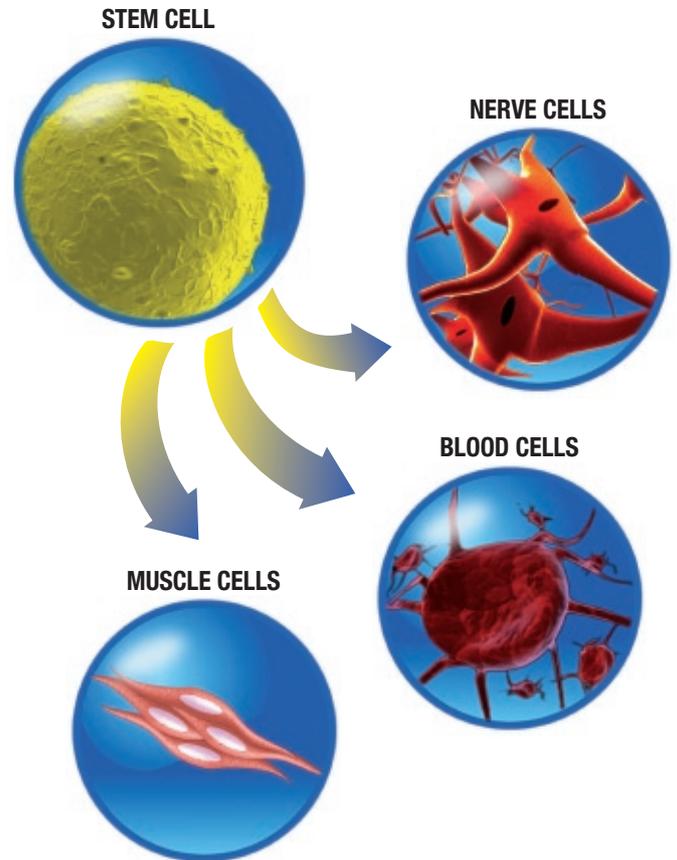


# STEM CELL MARKERS

Stem cells are unspecialized precursor cells characterized by two unique abilities. First, they are capable of reproducing themselves (self-renewal), thereby sustaining a stem cell pool. Second, they are able to develop into other cell types (differentiation) carrying out particular tissue functions. Thus, stem cells are essential for the development, turnover and repair of tissues. Because of their capacities, stem cells are ideal candidates for the treatment of diseases and regenerative medicine restoring lost or damaged cells or tissues.

## Embryonic Stem Cells

Stem cells are comprised of two general types, referred to as somatic (fetal or adult) or embryonic. Embryonic stem cells (ESCs) have attracted a lot of attention because of their origin and plasticity. Originating from the inner cell mass of a blastocyst, which forms a few days after fertilization, ESCs are considered pluripotent, capable of transforming into cells from all three somatic germ layers (ectoderm, mesoderm and endoderm) as well into germ cells. In contrast, adult stem cells are considered to be multipotent giving rise to only cell types of one particular lineage (see also Table 1). In general, potency becomes gradually restricted by epigenetic modifications along development and differentiation. The recent interest in ESCs has been catalyzed by the establishment of the first human ESC line in 1998 [1], 17 years after generation of the first murine ESCs lines [2, 3].



### LITERATURE

- [1] Embryonic stem cell lines derived from human blastocysts: J.A. Thomson, et al.; Science **282**, 1145 (1998)
- [2] Establishment in culture of pluripotential cells from mouse embryos: M.J. Evans & M.H. Kaufman; Nature **292**, 154 (1981)
- [3] Isolation of a pluripotent cell line from early mouse embryos cultured in medium conditioned by teratocarcinoma stem cells: G.R. Martin; PNAS **78**, 7634 (1981)

Potency	Sum of developmental options accessible to cell
Totipotent	Ability to form all lineages of organism; in mammals only the zygote and the first cleavage blastomeres are totipotent.
Pluripotent	Ability to form all lineages of body. Example: embryonic stem cells.
Multipotent	Ability of adult stem cells to form multiple cell types of one lineage. Example: hematopoietic stem cells.
Unipotent	Ability to form one cell type. Example: spermatogonial stem cells (can only generate sperm).
Reprogramming	Notion that somatic stem cells have broadened potency and can generate cells of other lineages, a concept that is controversial in mammals.

