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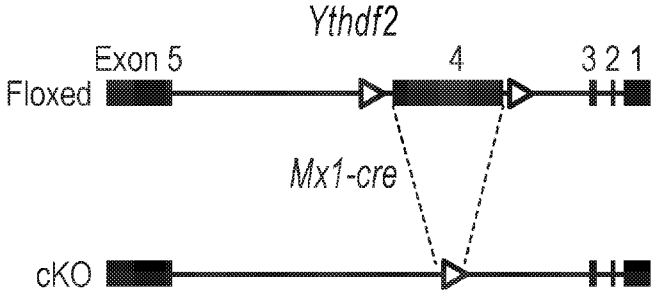

FIG. 1A

(57) Abstract: The present invention relates to methods for expanding a stem cell population, as well as other cell populations. More particularly, the invention relates, inter alia, to methods and compositions for expanding a stem cell and/or other cell population, particularly a hematopoietic stem cell population.

WO 2019/074980 A1

METHODS AND COMPOSITIONS FOR EXPANSION OF CELL POPULATION

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is being filed as a PCT application, and claims the benefit of priority to U.S. Patent Application No. 62/570,076 filed on October 9, 2017, as well as U.S. Patent Application No. 62/695,820 filed on July 9, 2018, both of which are hereby incorporated by reference herein in their entireties.

FIELD OF THE INVENTION

[0002] The present invention relates to methods and compositions for expanding a cell population, and particularly stem cell populations such as a hematopoietic stem cell population.

BACKGROUND

[0003] Hematopoietic stem cells (HSCs) are clonogenic cells, which possess the properties of both self-renewal (expansion) and multilineage potential giving rise to all types of mature blood cells. HSCs are responsible for hematopoiesis and undergo proliferation and differentiation to produce mature blood cells of various lineages while still maintaining their capacity for self-renewal. The ability to self-renew maintains the HSC population for the lifespan of an animal and also allows HSCs to repopulate the bone marrow of lethally irradiated congenic hosts.

[0004] Early HSC development displays a hierarchical arrangement, starting from long-term (LT-) HSCs, which have extensive self-renewal capability, followed by the expansion state, which corresponds to short-term (ST-) HSCs (having limited self-renewal ability) and proliferative multipotent progenitors (MPPs) (having

multipotent potential but no self-renewal capability). MPP is also a stage of priming or preparation for differentiation. An MPP differentiates and commits to become either a common lymphoid progenitor (CLP), which gives rise to all the lymphoid lineages, or a common myeloid progenitor (CMP), which produces all the myeloid lineages. During this process, the more primitive population gives rise to a less primitive population of cells, which is unable to give rise to a more primitive population of cells. The intrinsic genetic programs that control these processes including the multipotential, self-renewal, and activation (or transient amplification) of HSCs, and lineage commitment from MPP to CLP or CMP, remain largely unknown.

[0005] To sustain constant generation of blood cells for the lifetime of an individual, HSCs located in bone marrow niches (Zhang, J. et al. *Nature 425,* 836-841, 2003; Calvi, L. M. et al. *Nature 425*, 841-846, 2003; Kiel, M. J., et al. *Cell 121*, 1109-1121, 2005; Arai, F. et al. *Cell 118*, 149-161, 2004) must achieve a balance between quiescence and activation so that immediate demands for hematopoiesis are fulfilled, while long-term stem cell maintenance is also assured. In adults, homeostasis between the quiescent and activated states of stem cells is important to protect HSCs from losing their potential for self-renewal and, at the same time, support ongoing tissue regeneration (Li, L. and Xie, T. *Annu. Rev. Cell. Dev. Biol. 21*, 605-631, 2005). Over-activation and expansion of stem cells risks both eventual depletion of the stem cell population and a predisposition to tumorigenesis. Although some factors important for stem cell activation have been identified (Heissig, B. et al. *Cell 109*, 625-637, 2002), the molecular events governing the transition between quiescence and activation are poorly understood.

[0006] HSCs are responsible for life-long hematopoiesis under homeostatic and stress conditions, which relies on an exquisite balance between stem cell self-

renewal and differentiation (Li et al. *Science*, 327: 542-545, 2010; Weissman et al. *Cell*, 100: 157-168, 2000). Thus, HSC transplantation is a life-saving therapy for a broad spectrum of disorders, including hematologic, immune, and genetic diseases, as well as cancers (Walasek et al. *Annals of the New York Academy of Sciences* 1266: 138-150, 2012). However, HSC-based treatment can be limited primarily by the lack of HLA-matched donor bone marrow (BM). Allogeneic transplantation offers an alternative approach, but graft vs host disease (GvHD) remains a life-time challenge, since taking immune suppression medicine has numerous side effects, such as delayed immunological recovery, thrombotic microangiopathy (Sung et al. *Stem Cells Translational Medicine*, 2: 25-32 (2013) ;Shlomchik et al. *Nature Reviews. Immunology*, 7: 340-352, 2007). Transplantation of HSCs from hUCB reduces the risk of GvHD; however, the lower number of HSCs in hUCB than in BM or mobilized peripheral blood limits its application (Walasek et al. *Annals of the New York Academy of Sciences*, 1266: 138-150, 2012). Targeting single molecules or pathways has been studied for hUCB HSC expansion (Huang et al. Leukemia, 30: 144-153, 2016; Boitano et al. *Science*, 329: 1345-1348, 2010; Fares et al. *Science*, 345; 1509-1512, 2014; Ansellem et al. *Nature Medicine*, 9: 1423-1427, 2003; Antonchuk et al. *Cell*, 109: 39-45, 2002; Rentas et al. *Nature*, 532: 508-511, 2016; Himburg et al. *Nature Medicine*, 16: 475-482, 2010; North et al. *Nature*, 447: 1007-1011, 2007; Guo et al. *Nature Medicine*, 2018); Varnum-Finney et al. *Nature Medicine*, 6: 1278-1281, 2000; and Chou et al. *Experimental Hematology*, 41: 479-490 e474, 2013). However, other approaches are sought in order to relatively favor stem cell self-renewal versus differentiation (Zhao et al. *Molecular Cell Biology*, 18: 31-42, 2017).

[0007] m^6A is a prevalent internal modification in mRNAs that regulates the outcome of gene expression by modulating RNA processing, localization, translation, and eventual decay, which is modulated by "writers," "erasers" and "readers" of the mark (Roundtree et al. *Cell*, 169: 1187-1200, 2017; Li et al. *Annual Review of Genomics and Human Genetics*, 15: 127-150, 2014). Recent studies have elucidated the roles of m^6A modification in stem cell fate determination and endothelial-to-hematopoietic transition during embryogenesis (Batista et al. *Cell Stem Cell*, 15: 707-719, 2014; Geula et al. *Science*, 347: 1002-1006, 2015; Yoon et al. *Cell*, 2017; Zhang et al. *Nature*, 549: 273-276, 2017; Zhao et al. Nature, 542: 475-478, 2017) as well as in leukemia development (Li et al. *Cancer Cell*, 31: 127-141, 2017; Vu et al. *Nature Medicine*, 2017; Barbieri et al. *Nature*, 2017; Weng et al. *Cell Stem Cell*, 22: 191-205 e199, 2018). Interestingly, deficiency in m^6A writer complex, *Mettl3* and *Mettl14*, leads to distinct outcomes in different types of stem cells. For example, *Mettl3* or *Mettl14* KO promoted differentiation in HSCs (Vu et al. *Nature Medicine,* 2017; Weng et al. *Cell Stem Cell*, 22: 191-205 e199, 2018; Barbieri et al. *Nature*, 2017) while resulting in enhanced stem cell self-renewal and maintenance in mouse embryonic stem cells (mESCs) and embryonic neuronal stem cells (NSCs) (Batista et al. *Cell Stem Cell*, 15: 707-719, 2014; Yoon et al. *Cell*, 2017). Besides, the physiological function of m^6A in stem cells and leukemia are mediated through different mechanisms. In stem cells, m^6A modifications regulate stem cell fate determination by m^6A-mediated decay of mRNAs encoding stem cell fate determinant (Batista et al. *Cell Stem Cell*, 15: 707-719, 2014; Yoon et al. *Cell*, 2017) while in acute myeloid leukemia (AML), *Mettl3* and *Mettl14* promote leukemogenesis as m^6A modifications stabilize the mRNAs of oncogenes and/or increase their translation (Vu et al. *Nature Medicine*, 2017; Barbieri et al. *Nature*,

2017; Weng et al. *Cell Stem Cell*, 22: 191-205 e199, 2018). Furthermore, previous studies have reported that the leukemogenic functions of *FTO* and *Mettl14* are independent of YTHDF reader proteins (Li et al. *Cancer Cell*, 31: 127-141, 2017; Weng et al. *Cell Stem Cell*, 22: 191-205 e199, 2018).

[0008] As the m^6A RNA modification is modulated by "writers," "erasers" and "readers" of the mark (Wang et al. *Nature*, 505(7481): 117-120, 2014), processes that install, recognize and remove this and other marks may have various implications for cellular, developmental, and disease processes. For example, studies have shown that the m^6A mark may act as a key post-transcriptional modification to promote initiation of microRNA (miRNA) biogenesis (Alarcon et al. *Nature*, 519(7544): 482-485, 2015). Evidence also points to m^6A RNA modifications possibly being involved in the differentiation of stem cells to specific lineages (Batista, *Cell stem Cell*, 15(6): 707-719, 2014; Zhang et al. *Nature*, 549(7671): 273-276, 2017), and in regulating gene expression (Dominissini et al., *Nature* 485(7397):201-206, 2012; Haussmann et al, *Nature* 540(7632): 301-304, 2016). A m^6A transferase METTL3 has been identified as a regulator for terminating murine naïve pluripotency (Geula et al. *Science*, 347(6225): 1002-1006, 2015). The m^6A "writer" protein METTL3 has also been demonstrated in mouse T cells to disrupt T cell homeostasis and differentiation (Li et al. *Nature*, 548(7667): 338-342, 2017), and m^6A RNA methylation has been found to promote XIST-mediated transcriptional repression (Patil et al. *Nature*, 537(7620): 369-373, 2016). M^6A RNA modifications have also been shown to regulate the ultraviolet-induced DNA damage response (Xiang et al. *Nature*, 543(7646): 573-576, 2017). Study of the maternal-to-zygotic transition (MZT) as in zebrafish also indicated a role for m^6A mRNA methylation in transcriptome switching and animal development (Zhao et al. *Nature*, 542(7642):

475-478, 2017). Accordingly, while accumulative evidence has brought insights into the biological functions of m^6A (Lence et al. *Nature*, 540 (7632); 242-247, 2016), the function of m^6A in adult stems cells are largely unknown.

