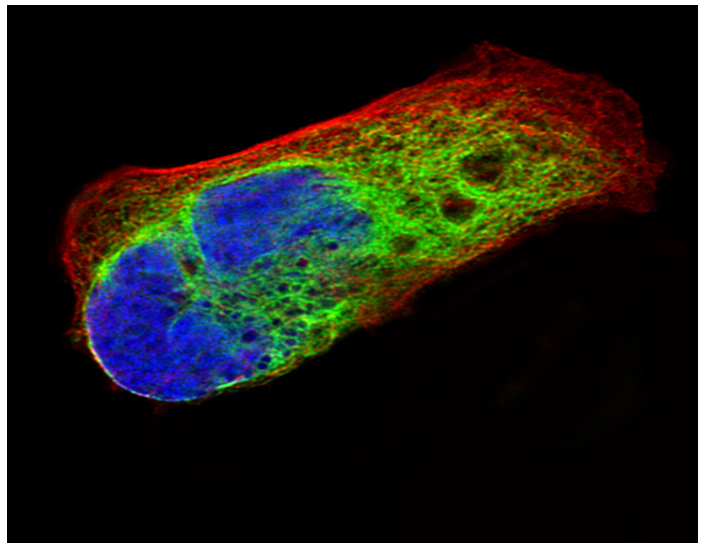
**Figure 4.** Immunohistochemical staining of human testis cancer with the intracellular marker anti-NANOG monoclonal antibody (AMAb91393) shows strong nuclear immunoreactivity in tumor cells, in brown.



**Figure 5.** Immunofluorescent staining of human cell line HEK 293 with 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 CSC markers (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, FN1B, GPIIA, MDF2, MSK12      | HPA059297      | Polyclonal | IHC*, WB               | 91% / 91%                                |
| Anti-ITGB1   | CD29, FN1B, 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%                                |

Table 4. Extracellular CSC markers (not CD).

| 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%                                |

\* Products with enhanced validation for indicated application



Table 5. Intracellular CSC 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-CTNBL1  | 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, FKHL1, 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

## 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 ovary 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 expression 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- $\beta$  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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