**TABLE 1:** Potency Definitions. Adapted from: *Stem cells, the molecular circuitry of pluripotency and nuclear reprogramming*: R. Jaenisch & R. Young; Cell **132**, 567 (2008)

## Embryonic Stem Cell Markers

Product	Specificity	Application	Prod. No.	Size
MAB to Thy-1 [CD90] (human) (BC9-G2)	Human	FC, IP, WB, Blocking	ALX-805-085-L002	2 ml
MAB to Thy-1 [CD90] (human) (AF9)	Human	IHC, WB	BML-TA1278-0100	100 µl
MAB to CD9 (human) (Gi15)	Human	IP, WB	ALX-805-027-C100	100 µg
MAB to E-cadherin (ECCD-2)	Human, mouse, dog	IHC, WB, Blocking	ALX-804-202-C100	100 µg
MAB to E-cadherin (HECD-1)	Human, guinea pig	FC, ICC, IHC, WB, Blocking	ALX-804-201-C100	100 µg
MAB to E-cadherin (human) (SHE78-7)	Human	FC, IHC, WB, Blocking	ALX-804-203-C100	100 µg
MAB to E-cadherin (mouse) (ECCD-1)	Mouse	Blocking	ALX-804-263-C100	100 µg
MAB to β1 Integrin [CD29] (human) (DF5)	Human	ICC, WB	BML-IG6060-0100	100 µl
MAB to β1 Integrin [CD29] (human) (DF7)	Human	ICC, WB	BML-IG6061-0100	100 µl
MAB to CD49b/CD29 Complex (human) (Gi14)	Human	FC, IHC, IP	ALX-805-030-C100	100 µg
MAB to CD49f [α6 Integrin] (human) (MAR6)	Human	FC, IHC, IP	ALX-804-621-C100	100 µg
MAB to BCRP (BXP-53)	Human, mouse	ICC, IHC, WB	ALX-801-036-C125 ALX-801-036-C250	125 µg 250 µg
MAB to BCRP (human) (BXP-21)	Human	ICC, IHC, WB	ALX-801-029-C125 ALX-801-029-C250	125 µg 250 µg
MAB to BCRP (human) (BXP-34)	Human	FC, ICC, IHC	ALX-801-027-C125 ALX-801-027-C250	125 µg 250 µg
MAB to Dnmt3b (52A1018)	Human, mouse	ICC, IHC, IP, WB	ALX-804-233-C100	100 µg
PAb to Galanin	Human, rat, others	IHC	BML-GA1161-0025 BML-GA1161-0100	25 µl 100 µl



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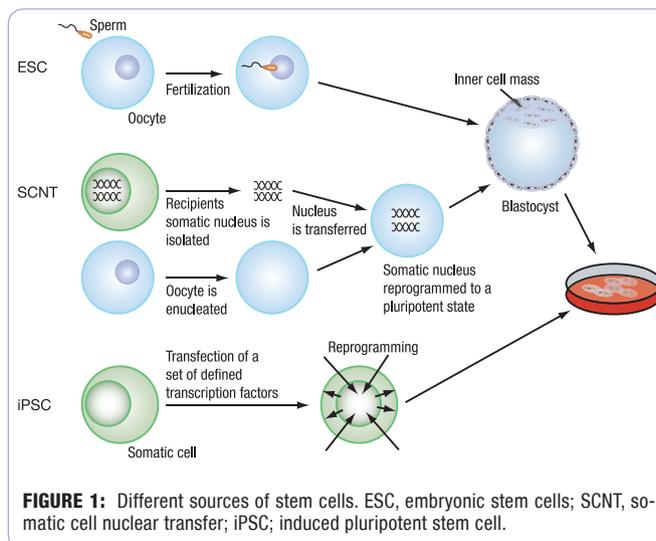
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# (INDUCED-) PLURIPOTENT STEM CELLS