[0009] Hematopoietic stem cells (HSCs) in bone marrow (BM) maintain homeostasis hematopoiesis throughout life and also support regeneration after myeloablation (Weissman, 2000). Quiescent HSCs perform superiorly to proliferative HSCs in lethally irradiated mice, which largely attributes to the quiescent state that protects HSCs from DNA damage (Arai et al., 2004; Fleming et al., 1993; Wilson et al., 2008) (Walter et al., 2015). However, a recent study showed that DNA damage accumulation in HSCs was associated with broad attenuation of DNA repair and response pathways that were dependent upon HSC quiescence (Beerman et al., 2014). In fact, the majority of HSCs, despite their quiescence, are sensitive to DNA damage from chemotherapeutic drugs, such as 5-Fluorouracil (5FU) (Lerner and Harrison, 1990). The unresolved issue is how the hematopoietic system overcomes the consequence of myeloablation. In respect to the remarkable heterogeneity of HSCs during development and in adult (Benveniste et al., 2010; Benz et al., 2012; Fleming et al., 1993; Morita et al., 2010; Zhou et al., 2016), the existence of a reserve HSC (rHSC) subpopulation was proposed, with the features of drug-resistance and capacity to regenerate the bulk of HSCs to overcome stress-caused myeloablation (Haug et al., 2008; Li and Clevers, 2010; Wilson et al., 2008). Thus far, however, no functional evidence has been provided in supporting existence of rHSCs in the blood system.

[0010] HSCs are preserved in complex BM niches for their maintenance and regeneration (Li and Clevers, 2010; Mendelson and Frenette, 2014; Morrison and Scadden, 2014; Scadden, 2014; Schofield, 1978). In the past decades, multiple

studies have uncovered the complexity of HSC bone marrow niche components, including: endosteal (inner bone surface) cells *(*Calvi et al., 2003; Zhang et al., 2003*),* sinusoidal endothelial cells (Hooper et al., 2009; Kiel et al., 2005), *Cxcl12* abundant reticular (CAR) cells (Sugiyama et al., 2006), $Nestin^+$ and $NG2^+$ perivascular cells (Kunisaki et al., 2013; Mendez-Ferrer et al., 2010), $LepR^+$ and $Prx\text{-}1^+$ mesenchymal stem and progenitor cells (Ding and Morrison, 2013; Ding et al., 2012; Greenbaum et al., 2013), non-myelinating Schwann cells (Yamazaki et al., 2011), and megakaryocytes (Bruns et al., 2014; Zhao et al., 2014). However, whether and how the BM niche complexity contributes to HSC heterogeneity regulation remain largely unclear (Itkin et al., 2016). Furthermore, the first HSC niche was initially identified as the spindle shaped N-Cadherin$^+$ (N-cad$^+$) pre-osteoblastic cells in the endosteum of the trabecular bone region (Calvi et al., 2003; Xie et al., 2009; Zhang et al., 2003), but the nature and function of N-cad$^+$ niche cells in BM remain unclear.

[0011] Accordingly, there remains a need for elucidation and understanding of the role of m^6A and m^6A mRNA pathways to provide insight into molecular regulation of stem cell proliferation and differentiation. There remains a further need for methods of expanding populations of stem cells, both in vivo and ex vivo, and methods of providing treatment with such expanded stem cell populations, such as via transplant into a suitable subject.

SUMMARY

[0012] In one embodiment of the present disclosure, a method for expanding a population of stem cells is provided, the population of stem cells being obtained from a tissue selected from the group consisting of peripheral blood, cord blood and

bone marrow. The method includes modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the population of stem cells, to expand the number of stem cells.

[0013] In yet another embodiment, a method for ex vivo expansion of a substantially undifferentiated stem cell population is provided, comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the undifferentiated stem cell population to expand the number of undifferentiated stem cells without significant differentiation of the stem cell population.

[0014] According to yet another embodiment, a method for ex vivo expansion of an hematopoietic stem cell (HSC) population is provided, the HSC population being obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the HSC population to expand the HSC population to a sufficient quantity while maintaining a multilineage differentiation potential in the HSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

[0015] According to yet another embodiment, a method for ex vivo expansion of hematopoietic stem cells (HSCs) by at least 2-fold is provided, the expanded HSCs being competent to reconstitute an HSC lineage upon transplantation into a mammal in need thereof, the method comprising introducing a mutation into the stem cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of HSCs in a suitable culture medium.

[0016] According to a further embodiment, a kit for expanding an hematopoietic stem cell population (HSC) population for subsequent transplantation

into a subject in need thereof is provided, the kit comprising a system for introducing a mutation into the HSC population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

[0017] According to yet another embodiment, a kit for expanding an hematopoietic stem cell population (HSC) population for subsequent transplantation into a subject in need thereof is provided, the kit comprising an inhibitor of a m^6A mRNA modification reader, and instructions for use thereof.

[0018] In yet a further embodiment, a method for administering an hematopoietic stem cell (HSC) to a subject in need thereof is provided, the method comprising: (a) introducing, into a sample containing an HSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the HSCs to the subject.

[0019] In yet a further embodiment, a method for administering an hematopoietic stem cell (HSC) to a subject in need thereof is provided, the method comprising: (a) culturing, in a suitable culture media, a sample containing an HSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the HSCs to the subject.

[0020] In another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided, comprising: (a) introducing, into a sample

containing an HSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the HSCs to the subject.

[0021] In another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided, comprising: (a) culturing, in a suitable culture media, a sample containing an HSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the HSCs to the subject.

[0022] In one embodiment, a method for expanding a population of hematopoietic cells (HSCs) comprising culturing the population of HSCs under conditions sufficient to result in an expansion of the HSC population by at least 2-fold is provided, wherein the expanded population of HSCs is suitable for transplantation into a mammal in need thereof.

[0023] In a further embodiment, a method for expanding a population of hematopoietic stem cells (HSCs) is provided, comprising: (a) obtaining from a mammal a tissue sample comprising an HSC population; (b) expanding, in vitro, the HSC population from the sample, wherein: (i) the HSC population expands by at least 2-fold; and (ii) the expanded HSC population has at least a 5-fold increase in total colony-forming units.

[0024] In a further embodiment, a method for reconstituting a hematopoietic stem cell lineage in a subject in need thereof is provided, the method comprising: (a)

obtaining from a mammal a tissue sample comprising an HSC population; (b) expanding, in vitro, the HSC population from the sample, wherein: (i) the HSC population expands by at least 2-fold; and (ii) the expanded HSC population has at least a 5-fold increase in total colony-forming units; and (c) transplanting the expanded HSC population into a subject in need thereof.

[0025] In yet another embodiment, a method for expanding a hematopoietic stem cell population in a mammal in need of such expansion is provided, comprising administering to the mammal a therapeutically effective amount of a modulator of a N^6-Methyladenosine (m^6A) mRNA modification pathway for a period of time sufficient to expand the HSC population by at least 2-fold with HSCs that possess the ability to reconstitute a hematopoietic lineage in the mammal.

[0026] According to yet another embodiment, a method for ex vivo expansion of a mesenchymal stem cell (MSC) population is provided, the MSC population being obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the MSC population to expand the MSC population to a sufficient quantity while maintaining a multilineage differentiation potential in the MSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

[0027] According to yet another embodiment, a method for ex vivo expansion of mesenchymal stem cells (MSCs) by at least 2-fold is provided, the expanded MSCs being competent to reconstitute a MSC lineage upon transplantation into a mammal in need thereof, the method comprising introducing a mutation into the stem cells that results in deletion, replacement or reduced expression of a gene

expressing a m^6A mRNA modification reader and culturing the population of MSCs in a suitable culture medium.

[0028] According to a further embodiment, a kit for expanding a mesenchymal stem cell population (MSC) population for subsequent transplantation into a subject in need thereof is provided, the kit comprising a system for introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

[0029] According to yet another embodiment, a kit for expanding an mesenchymal stem cell population (MSC) population for subsequent transplantation into a subject in need thereof is provided, the kit comprising an inhibitor of a m^6A mRNA modification reader, and instructions for use thereof.

[0030] In yet a further embodiment, a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof is provided, the method comprising: (a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the MSCs to the subject.

[0031] In yet a further embodiment, a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof is provided, the method comprising: (a) culturing, in a suitable culture media, a sample containing a MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a number

sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the MSCs to the subject.

[0032] In another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided, comprising: (a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the MSCs to the subject.

[0033] In another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided, comprising: (a) culturing, in a suitable culture media, a sample containing a MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the MSCs to the subject.

[0034] In one embodiment, a method for expanding a population of mesenchymal cells (MSCs) comprising culturing the population of MSCs under conditions sufficient to result in an expansion of the MSC population by at least 2-fold is provided, wherein the expanded population of MSCs is suitable for transplantation into a mammal in need thereof.

[0035] In a further embodiment, a method for expanding a population of mesenchymal stem cells (MSCs) is provided, comprising: (a) obtaining from a mammal a tissue sample comprising a MSC population; (b) expanding, in vitro, the MSC population from the sample, wherein: (i) the MSC population expands by at

least 2-fold; and (ii) the expanded MSC population has at least a 5-fold increase in total colony-forming units.

[0036] In a further embodiment, a method for reconstituting a mesenchymal stem cell lineage in a subject in need thereof is provided, the method comprising: (a) obtaining from a mammal a tissue sample comprising a MSC population; (b) expanding, in vitro, the MSC population from the sample, wherein: (i) the MSC population expands by at least 2-fold; and (ii) the expanded MSC population has at least a 5-fold increase in total colony-forming units; and (c) transplanting the expanded MSC population into a subject in need thereof.

[0037] In yet another embodiment, a method for expanding a mesenchymal stem cell population in a mammal in need of such expansion is provided, comprising administering to the mammal a therapeutically effective amount of a modulator of a N^6-Methyladenosine (m^6A) mRNA modification pathway for a period of time sufficient to expand the MSC population by at least 2-fold with HSCs that possess the ability to reconstitute a mesenchymal lineage in the mammal.