Embryonic stem cell research raises ethical concerns and faces various technical challenges. The latter include the lack of sources and the presence of the immune barrier ESCs would face when used as allogenic (derived from other individuals) transplants. Other methods have been described which have the advantage of producing pluripotent stem cells, which may be more immune-compatible. Among them, somatic cell nuclear transfer (SCNT) is a method by which a somatic nucleus is transferred into an enucleated egg (see Figure 1). The resultant pluripotent cells may then be taken from the developing morula and blastocyst, or may be used for transplantation into the individual who provided the somatic nucleus. Because of the identical genetic background, the transplant is not rejected. SCNT allows researchers to clone mammals, of which the sheep named Dolly was the first example [1-6]. However, SCNT has been shown to be inefficient not only in non-human primates [7] and not yet been successful for humans. Recently, different groups were searching for defined factors to reprogram somatic cells. The idea of producing pluripotent cells with the same genetic background to the donor cell by de-differentiation through defined factors would prevent the use of embryos and rejection of transplants. Expression of four factors, OCT4, SOX2, c-MYC and KLF4 has been initially shown to be sufficient to reprogram somatic cells of mice [8]. These results were confirmed by others and procedures were improved giving cells even more closely resembling ESCs [9-11]. The same factors have been introduced into human somatic cells and generated iPSCs similar to ESCs in such terms like morphology, surface markers, gene expression and proliferation [12-14].



In contrast, another screen yielded OCT4, SOX2, NANOG and LIN28 as being sufficient for reprogramming, generating as well cells similar but not identical to human ESCs [15]. More recently, mouse and human somatic cells could be reprogrammed by the expression of OCT4, SOX2, and KLF4 only [16]. Although, the additional expression of c-MYC gave significantly more iPSCs [16], c-MYC may induce tumour growth [10]. Recently, a transcriptional repressor called Ronin has been shown to maintain ESC pluripotency independent of the before mentioned factors [17].

## LITERATURE

- [1] Viable offspring derived from fetal and adult mammalian cells: I. Wilmut, et al.; *Nature* **385**, 810 (1997)
- [2] Cloned transgenic calves produced from nonquiescent fetal fibroblasts: J.B. Cibelli, et al.; *Science* **280**, 1256 (1998)
- [3] A cat cloned by nuclear transplantation: T. Shin, et al.; *Nature* **415**, 859 (2002)
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- [7] Producing primate embryonic stem cells by somatic cell nuclear transfer: J.A. Byrne, et al.; *Nature* **450**, 497 (2007)
- [8] Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors: K. Takahashi & S. Yamanaka; *Cell* **126**, 663 (2006)
- [9] Directly reprogrammed fibroblasts show global epigenetic remodeling and widespread tissue contribution: N. Maherali, et al.; *Cell Stem Cell* **1**, 55 (2007)
- [10] Generation of germline-competent induced pluripotent stem cells: K. Okita, et al.; *Nature* **448**, 313 (2007)
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- [14] Reprogramming of human somatic cells to pluripotency with defined factors: I.H. Park, et al.; *Nature* **451**, 141 (2008)
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- [16] Generation of induced pluripotent stem cells without Myc from mouse and human fibroblasts: M. Nakagawa, et al.; *Nat. Biotechnol.* **26**, 101 (2008)
- [17] Ronin is essential for embryogenesis and the pluripotency of mouse embryonic stem cells: M. Dejosez, et al.; *Cell* **133**, 1162 (2008)

## (Induced-) Pluripotent Stem Cell Markers

Product	Specificity	Application	Prod. No.	Size
MAb to c-Myc (human) (4H3)	Human	ICC, IHC, IP, WB	ALX-804-627-L001	1 ml
MAb to c-Myc (human) (6A10)	Human	ICC, IP, WB	ALX-804-632-L001	1 ml

# Adult Stem Cell

Adult stem cells are undifferentiated cells residing in differentiated tissues. They maintain tissue function and integrity throughout an organism's lifespan by replacing dead or damaged differentiated cells. Adult stem cells are characterized by limited self-renewal and differentiation capacity, usually restricted to cell types of the tissue in which they reside. Stem cell activity has been demonstrated in many tissues or organs. However, localization or isolation of adult stem cells from specific sites has been difficult, also partly of the lack of specific markers. Another difficulty is that, most adult stem cells are problematic to maintain and expand *in vitro*. Adult stem cells rely on a physiological microenvironment called stem cell niche. The niche is thought to support the maintenance of stem cells as well as to regulate their function [1]. Niches of stem cells have been described for different tissues (see Table 2). For example, blood cell producing

haematopoietic stem cells (HSCs) from the bone marrow often reside along the endosteal surface of trabecular bone in close proximity to both bone-forming osteoblasts and blood vessel lining endothelial cells. Neural stem cells (NSCs) are also found in association with endothelial cells. But in contrast to HSCs, NSCs are found within the subventricular zone of the hippocampus or the olfactory bulb. Other niches which have been described include skeletal muscle, small intestine and testis. Important factors for the maintenance and propagation of adult stem cells include adhesion molecules, which may play a role in attachment or migration, as well as molecules of various signaling pathways (see Table 2 and Figure 2).

## LITERATURE

[1] The relationship between the spleen colony-forming cell and the haemopoietic stem cell: R. Schofield; *Blood Cells* 4, 7 (1978)

## Mesenchymal Stem Cell Markers

Product	Specificity	Application	Prod. No.	Format	Size
MAB to CD14 (mouse) (biG 57)	Mouse	FC	ALX-804-552-C100		100 µg
MAB to CD14 (biG 10)	Human, dog, pig, others	FC, WB, Blocking	ALX-804-496-C100		100 µg
MAB to CD14 (biG 14)	Human, dog, pig, others	ELISA, FC, WB, Blocking	ALX-804-497-C100		100 µg
MAB to CD14 (human) (biG 2/RoMo-1)	Human	FC, IP	ALX-804-498-C100		100 µg
MAB to CD14 (mouse) (biG 53)	Mouse	FC, Blocking	ALX-804-499-C100		100 µg
MAB to CD40 (mouse) (FGK45)	Mouse	FC, Activation	ALX-805-046B-C050 ALX-805-046-C100 ALX-805-046-C500	Biotin Purified Purified	50 µg 100 µg 500 µg
MAB to CD44std (human) (SFF-2)	Human	FC, IHC	ALX-801-078-C100 ALX-801-078B-T100 ALX-801-078F-T100	Purified Biotin FITC	100 µg 100 tests 100 tests
MAB to CD44std (human) (SFF-304)	Human	FC, IHC, WB	ALX-801-089-C100 ALX-801-089B-T100 ALX-801-089F-T100	Purified Biotin FITC	100 µg 100 tests 100 tests
MAB to CD44var(v10) (human) (VFF-14)	Human	IHC, WB	ALX-801-084-C100	Purified	100 µg
MAB to CD44var(v3) (human) (VFF-327v3)	Human	FC, IHC, WB	ALX-801-079-C100 ALX-801-079B-T100	Purified Biotin	100 µg 100 tests
MAB to CD44var(v4) (human) (VFF-11)	Human	IHC	ALX-801-080-C100 ALX-801-080F-T100	Purified FITC	100 µg 100 tests
MAB to CD44var(v4) (mouse) (10D1)	Mouse	IHC, WB	ALX-801-085-C100	Purified	100 µg
MAB to CD44var(v5) (human) (VFF-8)	Human	FC, IHC	ALX-801-087-C100 ALX-801-087B-T100	Purified Biotin	100 µg 100 tests
MAB to CD44var(v6) (human) (VFF-18)	Human	FC, IHC, WB	ALX-801-081-C100 ALX-801-081B-T100 ALX-801-081F-T100	Purified Biotin FITC	100 µg 100 tests 100 tests
MAB to CD44var(v6) (human) (VFF-7)	Human	FC, IHC, WB	ALX-801-088-C100 ALX-801-088B-T100 ALX-801-088F-T100	Purified Biotin FITC	100 µg 100 tests 100 tests
MAB to CD44var(v6) (mouse) (9A4)	Mouse	FC, IHC, WB	ALX-801-086-C100	Purified	100 µg
MAB to CD44var(v7) (human) (VFF-9)	Human	FC, WB	ALX-801-082-C100 ALX-801-082F-T100	Purified FITC	100 µg 100 tests