[0038] According to year another embodiment, a method for ex vivo expansion of a mesenchymal stem cell (MSC) population is provided, the MSC population being obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the MSC population to expand the MSC population to a sufficient quantity while maintaining a multilineage differentiation potential in the MSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

[0039] According to yet another embodiment, a method for ex vivo expansion of mesenchymal stem cells (MSCs) by at least 2-fold is provided, the expanded

MSCs being competent to reconstitute a MSC lineage upon transplantation into a mammal in need thereof, the method comprising introducing a mutation into the stem cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of MSCs in a suitable culture medium.

[0040] According to a further embodiment, a kit for expanding a mesenchymal stem cell population (MSC) population for subsequent transplantation into a subject in need thereof is provided, the kit comprising a system for introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

[0041] According to yet another embodiment, a kit for expanding an mesenchymal stem cell population (MSC) population for subsequent transplantation into a subject in need thereof is provided, the kit comprising an inhibitor of a m^6A mRNA modification reader, and instructions for use thereof.

[0042] In yet a further embodiment, a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof is provided, the method comprising: (a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the MSCs to the subject.

[0043] In yet a further embodiment, a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof is provided, the method

comprising: (a) culturing, in a suitable culture media, a sample containing a MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the MSCs to the subject.

[0044] In another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided, comprising: (a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the MSCs to the subject.

[0045] In another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided, comprising: (a) culturing, in a suitable culture media, a sample containing a MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the MSCs to the subject.

[0046] In one embodiment, a method for expanding a population of mesenchymal cells (MSCs) comprising culturing the population of MSCs under conditions sufficient to result in an expansion of the HSC population by at least 2-fold is provided, wherein the expanded population of MSCs is suitable for transplantation into a mammal in need thereof.

[0047] In a further embodiment, a method for expanding a population of mesenchymal stem cells (MSCs) is provided, comprising: (a) obtaining from a mammal a tissue sample comprising a MSC population; (b) expanding, in vitro, the MSC population from the sample, wherein: (i) the MSC population expands by at least 2-fold.

[0048] In a further embodiment, a method for reconstituting a mesenchymal stem cell lineage in a subject in need thereof is provided, the method comprising: (a) obtaining from a mammal a tissue sample comprising a MSC population; (b) expanding, in vitro, the MSC population from the sample, wherein: (i) the MSC population expands by at least 2-fold; and (c) transplanting the expanded MSC population into a subject in need thereof.

[0049] In yet another embodiment, a method for expanding a mesenchymal stem cell population in a mammal in need of such expansion is provided, comprising administering to the mammal a therapeutically effective amount of a modulator of a N^6-Methyladenosine (m^6A) mRNA modification pathway for a period of time sufficient to expand the MSC population by at least 2-fold with MSCs that possess the ability to reconstitute a mesenchymal lineage in the mammal.

[0050] In a further embodiment, a method of isolating mesenchymal stem cells (MSCs) from a biological sample is provided, the method comprising contacting the biological sample having a population of MSCs with one or more N-cadherin antibodies.

[0051] In a further embodiment, an isolated population of mesenchymal stem cells is provided, as made by any of the processes described herein. According to yet another embodiment, an expanded, isolated population of mesenchymal stem cells is provided, as made by any of the processes described herein.

[0052] According to yet another embodiment, a kit for isolating a mesenchymal stem cell (MSC) population for subsequent transplantation into a subject in need thereof is provided. The kit comprises a system for contacting a biological sample comprising MSCs with one or more N-cadherin antibodies, and instructions for use thereof.

[0053] According to yet another embodiment, a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof is provided. The method comprises: (a) isolating MSCs from a biological sample comprising a population of MSCs, by contacting the biological sample with one or more N-cadherin antibodies, and (b) administering the isolated MSCs to the subject.

[0054] According to yet another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided. The method comprises: (a) isolating mesenchymal stem cells (MSCs) from a biological sample comprising a population of MSCs, by contacting the biological sample with one or more N-cadherin antibodies; and (b) administering the isolated MSCs to the subject.

[0055] According to yet another embodiment, a method for treating a subject in need of a transplant, selected from the group consisting of a bone marrow transplant, a peripheral blood transplant and an umbilical cord blood transplant, is provided. The method comprises administering to the subject a population of isolated MSCs obtained by any of the methods described herein.

[0056] In yet another embodiment, a method for expanding a population of chimeric antigen receptor (CAR) T-cells prepared by modifying T-cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow, is provided. The method comprises modulating a N^6-Methyladenosine

(m^6A) mRNA modification pathway in the population of CAR T-cells, to expand the number of CAR-T cells.

[0057] In a further embodiment a method for ex vivo expansion of a chimeric antigen receptor (CAR) T-cell population is provided. The method comprises modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the CAR T-cell population to expand the number of CAR T-cells.

[0058] According to yet another embodiment, a method for ex vivo expansion of a chimeric antigen receptor (CAR) T-cell population prepared by modifying T-cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow, is provided. The method comprises modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the CAR T-cell population to expand the CAR T-cell population to a sufficient quantity which is sufficient for subsequent transplantation into a subject in need thereof.

[0059] In yet another embodiment, a method for ex vivo expansion of chimeric antigen receptor (CAR) T-cells, the expanded CAR T-cells being competent to treat a cancer and/or blood disorder upon transplantation into a mammal in need thereof, is provided. The method comprises introducing a mutation into the CAR T-cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of CAR T-cells in a suitable culture medium.

[0060] In a further embodiment, a kit for expanding a chimeric antigen receptor (CAR) T-cell (HSC) population for subsequent transplantation into a subject in need thereof, is provided. The kit comprises a system for introducing a mutation into the CAR T-cell population that results in deletion, replacement or reduced

expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

[0061] In yet a further embodiment, a method for administering chimeric antigen receptor (CAR) T-cell to a subject in need thereof is provided. The method comprises: (a) introducing, into a sample containing CAR T-cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; and (c) administering the CAR T-cells to the subject.

[0062] In another embodiment, a method for administering a CAR T-cell to a subject in need thereof, is provided. The method comprises: (a) culturing, in a suitable culture media, a sample containing a CAR T-cell population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the CAR T-cells to the subject.

[0063] In a further embodiment, a method for treating cancer and/or a blood disorder in a subject in need thereof is provided. The method comprises: (a) introducing, into a sample containing a CAR T-cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; and (c) administering the CAR T-cells to the subject.

[0064] In yet a further embodiment, a method for treating cancer and/or a blood disorder in a subject in need thereof, is provided. The method comprises: (a) culturing, in a suitable culture media, a sample containing a CAR T-cell population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the CAR T-cells to the subject.

[0065] In one embodiment, a method for expanding a population of chimeric antigen receptor (CAR) T-cells is provided. The method comprises culturing the population of CAR T-cells under conditions sufficient to result in an expansion of the CAR T-cell population by at least 2-fold, wherein the expanded population of CAR T-cells is suitable for transplantation into a mammal in need thereof.

[0066] In yet another embodiment, a method for expanding a population of chimeric antigen receptor (CAR) T-cells is provided. The method comprises: (a) obtaining from a mammal a tissue sample comprising a T-cell population; (b) modifying the T-cell population with chimeric antigen receptors to provide CAR T-cell population; and (c) expanding, in vitro, the CAR T-cell population from the sample, wherein: (i) the CAR T-cell population expands by at least 2-fold.

[0067] In a further embodiment, a method for treating a subject suffering from cancer and/or a blood disorder is provided. The method comprises: (a) obtaining from a mammal a tissue sample comprising a T-cell population; (b) modifying the T-cell population with a chimeric antigen receptor (CAR) to form a CAR T-cell population; (c) expanding, in vitro, the CAR T-cell population from the sample, wherein: (i) the CAR T-cell population expands by at least 2-fold; and (d) transplanting the expanded CAR T-cell population into the subject.

[0068] In yet a further embodiment, a method for expanding a chimeric antigen receptor (CAR) T-cell population in a mammal in need of such expansion is provided. The method comprises administering to the mammal a therapeutically effective amount of a modulator of a N^6-Methyladenosine (m^6A) mRNA modification pathway for a period of time sufficient to expand the CAR T-cell population by at least 2-fold with CAR T-cells that possess the ability to treat cancer and/or a blood disorder in the mammal.

[0069] In yet another embodiment, a method of treating a subject suffering from a blood disorder is provided. The method comprises (a) obtaining a population of cells selected from the group consisting of stem cells and T-cells, from a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow; (b) optionally, in a case where the population of cells comprises T-cells, modifying the T-cells with a chimeric antigen receptor (CAR) to provide CAR T-cells; (c) expanding the population of cells by modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the cells, to expand the number of cells; and (d) transplanting the expanded cells to the subject to treat the blood disorder.

[0070] These and other aspects of the invention are further disclosed in the detailed description and examples which follow.

BRIEF DESCRIPTION OF THE DRAWINGS

[0071] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein.