incorporating

## Mesenchymal Stem Cell Markers

Product	Specificity	Application	Prod. No.	Format	Size
MAb to CD44var(v7-8) (human) (VFF-17)	Human	WB	ALX-801-083-C100	Purified	100 µg
			ALX-801-083B-T100	Biotin	100 tests
			ALX-801-083F-T100	FITC	100 tests
PAb to CD44var(v3-v10) (human)	Human	IHC, WB	ALX-210-234-M001		1 mg
MAb to CD45 (human) (MEM-28)	Human	FC, IHC, IP, WB	ALX-805-041-C100	Purified	100 µg
			ALX-805-041F-T100	FITC	100 tests
MAb to CD45RA (human) (MEM-56)	Human	FC, IHC, IP, WB	ALX-805-067-C100	Purified	100 µg
			ALX-805-067F-T100	FITC	100 tests
MAb to CD45RB (human) (MEM-55)	Human	FC, IHC, IP, WB	ALX-805-068-C100	Purified	100 µg
MAb to CD45RB (human) (MEM-143)	Human	FC	ALX-805-069-C100	Purified	100 µg
MAb to Thy-1 [CD90] (human) (BC9-G2)	Human	FC, IP, WB, Blocking	ALX-805-085-L002		2 ml
MAb to Thy-1 [CD90] (human) (AF9)	Human	IHC, WB	BML-TA1278-0100		100 µl
MAb to NGFR (human) (MGR15)	Human	FC, IHC	ALX-804-574-C050		50 µg
MAb to NGFR(human) (Nagy-1)	Human	FC, IP	ALX-804-833-C100		100 µg
PAb to NGFR	Human, rat, others	IP, WB	ALX-210-230-R100		100 µl
PAb to NGFR (human) (AT101)	Human	WB	ALX-210-921-C050		50 µg

## Haematopoietic Stem Cell Markers

Product	Specificity	Application	Prod. No.	Size
MAb to BCRP (BXP-53)	Human, mouse	ICC, IHC, WB	ALX-801-036-C125	125 µg
			ALX-801-036-C250	250 µg
MAb to BCRP (human) (BXP-21)	Human	ICC, IHC, WB	ALX-801-029-C125	125 µg
			ALX-801-029-C250	250 µg
MAb to BCRP (human) (BXP-34)	Human	FC, ICC, IHC	ALX-801-027-C125	125 µg
			ALX-801-027-C250	250 µg
PAb to Cathepsin G (human)	Human	ELISA, WB	BML-SA354-0100	100 µl
PAb to CXCR4 (human)	Human	ICC, IHC, WB, Blocking	ALX-210-820-C200	200 µg
PAb to CXCR4 (mouse)	Mouse	ICC, IHC, WB,	ALX-210-819-C200	200 µg
PAb to Neutrophil Elastase (human)	Human	ELISA, WB	BML-SA469-0100	100 µl
MAb to Prion Protein (F89/160.1.5)	Human, bovine, ovine	IHC, WB	ALX-803-042-C200	200 µg
PAb to Prion Protein (sheep)	Sheep	IHC, WB	ALX-210-200-R100	100 µl
MAb to SerpinB6/PI-6 (human) (3A)	Human	ELISA, FC, ICC, IHC, IP, WB	BML-SA622-0100	100 µg
MAb to SerpinB8/PI-8 (human) (PI-8)	Human	ELISA, IHC, WB,	ALX-804-655-C125	100 µg
MAb to SerpinB9/PI-9 (human) (7D8)	Human	ELISA, FC, ICC, IHC, IP, WB	BML-SA621-0100	100 µg
MAb to SerpinB9/PI-9 (human) (PI9-17)	Human	IHC, WB	ALX-804-457-C125	125 µg
MAb to SLAM (human) (IPO-3)	Human	ELISA, FC, ICC, IHC, IP, FUNC	ALX-804-246-C100	200 µg
MAb to Thy-1 [CD90] (human) (BC9-G2)	Human	FC, IP, WB, Blocking	ALX-805-085-L002	2 ml
MAb to Thy-1 [CD90] (human) (AF9)	Human	IHC, WB	BML-TA1278-0100	100 µl

## Endothelial Progenitor Cell (EPC) Markers

Product	Specificity	Application	Prod. No.	Format	Size
MAB to CD14	see Page 4				
MAB to CD31 (human) (Gi18)	Human	FC, IHC, WB	ALX-805-003A-C100 ALX-805-003B-T100 ALX-805-003F-T100	Purified Biotin FITC	100 µg 100 tests 100 tests
MAB to CD31 (human) (Gi34)	Human	IP, WB	ALX-805-029-C100		100 µg
MAB to CD45	see Page 5				
MAB to eNOS (phosphorylated) (pSer <sup>1177</sup> ) (15E2)	Human	WB	ALX-804-396-C100		100 µg
MAB to eNOS (H32)	Human, mouse, rat, pig, others	IHC, IP, WB	BML-SA258-0025 BML-SA258-0100		25 µg 100 µg
PAb to eNOS	Human, bovine	WB	ALX-210-511-R100		100 µl
PAb to eNOS	Human, mouse, rat, dog, pig, others	IHC, WB	ALX-210-509-R100		100 µl
PAb to eNOS	Human, mouse, rat, dog	ICC, WB	ALX-210-505/1-R100		100 µl

## Neural Stem Cell Markers

Product	Specificity	Application	Prod. No.	Size
MAB to GFAP (EB4)	Wide range	IHC, WB	BML-GA1170-0100 BML-GA1170-0500	100 µl 500 µl
MAB to NCAM [CD56] (MEM188)	Human	FC, WB	BML-NA2116-0100 BML-NA2116-0500	100 µl 500 µl
MAB to βIII-Tubulin (human) (TU-20)	Human	ICC, IHC, WB	ALX-804-405-C100	100 µg

Tissue	Stem Cell	Supporting Cells	Signaling Pathway	Adhesion
Mouse skeletal muscle	Satellite cell	NI	Notch	β1 integrin
Mouse bone marrow	HSC	Osteoblasts, vascular cells	SLF, Wnt, Notch, ANG1, OPN	β1 integrin
Mouse small intestine	CBC	Crypt fibroblasts, Paneth cells	Wnt, BMP	β-catenin
Mouse skin	Interfollicular keratinocyte	NI	Wnt, Shh, Notch	E-cadherin, β-catenin, β1 integrin
Mouse skin	Follicular bulge stem cell	Dermal fibroblasts	Wnt, BMP	β-catenin, β1 integrin
Mouse brain (lateral ventricle)	SVZ stem cell	Vascular cells, astrocytes	Shh, BMP	N-cadherin, β-catenin
Rat brain (hippocampus)	SGZ stem cell	Vascular cells, astrocytes	Shh, Wnt	N-cadherin, β-catenin
Mouse testis	SSC	Sertoli cells, vasculature, interstitial cells	GDNF, SLF	α6 integrin, β1 integrin

**TABLE 2:** Example of mouse stem cell niches. ANG1, angiopoietin-1; BMP, bone morphogenetic protein; CBC, crypt base columnar cell; GDNF, glial cell-line-derived neurotrophic factor; HSC, haematopoietic stem cell; NI, none identified; OPN, osteopontin; SGZ, subgranular zone; Shh, sonic hedgehog; SLF, steel factor; SSC, spermatogonial stem cell; SVZ, subventricular zone. Adapted from: *Stem cells, the molecular circuitry of pluripotency and nuclear reprogramming*; R. Jaenisch & R. Young; *Cell* **132**, 567 (2008)

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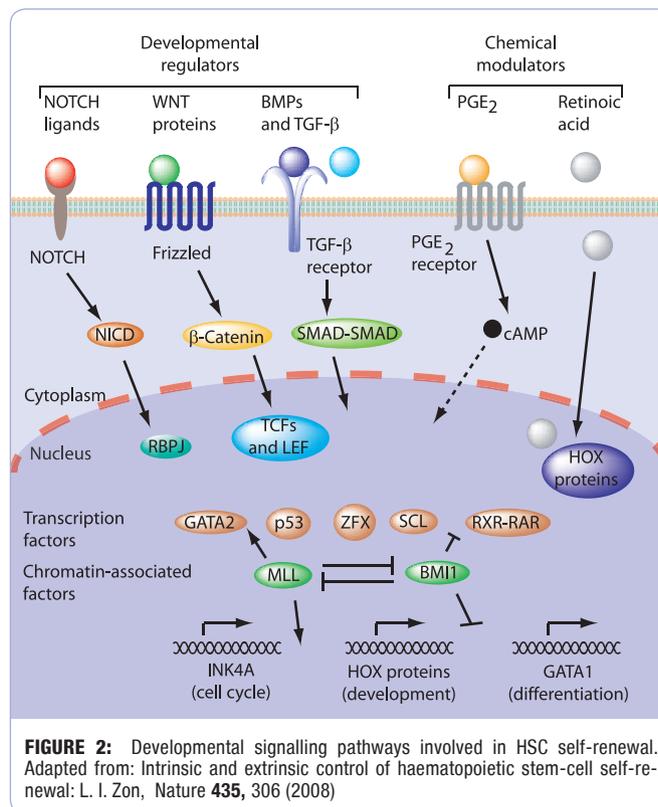
# Stem Cell Signaling Pathways

WNT, fibroblast growth factor (FGF), Notch, Hedgehog, and transforming growth factor  $\beta$ /bone morphogenetic protein signaling pathways are hallmarks of stem cell signaling. These multiple pathways are implicated in the maintenance of tissue homeostasis by regulating self-renewal of normal stem cells as well as proliferation or differentiation of progenitor (transit-amplifying) cells. Interruption of these stem cell signaling pathways can lead to carcinogenesis.