[0072] Figs 1A-1H: Ythdf2 KO leads to increase in phenotypic HSCs in mice. Fig. 1A is a shematic showing a deletion of Ythdf2 in the HSPCs of *Mx1-cre;Ythdf2*$^{f/f}$ conditional KO (cKO) mice; Fig. 1B shows a Western blot (left) and histogram (right) showing intracellular flow validation of knockout Ythdf2 in mouse HSPCs; Fig. 1C are representative flow cytometric analysis plots of HSPCs in BM from *wt* and *Ythdf2* KO mice (n = 5 for each group); Figs. 1D and 1E are bar graphs showing the frequency in total nucleated cells (TNC) (1D) and absolute cell number (1E) of HSPCs in BM from *wt* and *Ythdf2* KO mice (n = 5 for each group); Fig. 1F is a bar graph showing the absolute number of BM TNC from *wt* and *Ythdf2* KO mice (n= 5 for each group); and Figs.1G and 1H are bar graphs showing the absolute number of committed progenitors (1G) and lineage cells (1H) in BM of *wt* and *Ythdf2* KO mice (n = 5 for each group). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant

[0073] Figs. 2A-2J: Ythdf2 KO results in expansion of functional HSCs in mice. Fig. 2A depicts an experimental scheme for limiting dilution transplantation assay (LDA) to determine the frequency of functional HSCs; Fig. 2B is a graph showing Primary LDA to determine the CRU frequency by ELDA (Extreme Limiting Dilution Analysis) (n = 10 per group) at 16 weeks post transplantation; Fig. 2C is a graph showing a competitive reconstitution assay by transplanting 200K whole bone marrow (WBM) cells with 200K rescue cells into irradiated recipients. (n = 10 for each group); Figs 2D and 2E are bar graphs showing the frequency in TNC (2D) and absolute cell number (2E) of donor derived HSPCs in BM from transplantation recipient mice as (2C) (n = 10 for each group); Figs. 2F and 2G are bar graphs showing absolute cell number of donor derived (CD45.2^{+}) committed progenitors (2F) and lineage cells (2G) in BM from primary 200K BM transplantation recipient

mice (n= 9-10 for each group); and Fig. 2H shows a plot with secondary LDA to determine the long-term CRU frequency by ELDA at 16 weeks after secondary transplantation (n = 10); Figs. 2I and 2J are, respectively, a bar graph showing quantification of functional mouse hematopoietic stem cells (HSCs) by transplantation assay with peripheral blood analysis for total engrafted donor cells at 4 weeks after transplantation (2I), and a bar graph showing quantification of functional mouse HSCs by transplantation assay with the percentage of B, T and myeloid lineage cells at 4 weeks after transplantation (2J). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0074] Figs. 3A-3I: Ythdf2 functions as an m^{6}A reader and regulates HSC gene expression by mediating mRNA decay. Fig. 3A is a schematic of irCLIP-seq workflow; Fig. 3B is a schematic showing Ythdf2 binding motif identified by MEME with all irCLIP peaks found in all three replicates; Fig. 3C is a pie chart depicting the fraction of Ythdf2 binding peaks in each of five transcript segments; Fig. 3D is a chart showing a GO enrichment analysis of Ythdf2 targets from intersect genes of three Ythdf2 irCLIP-seq replicates; Fig. 3E shows representative tracks of *Tal1* harboring m^{6}A peaks and Ythdf2 irCLIP peaks, with coverage of m^{6}A immunoprecipitation and input fragments indicated in red and grey, respectively, and Ythdf2 irCLIP reads highlighted in yellow; Fig. 3F is a chart showing qPCR analysis of total mRNA of sorted LSK cells from *wt* and *Ythdf2* KO mice. All Ct values were first normalized to *Actb* control (not m^{6}A-tagged). Then the ratio (*Ythdf2* KO over *wt*) was calculated. (n = 3); Fig. 3G shows representative images (left) and quantification via bar graph (right) of staining intensity of *wt* (n = 65) and *Ythdf2* KO (n = 54) HSPCs for TAL1 (green); Fig. 3H shows images depicting fluorescence in situ hybridization of *Tal1* mRNA (red) and fluorescence immunostaining of Dcp1a (P-body marker) (magenta),

Ythdf2 (green) in *wt* and *Ythdf2* KO HSPCs, where arrows indicate co-localized staining. Scale bars, 5 μm; Fig. 3I shows Quantification of *Tal1* mRNA and DCP1a co-localization in sorted LSK cells from *wt* and *Ythdf2* KO mice. Percentage indicates the average frequency of the *Tal1* mRNA that co-localized with DCP1a over total *Tal1* mRNA level in each LSK cells (n = 9-17). Data shown as mean ± s.e.m. Unpaired t-test.

[0075] Figs. 4A-4I: Role of YTHDF2 in human cord blood HSCs by m^{6}A-seq and RNA-seq analysis. Fig. 4A shows metagene profiles depicting sequence coverage in windows surrounding the TSS (left) and stop codon (right), where coverage of m^{6}A IP and control (input) fragments indicated in red and grey, respectively; Fig. 4B depicts pie charts presenting the fraction of m^{6}A peaks in each of five non-overlapping transcript segments; Fig. 4C depicts a Venn diagram showing shared and unique m^{6}A-tagged genes in mouse and hUCB HSPCs; Fig. 4D depicts a chart with a GO enrichment analysis of m^{6}A-tagged transcripts shared in both mouse and hUCB HSPCs; Fig. 4E shows representative tracks of *HOXB4* harboring m^{6}A peaks, where color codes are the same as in Fig 4A; Fig. 4F depicts a schematic of lentivirus mediated YTHDF2 KD in hUCB CD34$^+$ HSPCs for RNA-seq; Fig. 4G is a plot of a cumulative distribution of $\log_2$ (fold change) for m^{6}A-marked genes (purple line) and non-m^{6}A-marked genes (black line), with control and *YTHDF2* KD hUCB CD34$^+$ cells; Fig. 4H shows representative coverage plots from the RNA-seq analysis, showing increased reads of m^{6}A-tagged gene *HOXB4* but not a non-m^{6}A-tagged gene *ACTB* in *YTHDF2* KD compared to control hUCB CD34$^+$ cells; and Fig. 4I is a bar graph showing relative mRNA expression levels of non-m^{6}A labeled *ACTB* (as control) and m^{6}A-marked transcription factor related to stem cell self-renewal in control and *YTHDF2* KD hUCB CD34$^+$ cells. RPKM from RNA-seq

analysis were normalized to controls. Adjusted P value were indicated. n.s., nonsignificant.

[0076] Figs 5A-5F: *YTHDF2* KD facilitates expansion of human cord blood HSCs *ex vivo*. Figs. 5A-5B are bar graphs depicting the fold change of frequency (5A) and absolute number (5B) of indicated cells in *YTHDF2* KD over control cells after 7 days culture; Fig. 5C shows a bar graph depicting CFU output from transduced $CD34^+$ $CD38^-$ hUCB cells and images of CFU-granulocyte erythrocyte monocyte megakaryocyte (GEMMs) (scale bar, 200μm); Fig. 5D includes images of burst forming unit-erythroid (BFU-E) (left) and colony-forming unit-granulocyte/macrophage (CFU-GM) (right) from 7-days cultured control or *YTHDF2* KD hUCB cells (scale bar, 200μm), where independent cord blood samples were used and repeated twice for the panels; Fig. 5E is a bar graph showing apoptosis analysis of $CD34^+$ $CD38^-$ cells in 7-day cultures of transduced $CD34^+$ hUCB cells by Annexin V staining (n = 3 independent CB samples); Fig. 5F is a bar graph showing the fold change of Tthdf2 knockdown (KD) to control in indicated human cord blood HSCs (n=3 individual human samples), where lentivirus was used to deliver control shRNA or human Ythdf2 shRNA into sorted $CD34^+$ $CD38^-$ blood cord HSCs. Dashed lines indicate 95% confidence intervals. Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0077] Figs. 6A-6G: *YTHDF2* KD facilitates expansion of human cord blood functional long-term HSCs. Fig. 6A is an image showing an experimental scheme for measuring frequency of HSCs after *in vivo* expansion; Fig. 6B includes representative flow plots of $hCD45^+$ GFP^+ reconstitution from primary recipient mice receiving the highest two cell doses. hCD45 = human CD45; Fig. 6C is a plot showing $hCD45^+$ GFP^+ engraftment in BM from the primary recipient mice that

received the highest two doses (n = 8); Fig. 6D is a plot showing HSC frequency determined by primary LDA. Dashed lines indicate 95% confidence intervals; Fig. 6E includes representative flow plots of $hCD45^+$ GFP^+ reconstitution from secondary recipient mice receiving the highest two cell doses; Fig. 6F is a plot showing $hCD45^+$ GFP^+ engraftment in BM from the secondary recipient mice that received the highest two doses (n = 6); Fig. 6D is a graph showing HSC frequency determined by secondary LDA. Dashed lines indicate 95% confidence intervals. Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0078] Figs. 7A-7I: *Ythdf2* KO HSCs show no signs of lineage bias or differences in quiescence and homing ability but exhibit lower apoptotic rate. Fig. 7A is bar graph showing absolute cell number of HSPCs in BM from *Mx1-cre*$^-$*;Ythdf2*$^{f/f}$ and *Mx1-cre*$^+$*;Ythdf2*$^{f/f}$ mice without pI:pC injection (n=3 per group); Fig. 7B is a bar graph showing cell cycle analysis of HSPCs in *wt* (n = 3) and *Ythdf2* KO (n = 4) mice; Fig. 7C is a bar graph showing apoptosis analysis of BM HSPCs in *wt* and *Ythdf2* KO mice (n = 5 for each group); Fig. 7D shows images and the weight of spleens from *wt* and *Ythdf2* KO mice; Figs. 7E-7H are bar graphs showing absolute number of TNC (7E), LSK $CD48^-$ $CD150^+$ HSCs (7F), committed progenitors (7G) and lineage cells (7H) in the spleen of *wt* (n = 3) and *Ythdf2* KO (n = 4) mice; Fig. 7I is a bar graph showing Homing ability of *wt* and *Ythdf2* KO cells was determined by transplanting 1×10^6 CFDA SE-labelled BM cells into lethally irradiated mice. 18 hours later, BM was analyzed for homed events (n = 6 mice per group). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0079] Figs. 8A-8F: Transplantation recipient mice of *Ythdf2* KO BM display no lineage changes or defects 16 weeks post transplantation. Figs. 8A to 8C are bar graphs depicting absolute cell number of donor derived ($CD45.2^+$) TNC

(8A), committed progenitors (8B) and lineage cells (8C) in the BM from secondary 200K transplantation recipient mice at 16 weeks after secondary transplantation (n= 7-10 for each group); Figs. 8D to 8F are bar graphs depicting absolute cell number of donor derived ($CD45.2^+$) TNC (8D), committed progenitors (8E), and lineage cells (8F) in the spleen from secondary 200K transplantation recipient mice at 16 weeks after secondary transplantation (n= 7-10 for each group). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0080] Figs. 9A-9K: *Ythdf2* KO has long-term effect on mouse HSC expansion *in vivo* without inducing lineage bias. Fig 9A is a schematic showing BM and spleen collected from *wt* and *Ythdf2* KO mice were analyzed by flow cytometry at 5-7 months post pI:pC inductions; Figs. 9B to 9E are bar graphs showing: absolute cell number of TNC (Fig. 9B), HSPCs (Fig. 9C), committed progenitors (Fig. 9D) and lineage cells (Fig. 9E) in the BM of *wt* and *Ythdf2* KO mice at 5-7 months post induction. (n = 4-7 mice per group); Fig. 9F is a bar graph showing the weight of spleens from *wt* and *Ythdf2* KO mice at 5-7 months post induction. (n = 4-7 mice per group); Figs. 9G to 9J are bar graphs showing: absolute cell number of TNC (Fig. 9G), LSK $CD48^-$ $CD150^+$ HSCs (Fig. 9H), committed progenitors (Fig. 9I) and lineage cells (Fig. 9J) in the spleen of *wt* and *Ythdf2* KO mice at 5-7 months post induction. (n = 4-7 mice per group); Fig. 9K is a schematic and graph showing 5 months post pI:pC injection, 75k WBM from *wt* and *Ythdf2* KO mice were transplanted with 200K rescue cells into lethally irradiated recipients. Peripheral blood from transplantation recipients were analyzed every 4 weeks post transplantation to determine the donor derived engraftment (n = 10 for each group). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0081] Figs. 10A-10D: Molecular characterization of m^6A modification in mouse HSPCs. Fig. 10A shows plots of metagene profiles depicting sequence coverage in windows surrounding the TSS (up) and stop codon (down), where coverage of m^6A IP and control (input) fragments indicated in red and grey, respectively; Fig. 10B shows pie charts presenting the fraction of m^6A peaks in each of five transcript segments; Fig. 10C shows plots of the fraction of genes in mouse HPSCs with m^6A peaks in each of the segments as a function of expression level; Fig. 10D shows graphs of m^6A-tagged and non-m^6A-tagged mRNA degradation rates as determined by analysis of the expression level at 0 hour and 4 hours post actinomycin D treatment in HSPCs.