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- Notch-Signaling
- TGF- $\beta$  Signaling
- Hedgehog-Signaling

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# Stem Cell Migration

Most knowledge about the migration of stem cells came from the study of hematopoietic stem cells (HSCs) [1, 2]. During embryogenesis, HSCs egress from the fetal liver and migrate via the circulation to the bone marrow, from where they give rise of immature and mature blood cells into the circulation. Mobilization and homing (migration to a target tissue) of HSCs are regulated by different proteases, cytokines, chemokines and the corresponding receptors. Among them, the chemokine receptor CXCR4 and its ligand stromal cell-derived factor

1 (SDF-1, CXCL12) are of particular importance. The identification of molecules that mediate stem cell-specific homing is of interest for fulfilling the promises of regenerative medicine, e.g. for targeted administration of stem cells.

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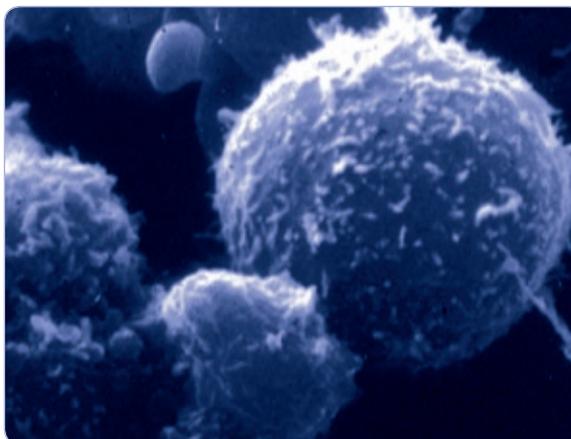
## Haematopoietic Stem Cell Markers

Product	Specificity	Application	Prod. No.	Size
PAb to CXCR4 (human)	Human	ICC, IHC, WB, Blocking	ALX-210-820-C200	200 $\mu$ g
PAb to CXCR4 (mouse)	Mouse	ICC, IHC, WB,	ALX-210-819-C200	200 $\mu$ g

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# Cancer Stem Cells

One hypothesis proposes a defined subset of tumor cells of being responsible for initiation and propagation of tumorigenesis. These cells have been named cancer stem cells (CSCs) and are believed to be capable of self-renewing and multidirectional differentiation [1, 2]. Cancer stem cells may explain the cellular heterogeneity seen in tumors, as well as cancer relapses often seen after treatment. The hypothesis about CSCs assumes that these cells may arise from stem cells or early progenitor cells, by accumulation of genetic modifications or epigenetic alterations. Given their potential role in tumorigenesis, CSCs are important targets for research and therapy.



## LITERATURE

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 [2] Cancer stem cells in solid tumours: accumulating evidence and unresolved questions: J.E. Visvader & G.J. Lindeman; Nat. Rev. Cancer **8**, 755 (2008)

## Cancer Stem Cell (CSC) Markers

Product	Specificity	Application	Prod. No.	Format	Size
MAb to CD19 (human) (LT19)	Human	FC, IP	ALX-805-049-C100 ALX-805-049F-T100	Purified FITC	100 µg 100 tests
MAb to CD20 (human) (MEM-97)	Human	FC, IP	ALX-805-047-C100		100 µg
MAb to CD31 (human) (Gi18)	Human	FC, IHC, WB	ALX-805-003A-C100 ALX-805-003B-T100 ALX-805-003F-T100	Purified Biotin FITC	100 µg 100 tests 100 tests
MAb to CD31 (human) (Gi34)	Human	IP, WB	ALX-805-029-C100		100 µg
MAb to CD44	see Page 4/5				
MAb to Thy-1 [CD90] (human) (BC9-G2)	Human	FC, IP, WB, Blocking	ALX-805-085-L002		2 ml
MAb to Thy-1 [CD90] (human) (AF9)	Human	IHC, WB	BML-TA1278-0100		100 µl
MAb to EpCAM [CD326] (human) (VU-1D9)	Human	FC, IHC, IP, WB, Blocking	ALX-804-330-C100		100 µg

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