[0082] Figs 11A-11E: Define Ythdf2 functionality in mouse HSPCs by irCLIP-seq. Fig. 11A is an image showing immunoprecipitation of Ythdf2 in control or Flag-Ythdf2 overexpressed HPC7 cells; Fig. 11B is an irCLIP membrane image showing IR800 labeled RNA-Ythdf2 complex, where red box indicate the RNA-Ythdf2 complex collected for library construction, and with samples without UV crosslinking serve as controls; Fig. 11C is a Venn diagram showing intersection genes identified in three independent Ythdf2 irCLIP-seq experiments; Fig. 11D is a Venn diagram showing overlap of Ythdf2 binding targets and m^6A labeled mRNAs; Fig. 11E shows representative tracks of *Gata2* harboring m^6A peaks and Ythdf2 irCLIP peaks, where coverage of m^6A immunoprecipitation and input fragments are indicated in red and grey, respectively, and Ythdf2 irCLIP reads are highlighted in yellow.

[0083] Figures 12A-12F: *Ythdf2* KO increased m^6A-tagged mRNA expression, contributing to HSC expansion. Fig. 12A is a bar graph showing total RNA was extracted from 15,000 sorted BM LSK $Flk2^-$ cells; Fig. 12B shows

quantification of m^6A RNA methylation in *wt* and *Ythdf2* KO Lin^- cells (n = 6); Fig. 12C shows quantification (right) and histogram (left) showing intracellular flow validation of increased expression of TAL1, GATA2, RUNX1 and STAT5 in *Ythdf2* KO LT-HSCs comparing to *wt* LT-HSCs (n = 3 mice per group); Fig. 12D shows fluorescence in situ hybridization of *Gata2* mRNA (red) and fluorescence immunostaining of Dcp1a (P-body marker) (magenta), Ythdf2 (green) in *wt* and *Ythdf2* KO HSPCs. Arrows indicate co-localized staining. Scale bars, 5 μm; Fig. 12E shows quantification of *Gata2* mRNA and DCP1a co-localization in sorted LSK cells from *wt* and *Ythdf2* KO mice. Percentage indicates the average frequency of the *Gata2* mRNA that co-localized with DCP1a over total *Gata2* mRNA level in each LSK cells (n = 12-20); Fig. 12F shows percentage of GFP^+ cells in the $CD45^+$ population at 4 weeks post transplantation (n = 10). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0084] Figures 13A-13G: YTHDF2 regulates expression of transcription factors related to stem cell self-renewal in human cord blood stem cells. Fig. 13A is a Venn diagram showing intersection genes identified in three independent m^6A-seq experiments, using three independent cord blood samples; Fig. 13B shows pie charts with the percentage of mRNAs and non-coding RNAs containing m^6A peaks; Fig. 13C is a bar graph showing GO enrichment analysis of the transcription factors harboring m^6A modifications in hUCB $CD34^+$ cells; Fig. 13D shows images of Western blotting of YTHDF2 (up) and β-Actin (down) in sorted GFP^+ control and *YTHDF2* KD hUCB cells, showing knockdown efficiency of YTHDF2; Fig. 13E shows a bar graph with expression level (left) and representative track plots (right) of YTHDF2 from RNA-seq analysis of control and *YTHDF2* KD hUCB $CD34^+$ cells, showing knockdown efficiency of YTHDF2. Figs. 13F through 13G are

representative track plots of indicated transcription factors harboring m^6A peaks (up) and their representative coverage plots from the RNA-seq analysis (bottom). Adjusted P values are indicated.

[0085] Figs. 14A-14C: YTHDF2 KD in hUCB cells resulted in HSC expansion without changing lineage output. Fig. 14A depicts representative flow plots of GFP^+ $CD34^+$ $CD38^-$ $CD45RA^-$ $EPCR^+$ HSCs in control and *YTHDF2* KD hUCB cells post 7 days culture; Fig. 14B depicts confirmation of YTHDF2 protein knockdown and overexpression in transduced Hela cells; Fig. 14C depicts CFU production by YTHDF2 OE and control transduced $CD34^+$ $CD38^-$ CB from day 10 cultures (n = 3 independent human samples). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0086] Figs. 15A-15D: YTHDF2 KD in hUCB cells resulted in HSC expansion without changing lineage output. Fig. 15A includes representative flow plots of $hCD45^+$ GFP^+ monocyte, megakaryocyte (MK cell), B cell and erythrocyte in primary NSG recipient BM.; Figs. 15B and 15C are bar graphs depicting the percentage of lineage cells in $hCD45^+$ GFP^+ (Fig. 15B) and in total $CD45^+$ (Fig. 15C) BM cells from primary NSG recipients at 10 weeks post transplantation (n = 13-15); Fig. 15D is a bar graph depicting a summary of human donor derived lineage chimerisms in total $CD45^+$ BM cells from secondary NSG recipients at 12 weeks post transplantation (n = 6). Data shown as mean ± s.e.m. Unpaired t-test. n.s., nonsignificant.

[0087] FIG. 16: expansion of mesenchymal stem cells *in vivo*. Fig. 16 is a bar graph showing the frequency of N-Cad+ CD105+ in TNC with both *wt* Ythdf2 and a Ythdf2 knockout (KO).

[0088] Figs. 17A-17J: functional identification of rHSC population. Fig. 17A is a schematic representation of FACS sorting for rHSCs, pHSCs, ST-HSCs and MPPs; Fig. 17B shows a quantification of rHSCs and pHSCs function by transplantation assay. PB analysis for total engrafted donor cells at the indicated number of weeks post transplantation and the percentage of donor-derived B, T and myeloid lineage cells at 20 weeks post transplantation (n = 10 mice per group); Fig. 17C shows donor derived cells from rHSCs or pHSCs transplanted mice at 40 weeks post transplantation; Fig. 17D H2B-GFP label retaining cells in rHSCs and pHSCs at 130 days post chasing (n=4 mice per group); Fig. 17E shows cell cycle gene expression in rHSCs and pHSCs (n=3 replicates from 20 mice); Fig. 17F shows rHSCs and pHSCs transplanted recipients received 5FU injection at 4 weeks post transplantation as indicated. PB analysis for donor engraft cells at indicated weeks post transplantation. The percentage of donor-derived B, T and myeloid lineage cells were shown at 20 weeks post transplantation (n=10 mice per group); Fig. 17G shows rHSCs and pHSCs at day 3 post 5FU treatment (pool from 15 mice); Fig. 17H shows DNA damage gene expression in rHSCs and pHSCs (n=3 replicated from 20 mice); Fig. 17I shows DNA damage genes in rHSCs from control mice and mice at day 3 post 5FU (n=20 in control mouse group, n=40 in D3 5FU mouse group). * $P<0.05$, ** $P<0.01$, ***$P<0.001$. Error bars, s.e.m; Fig. 17J shows heat map of stress response genes in rHSCs, pHSCs and 5FU rHSCs.

[0089] Figs 18A-18I: rHSCs located by endosteal region in BM niche. Fig. 18A shows representative whole-mount images of mouse sternal bone marrow (BM), with bone (white, generated by second harmonic generation, SHG), MKs (yellow, distinguished by size, morphology and CD41 expression). Green arrowheads denoted phenotypic Lin^- $CD48^-CD41^-CD150^+CD49b^-$rHSCs, White arrowheads

denoted phenotypic Lin^-CD48^- $CD41^-CD150^+CD49b^+$ pHSCs; Fig. 18B shows representative image of rHSCs, pHSCs and 5FU rHSCs. White arrows denoted phenotypic $Lin^-CD48^-CD41^-CD150^+CD49b^-$rHSCs, phenotypic $Lin^-CD48^-CD41^-$ $CD150^+CD49b^+$ pHSCs and phenotypic $Lin^-CD48^-CD41^-$ $CD150^+CD49b^-$ 5FU rHSCs; Figs. 18C-E show relative distance between rHSCs, pHSCs and 5FU rHSCs to vessels, MKs or bones (n=144 rHSCs, n=685 pHSCs, n=707 5FU rHSCs); Fig. 18F shows absolute number of healthy, apoptotic and dead VE-Cad^+ $CD31^+$ vessel cells in control mice and mice at 1 day post 5FU treatment; Figs. 18F-G show absolute number of $AnnexinV^+$ $SytoxG^-$ apoptotic Ve-Cad^+ $CD31^+$ endothelial cells in central marrow (CM) or N-cad- $tomato^+$ cells in both CM and bone from control mice and mice 1 day post 5FU treatment. N=3 in each group. * $P<0.05$, ** $P<0.01$, ***$P<0.001$. Error bars, s.e.m; Figs. 18H-I show representative image of N-cad-$tomato^+$ and Ve-Cad^+ $CD31^+$ vessels in control mice and in mice at 3 days post 5FU treatment.

[0090] Figs. 19A-19J: N-cad^+ cells maintain functional HSCs in BM niche. Fig. 19A shows a scheme for DT administration to *N-cad-CreER^T;iDTR* mice used for the experiments shown in B-G. D indicated day (e.g., D0 indicates day 0); Fig. 19B shows N-cad^+ cell ablation efficiency as indicated by $Tomato^+$ cells in *N-cad-CreER^T;iDTR* mice; Figs. 19C-D show flow cytometric analyses to determine the absolute numbers of total nucleated cells (TNC) and HSPCs in the bone marrow (BM) from *N-cad-CreER^T;iDTR* mice post TMX and DT injections (n=5 mice per group); Figs. 19E-H show quantification of functional HSCs by transplantation assay in primary 1° and secondary 2° transplantation. Total BM cells from PB analysis for total engrafted donor cells at the indicated number of weeks post transplantation and the percentage of donor-derived B, T and myeloid lineage cells at 16 weeks post

transplantation (n = 10 mice per group); Figs. 19I-J show flow cytometric analyses to determine the absolute numbers of HSPCs in the bone marrow (BM) from *N-cad-CreER^{T};SCFf/f* (*N-cad-CreER^{T}_;SCFf/f*, n=4 mice, *N-cad-CreER^{T+};SCFf/f*, n=6 mice) and *N-cad-CreER^{T+};Cxcl12f/f* mice (*N-cad-CreER^{T}_;Cxcl12f/f*, n=3 mice, *N-cad-CreER^{T+};Cxcl12f/f,* n=6 mice) post TMX and DT injections. (* P<0.05, ** P<0.01, ***P<0.001. Error bars, s.e.m.).

[0091] Figs 20A-20K: transcriptome analysis for hematopoietic cells and niche cells. Figs. 20A-B shows pearson distance tree and PCA analysis for hematopoietic stem and progenitor cells (HSPCs); Figs. 20C-D show pearson distance tree and PCA analysis for BM niche cells; Fig. 20E shows HSC signature gene expression in hematopoietic stem and progenitor cells; Fig. 20F shows BM niche signature gene expression in niche cells; Fig. 20G shows term analysis for BM niche cells; Fig. 20H shows stromal cell development gene expression in niche cells from endosteal and perivascular zones; Fig. 20I shows lineage tracing for *N-cad-CreER^{T}; R26-tdT; Nestin-GFP* mice after 3 TMX injections, and *N-cad-CreER^{T}; R26-ZsG; Cxcl12-DsR* mice after 3 TMX injections; Fig. 20J shows enzymatically digested bone marrow cells from *N-cad-CreERT; R26-tdT* mice post TMX injections. LepR and Pdfgrα stained by antibodies shown as red peak. Isotype control shown as gray peak; Fig. 20K shows CFU-F activity in niche cells from endosteal and perivascular zones.

[0092] Fig. 21A-21G: *in vitro* differentiation potential and localization of N-cad^{+} derived cells. Fig. 21A shows experimental design; Fig. 21B shows live CFU-F colonies cultured from enzymatically digested bone marrow, stained with Cell Trace^{TM} and Tomato^{+} cells in one colony in high magnification; Figs. 21C-E show *in vitro* differentiation of stromal cells derived from *N-cad-CreER^{T}; R26-tdT* mice: live

tdTomato$^+$ cells and Alkaline Phosphatase staining of culture 21 days after osteo-differentiation (21C); live Tomato$^+$ cells and Oil Red O lipid staining 21 days after adipo-differentiation (21D); aggrecan antibody stained and toluidine blue stained chondrocytes at 21 days after chondro-differentiation of Tomato$^+$ cells (21E); Figs. 21F-G show(F-G) experimental design; Fig. 21H shows localization of cells derived from *N-cad-CreERT; R26-tdT* mice post TMX injection at 6 hours, 14 hours, 24 hours, 1 week and 4 weeks; Fig. 21 I shows percentage of Tomato$^+$ cells post TMX injection at 1 week, 2 weeks, 4 weeks and 6 weeks in trabecular, cortical bone and central marrow (n=2 mice in 1 and 2 weeks group, n=3 mice in 4 and 6 weeks group. * P<0.05, ** P<0.01, ***P<0.001. Error bars, s.e.m.).

[0093] Figs. 22A-22K: N-cad$^+$ stromal cells give rise to osteoblasts and adipocytes in adult mice. Fig. 22A shows representative femur sections from *N-cad-CreER^T; R26-tdT; Col2.3-GFP* mice of different time points post TMX injection showing the anatomical distribution and increasing generation of Tomato$^+$Col2.3-GFP$^+$ osteoblasts. Scale bar, 100μm; Figs. 22B-C show higher-power images of *N-cad-CreER^T; R26-tdT; Col2.3-GFP* mice at early time points post TMX in region i, ii, iii, iv, v and vi shown in 6hr (22B) and 14hr (22C). Hollow arrowheads show Tomato$^+$Col2.3GFP$^+$ osteoblasts (yellow cells) at 6 hours and 14 hours post TMX, whereas solid arrowheads indicate the *N-cad* recombined both in the trabecular (ii, iv, v) and cortical (iii, vi) region (green). These cells are potentially undifferentiated as shown by the absence of Col2.3-GFP. Scale bar, 50 μm; Figs. 22D-E show image quantification showing percentage of Tomato$^+$Col2.3-GFP$^+$ and Tomato$^+$Col2.3-GFP$^-$ cells in trabecular (22D) and compact bone (22E) at 6 hours, 14 hours, 24 hours, 2 weeks and 4 weeks post TMX injection; Fig. 22F shows image quantification comparing percentage of potential undifferentiated Tomato$^+$Col2.3-

GFP$^-$ between trabecular and compact bone. * P<0.05, ** P<0.01, ***P<0.001. Error bars, s.e.m; Fig. 22G shows representative image of trabecular bone (TB) and cortical bone (CB) in *N-cad-CreER^T; R26-tdT; Col2.3-GFP* mice at 4 weeks post TMX injection. Scale bar, 20 μm; Fig. 22H shows representative low and high-power image of femur section from *N-cad-CreER^T; R26-tdT* mice with Perilipin staining at 4 weeks post TMX injection. At periosteal region (i), bone marrow near trabecular region (ii) and central marrow(iii), solid arrowheads showed Tomato$^+$Perilipin$^+$ derived from N-cad$^+$ MSCs; Fig. 22I shows BODIPY staining showed the lipid droplet (green) inside the Tomato$^+$ Perilipin$^+$ adipocyte (arrowheads). Scale bar, 20 μm; Figs. 22J-K show image quantification of Tomato$^+$Perilipin$^+$ adipocytes in trabecular bone (22J) and periosteal region (22K) at 6 hours, 14 hours, 24 hours, 2 weeks and 4 weeks post TMX injection. (* P<0.05, ** P<0.01, ***P<0.001. Error bars, s.e.m.).

[0094] Figs. 23A-23J: N-cad$^+$ MSCs give rise to chondrocytes during development and post injury. Fig. 23A shows experimental design; Fig. 23B shows tomato$^+$ partially colocalized with Aggrecan$^+$ chondrocytes in rib at E14.5(2 days post TMX induction); Fig. 23C shows an Illustration of chondrocyte development in femur; Fig. 23D shows a representative femur section from 2-day-old *N-cad-CreER^T; R26-tdT* mice with TMX induction at E12.5. Note that Tomato$^+$ cells gave rise to Aggrecan$^+$ cartilage cells in articular surface (i) and the developing secondary ossification center (ii). Arrowheads indicated Tomato$^+$ Aggrecan$^+$ cells; Fig. 23E shows a representative femur section from 10-month-old *N-cad-CreER^T; R26-tdT* mice with TMX induction at E12.5. Tomato$^+$ cells from early embryonic stage differentiated to Perilipin$^+$ adipocytes; Fig. 23F shows a representative femur section from 2-month-old *N-cad-CreER^T; R26-tdT* mice with TMX induction at E12.5. Tomato$^+$ cells from early embryonic stage differentiated to Osteopontin+ hypertrophic

chondrocytes (i and ii) and osteoblasts (iii, iv, v and vi); Fig. 23G shows an experimental design for femoral groove injury to *N-cad-CreER^T; R26-tdT* mice with TMX induction at E12.5; Fig. 23H shows quantification of Tomato$^+$ chondrocytes in control mice and in mice 3 weeks after knee cartilage injury. (I) Representative section of distal femur from *N-cad-CreER^T; R26-tdT* mice without cartilage injury or 3 weeks after cartilage injury. Note that the clustered Tomato$^+$ Aggrecan$^+$ cells at the knee surface of control mice (i) significantly increased at the correspondent region in mice 3 weeks after knee cartilage injury (ii); Fig. 23J shows AHO staining of the sections in Figure 6H showing the Alcian blue positive chondrocytes in control (i) and in the location of cartilage injury(ii).

[0095] Figs. 24A-24K: BrdU assay and N-cad reporter mouse line post 5FU. Figs. 24A-F show representative images showing BrdU$^+$ cells in femur of mice at day 0, 2, 3, 4 and 6 post 5FU treatment. Note that BrdU$^+$ cells reduced at day 2 post 5FU, and reactivated from day 3 to day 6 post 5FU near bone (red dotted line) or vessel/adipose structure (green dotted line); Fig. 24G shows a model of dynamic of BrdU$^+$ cells; Fig. 24H shows a ratio of BrdU$^+$ cells in bone marrow to bone surface from day 3 to 6 post 5FU treatment; Fig. 24I shows a percentage of BrdU$^+$ cells near bone surface and near vessel/adipose structures from day 3 to 6 post 5FU treatment; Fig. 24J shows representative whole bone section showing N-cad driven tomato$^+$ cells in both bone surface and central marrow; Fig. 24K shows absolute number of N-cad driven tomato$^+$ cells in central marrow (CM) and in bone of *N-cad-TdT* mice of control group and mice 3 days post 5FU treatment. N=3 in each group. * P<0.05, ** P<0.01, ***P<0.001. Error bars, s.e.m.

[0096] Figs. 25A-25B: generation of *N-cad-CreER^T* mouse strain. Fig. 25A shows a generation of *N-cad-CreER^T* mouse strain; Fig. 25B shows lineage tracing for

N-cad-CreER^T, R26-tdT; Col2.3-GFP mice after three TMX injections; blood vessels stained by CD31 and Ve-cadherin antibodies.

[0097] Figs. 26A-26E: sorting strategy and signature gene expression of niche cells. Fig. 26A shows niche cells in endosteal zone harvested from digested bone cells; Fig. 26 B shows niche cells from Perivascular and sinusoid zones harvested from digested bone marrow cells; Fig. 26C shows localization of NG2-RFP$^+$ cells in endosteal and peri-arterial regions; Figs 26D-E show heatmaps of osteo-chondrogenic progenitor gene and adipogenic progenitor gene expression in niche cells.

[0098] Figs. 27A-27E: lineage tracing in *N-cad-CreERT; R26-tdT* mice at early time point post TMX induction. Figs. 27A-B show representative images of trabecular bone (TB) and cortical bone(CB) in *N-cad-CreERT; R26-tdT; Col2.3-GFP* mice at 24 hours and 2 weeks post TMX induction. Scale bar, 20μm; Figs. 27C-E show representative femur section with high power images of *N-cad-CreERT; R26-tdT* mice at 6 hours, 14 hours and 24 hours post TMX induction. Adipocytes shown with perilipin antibody staining.

[0099] Figs. 28A-28D: characterization of N-cad$^+$ MSCs from early development and in injury repair. Fig. 28A shows representative images of femur section showing N-cad$^+$ MSCs with Aggrecan staining in *N-cad-CreER^T; R26-tdT* 24 hours post TMX induction at postnatal D2; Fig. 28B shows a representative femur section from 2-month-old *N-cad-CreER^T; R26-tdT* mice with TMX induction at E12.5. Adipocytes shown with Perilipin antibody staining; Fig. 28C shows a representative femur section from 2-day-old *N-cad-CreER^T; R26-tdT* mice with TMX induction at E12.5. Developing bone cells shown with Osteopontin antibody staining; Fig. 28D shows a representative sagittal knee sections in E12.5 TMX induced *N-cad-CreER^T;*

R26-tdT mice of control group and 2 weeks after knee cartilage injury. Scale bar, 1mm.

[00100] **Fig. 29:** Image of surviving rHSCs (green, $CD150^+$ Lin^- $CD49b^-$) at day 3 post 5FU treatment were often detected as single cells adjacent to the bone surface (white, SHG), and proliferating HSCs were often associated with MKs ($CD150^+$ Lin^+) or near the vessels (red, CD31+).

[00101] **Fig. 30:** Plot showing production of human Thpo by 10K ncad+ hMSCs and 1000k total hMSCs *in vivo*.

DETAILED DESCRIPTION OF THE INVENTION

[00102] One embodiment of the invention is a method for expanding a population of stem cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow. This method comprises modulating a N6-methyladenosine (m^6A) mRNA modification pathway in the population of stem cells to expand the number of stem cells.

[00103] Another embodiment of the invention is a method for expanding a population of chimeric antigen receptor (CAR) T-cells cells obtained by modifying T-cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow. This method comprises modulating a N6-methyladenosine (m^6A) mRNA modification pathway in the population of CAR T-cells to expand the number of stem cells.

[00104] In the present invention the population of stem cells and/or T-cells may be obtained from any mammal, such as, e.g., a human, and from any tissue that contains stem cells and/or progenitor cells and/or T-cells. As noted above, in a

preferred embodiment the tissue may be peripheral blood, cord blood or bone marrow.

[00105] As used herein, "expand", "expanding" and like terms means to increase the number of stem cells and/or CAR-T cells in the population relative to the number of stem cells and/or CAR T-cells in the original population either in *vivo* or *ex vivo* using any of the methods disclosed herein. The expansion may be at least 40-fold compared to the original number of stem cells and/or CAR T-cells in the population. More preferably, the expansion is at least 2-fold, 4-fold, 5-fold, 8-fold, 10-fold, 15-fold, 20-fold or more compared to the original number of stem cells.

[00106] In the present invention "a population of stem cells" means a group of substantially undifferentiated cells that possess the ability to give rise to many different types of cells and which have the ability to self-renew. Representative, non-limiting examples of stem cells according to the present invention include bronchioalveolar stem cells (BASCs), bulge epithelial stem cells (bESCs), corneal epithelial stem cells (CESCs), cardiac stem cells (CSCs), epidermal neural crest stem cells (eNCSCs), embryonic stem cells (ESCs), endothelial progenitor cells (EPCs), hepatic oval cells (HOCs), hematopoetic stem cells (HSCs), hematopoietic stem and progenitor cells (HSPCs), keratinocyte stem cells (KSCs), mesenchymal stem cells (MSCs), neuronal stem cells (NSCs), pancreatic stem cells (PSCs), retinal stem cells (RSCs), and skin-derived precursors (SKPs).

[00107] Hematopoietic stem cells, for example, have the ability to self-renew (i.e., expand) and can give rise to all the types of progenitor cells (such as, e.g., CMP, GMP, MEP and CLP) and ultimately all the types of blood cells (such as *e.g.*, red blood cells, B lymphocytes, T lymphocytes, natural killer cells, neutrophils, basophils, eosinophils, monocytes, macrophages, and platelets) in the hematopoietic

system. Mesenchymal stem cells, as another example, are multipotent stromal cells that can differentiate into a variety of cell types (such as, e.g., osteoblasts, chondrocytes, myocytes and adipocytes).

[00108] In the present invention "a population of chimeric antigen receptor (CAR) T-cells" means a group of T-cells that have been modified with chimeric antigen receptors capable of binding specific antigens, such as antigens on the surface of cancer cells, and may possess the ability to target and kill such cancer cells. The CAR T-cells can be prepared by modifying T-cells with the chimeric antigen receptors, such as by introducing DNA coding for the chimeric antigen receptors into the T-cells, to express the chimeric antigen receptors on the surface of the T-cells (Davila et al. *Sci Transl Med* 6(224), 224ra25 (2014); Tasian et al. *Ther Adv Hematol* 6(5), 228-241 (2015).

[00109] In the present invention, "modulating", "modulation" and like terms mean altering the signal transduction pathway, e.g., a protein in the m^6A mRNA modification pathway, including but not limited to lowering or increasing the expression level of a protein, altering the sequence of such a protein (by mutation, pre-translational or post-translational modification or otherwise), or inhibiting or activating such a protein (whether by binding, phosphorylation, glycosylation, translocation or otherwise). Such modulation may be achieved genetically or pharmacologically.

[00110] In one aspect of the present invention, modulating the m^6A mRNA modification pathway comprises introducing a mutation into a population of stem cells and/or CAR-T cells, which mutation results in modulation of a molecule in the m^6A mRNA modification pathway. In another aspect present invention, modulation of the m^6A mRNA modification pathway also includes contacting the stem cells

and/or CAR T-cells with a modulator of a molecule in the m^{6}A mRNA pathway. Representative, non-limiting examples of such modulators include a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

[00111] In the present invention, the phrase "modulation of a molecule in the m^{6}A mRNA modification pathway" means altering the function of a member of the m^{6}A mRNA modification pathway, which altered function may have an effect similar to inhibiting or decreasing the function of a molecule involved in a process upstream and/or downstream of m^{6}A modification of mRNA. Non-limiting examples of such "modulation" include increasing or decreasing the expression or function of proteins involved in any of the incorporation of *N*^{6}-methyladenosine modifications in mRNA, removal of *N*^{6}-methyladenosine mRNA modifications to mRNA, and/or the recognizing and processing of *N*^{6}-methyladenosine modified mRNA. For example, the modulation may include increasing or decreasing N^6-methyladenosine modifications in mRNA, and/or that affecting the type and/or distributions of such modifications in mRNA, such as by modulating the activity of one or more of a m^{6}A writer (e.g. methyltransferase) and m^{6}A eraser (e.g. demethylase). As another example, the modulation may increase or decreases expression or function of proteins that recognize *N*^{6}-methyladenosine modifications to mRNA to mediate m^{6}A-dependent functions, such as by modulating the activity of a m^{6}A reader (e.g., an RNA binding protein that recognizes methylated adenosine). Thus, modulation of the molecule in the m^{6}A mRNA modification pathway modulator may result in modulation of the activity and/or expression of a molecule upstream or downstream of an m^{6}A mRNA modification process.

[00112] In one aspect, the modulation of the m^6A mRNA modification pathway involves modulation of a molecule selected from the group consisting of m^6A mRNA modification readers, m^6A mRNA modification writers, m^6A mRNA modification erasers and combinations thereof. Non-limiting examples of m^6A modification writers include methyltransferases that are capable of post-transcriptionally installing the m^6A modification in messenger RNA, and can include any selected from the group consisting of METTL3, METTL14, WTAP, KIAA1429 and combinations thereof. Non-limiting examples of m^6A modification erasers include demethylases that are capable of reversing the methylation, and can include any selected from the group consisting of FTI, ALKBH5 and combinations thereof. M^6A modification readers include proteins that are capable of selectively binding m^6A-methylated mRNA to exert regulatory functions through selective recognition of methylated mRNA. Suitable m^6A modification readers can include any selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, eIF3 and combinations thereof. According to one aspect, the m^6A modification readers comprise proteins of the YTH domain family of proteins, which includes Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2 and combinations thereof. (*see, e.g.,* Wang et al. *Nature*, 505(7481):117-120, 2014; Frayling et al. *Science*, 316: 889-894, 2007; Zheng et al. *Mol. Cell.*, 49: 18-29, 2012; Cao et al. *Open Biol.*, 6(4): 160003, 2016; Maity et al. *The FEBS Journal*, 283(9): 1607-1630, 2016).

[00113] As used herein, "introducing a mutation" means any conventional method for producing an alteration in the genetic makeup of the stem cell population and/or CAR T-cell population. Non-limiting examples for introducing a mutation into a stem cell population and/or CAR T-cell population include mutagenesis via ultra-violet light irradiation, chemical mutagenesis, targeted mutagenesis such as site

directed mutagenesis of a stem cell and/or CAR T-cell, and creation of a transgenic mouse. According to one aspect, a mutation may be introduced into the stem cell and/or CAR T-cell to delete, replace or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway, such as a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, a m^6A mRNA modification eraser and combinations thereof. In one aspect, the mutation is introduced to delete, replace or reduce expression of a gene that expresses a m^6A mRNA modification reader, such as any selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, eIF3 and combinations thereof. In a preferred aspect, a mutation is introduced to delete, replace or reduce expression of a gene that expresses Ythdf2. In yet another aspect, the mutation is introduced to delete, replace or reduce expression of a gene that expresses a m^6A mRNA modification writer, such as any selected from the group consisting of METTL3, METTL14, WTAP, KIAA1429 and combinations thereof. In yet another aspect, the mutation is introduced to delete, replace or reduce expression of a gene that expresses a m^6A mRNA modification eraser, such as any selected from the group consisting of FTI, ALKBH5 and combinations thereof.

[00114] In one aspect, the mutation can be introduced by exposing the stem cells and/or CAR T-cells to a Mx1-Cre targeting system (*see, e.g.,* Kuhn et al. *Science*, 269(5229): 1427-1429, 1995) that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway. In yet another aspect, a mutation is introduced that incorporates short hairpin RNA (shRNA) into the stem cells and/or CAR T-cells to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway. For example, the

shRNA may be introduced by exposing the stem cells and/or CAR T-cells to a vector to deliver shRNA, which may be a viral vector such as lentivirus (*see, e.g.,* Chira et al. *Oncotarget*, 6(31): 30675-30703, 2015). The shRNA may be capable of triggering gene silencing to regulate gene expression (*see, e.g.,* Paddison et al. *Genes Dev.*, 16(8): 948-958, 2002).

[00115] As used herein, "a modulator of a *N*^{6}-Methyladenosine mRNA modification pathway" (or "m^{6}A mRNA modification pathway modulator") is any agent that regulates the activity of any member of the m^{6}A mRNA modification pathway, which results in, *e.g.*, an increase or decrease in N^6-methyladenosine modifications in mRNA, and/or a change in the types and/or distributions of such modifications in mRNA, such as by modulating the activity of one or more of a m^{6}A writer (e.g. methyltransferase) and m^{6}A eraser (e.g. demethylase). As another example, the agent may be one that increases or decreases activity of proteins that recognize *N*^{6}-methyladenosine modifications to mRNA to mediate m^{6}A-dependent functions, such as by modulating the activity of a m^{6}A reader (e.g., an RNA binding protein that recognizes methylated adenosine). Thus, the m^{6}A mRNA modification pathway modulator may act on, or upstream of, or downstream of, an agent that affects the m^{6}A modification to mRNA.

[00116] In one embodiment, the m^{6}A mRNA modification pathway may be modulated by down-regulating and/or inhibiting a member of the m^{6}A mRNA modification pathway, such as down-regulating and/or inhibiting a m^{6}A mRNA modification reader. As used herein, "down-regulating" means inhibiting or reducing the amount of or inhibiting or decreasing the activity of a member of the m^{6}A mRNA modification pathway. Such down-regulation may be accomplished using, e.g. antisense RNA, siRNA, antibodies, or small molecules. As another example, the

m^6A mRNA modification reader may be down-regulated by contacting the stem cells and/or CAR T-cells with an inhibitor of an m^6A mRNA reader, to inhibit binding and/or recognizing of the m^6A modified mRNA by the m^6A mRNA reader. In one aspect, the m^6A mRNA modification reader that is down-regulated is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, eIF3 and combinations thereof. In a preferred aspect, the m^6A mRNA modification reader that is down-regulated is Ythdf2. Inhibitors of the m^6A mRNA modification reader may be any selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-

501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e (*see, e.g.* Helwak et al. *Cell*, 153(3): 654-655, 2013; Whisnant et al., *MBio* 4(2), 2013:e000193); (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-

502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p (*see, e.g.,* Hafner et al. *Cell*, 141(1): 129-141, 2010; Helwak et al. *Cell*, 153(3): 654-655, 2013); (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262 (*see, e.g.* Helwak et al. *Cell*, 153(3): 654-655, 2013; Selbach et al. Nature, 455(7209): 58-63, 2008; Yang et al. *J Biol Chem.*, 292(9): 3614-3623, 2017); (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-

888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-

mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296 (*see, e.g.,* Helwak et al. *Cell,* 153(3): 654-656, 2013; Selbach et al. *Nature*, 455 (7209):58-63, 2008; Baek et al, *Nature*, 455(7209):64-71, 2008; Leivonen et al. *Mol Cell Proteomics*, 10(7), 2011: M110.005322): (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t, hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141,

hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262 (*see, e.g.* Helwak et al. *Cell,* 153(3): 654-655, 2013; Hafner et al. Cell, 141(1): 129-141, 2010; Kishore et al, Nat Methods, 8(7):559-64, 2011; Memczak et al. *Nature*, 495(7441):333-8, 2013; Selbach et al. *Nature*, 455(7209):58-63, 2008; Chi et al. Nature. 460(7254):479-86, 2009).

[00117] In the present invention, the term "small molecule" includes any chemical or other moiety, other than polypeptides and nucleic acids, that can act to affect biological processes, particularly to modulate members of the m^6A mRNA modification pathway. Small molecules can include any number of therapeutic agents presently known and used, or that can be synthesized in a library of such molecules for the purpose of screening for biological function(s). Small molecules are distinguished from macromolecules by size. The small molecules of the present invention usually have a molecular weight less than about 5,000 daltons (Da), preferably less than about 2,500 Da, more preferably less than 1,000 Da, most preferably less than about 500 Da.

[00118] Small molecules include without limitation organic compounds, peptidomimetics and conjugates thereof. As used herein, the term "organic compound" refers to any carbon-based compound other than macromolecules such

as nucleic acids and polypeptides. In addition to carbon, organic compounds may contain calcium, chlorine, fluorine, copper, hydrogen, iron, potassium, nitrogen, oxygen, sulfur and other elements. An organic compound may be in an aromatic or aliphatic form. Non-limiting examples of organic compounds include acetones, alcohols, anilines, carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, nucleosides, nucleotides, lipids, retinoids, steroids, proteoglycans, ketones, aldehydes, saturated, unsaturated and polyunsaturated fats, oils and waxes, alkenes, esters, ethers, thiols, sulfides, cyclic compounds, heterocyclic compounds, imidizoles, and phenols. An organic compound as used herein also includes nitrated organic compounds and halogenated (e.g., chlorinated) organic compounds.

[00119] Preferred small molecules are relatively easier and less expensively manufactured, formulated or otherwise prepared. Preferred small molecules are stable under a variety of storage conditions. Preferred small molecules may be placed in tight association with macromolecules to form molecules that are biologically active and that have improved pharmaceutical properties. Improved pharmaceutical properties include changes in circulation time, distribution, metabolism, modification, excretion, secretion, elimination, and stability that are favorable to the desired biological activity. Improved pharmaceutical properties include changes in the toxicological and efficacy characteristics of the chemical entity.

[00120] In general, a polypeptide mimetic ("peptidomimetic") is a molecule that mimics the biological activity of a polypeptide, but that is not peptidic in chemical nature. While, in certain embodiments, a peptidomimetic is a molecule that contains no peptide bonds (that is, amide bonds between amino acids), the term

peptidomimetic may include molecules that are not completely peptidic in character, such as pseudo-peptides, semi-peptides, and peptoids.

[00121] As used herein, the term "biologic" means products derived from living sources as opposed to a chemical process. Non-limiting examples of a "biologic" include proteins, conditioned media, and partially purified products from tissues.

[00122] The terms "peptide," "polypeptide," and "protein" are used interchangeably herein. In the present invention, these terms mean a linked sequence of amino acids, which may be natural, synthetic, or a modification or combination of natural and synthetic. The term includes antibodies, antibody mimetics, domain antibodies, lipocalins, and targeted proteases. The term also includes vaccines containing a peptide or peptide fragment intended to raise antibodies against the peptide or peptide fragment.

[00123] "Antibody" as used herein includes an antibody of classes IgG, IgM, IgA, IgD, or IgE, or fragments or derivatives thereof, including Fab, F(ab')2, Fd, and single chain antibodies, diabodies, bispecific antibodies, and bifunctional antibodies. The antibody may be a monoclonal antibody, polyclonal antibody, affinity purified antibody, or mixtures thereof, which exhibits sufficient binding specificity to a desired epitope or a sequence derived therefrom. The antibody may also be a chimeric antibody. The antibody may be derivatized by the attachment of one or more chemical, peptide, or polypeptide moieties known in the art. The antibody may be conjugated with a chemical moiety. The antibody may be a human or humanized antibody. These and other antibodies are disclosed in U.S. Published Patent Application No. 20070065447.

[00124] Other antibody-like molecules are also within the scope of the present invention. Such antibody-like molecules include, e.g., receptor traps (such as

entanercept), antibody mimetics (such as adnectins, fibronectin based "addressable" therapeutic binding molecules from, *e.g.*, Compound Therapeutics, Inc.), domain antibodies (the smallest functional fragment of a naturally occurring single-domain antibody (such as, e.g., nanobodies; see, e.g., Cortez-Retamozo et al., Cancer Res. 2004 Apr 15;64(8):2853-7)).

[00125] Suitable antibody mimetics generally can be used as surrogates for the antibodies and antibody fragments described herein. Such antibody mimetics may be associated with advantageous properties (e.g., they may be water soluble, resistant to proteolysis, and/or be nonimmunogenic). For example, peptides comprising a synthetic beta-loop structure that mimics the second complementarity-determining region (CDR) of monoclonal antibodies have been proposed and generated. See, e.g., Saragovi et al., Science. Aug. 16, 1991;253(5021):792-5. Peptide antibody mimetics also have been generated by use of peptide mapping to determine “active” antigen recognition residues, molecular modeling, and a molecular dynamics trajectory analysis, so as to design a peptide mimic containing antigen contact residues from multiple CDRs. See, e.g., Cassett et al., Biochem Biophys Res Commun. Jul. 18, 2003;307(1):198-205. Additional discussion of related principles, methods, etc., that may be applicable in the context of this invention are provided in, e.g., Fassina, Immunomethods. October 1994;5(2):121-9.

[00126] As used herein, “peptide” includes targeted proteases, which are capable of, *e.g.*, substrate-targeted inhibition of post-translational modification such as disclosed in, e.g., U.S. Patent Application Publication No. 20060275823.

[00127] “Antisense” molecules as used herein include antisense or sense oligonucleotides comprising a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target mRNA (sense) or DNA (antisense) sequences.

The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen, Cancer Res. 48:2659, (1988) and van der Krol et al., BioTechniques 6:958, (1988).

[00128] Antisense molecules can be modified or unmodified RNA, DNA, or mixed polymer oligonucleotides. These molecules function by specifically binding to matching sequences resulting in inhibition of peptide synthesis (Wu-Pong, November 1994, BioPharm, 20-33) either by steric blocking or by activating an RNase H enzyme. Antisense molecules can also alter protein synthesis by interfering with RNA processing or transport from the nucleus into the cytoplasm (Mukhopadhyay & Roth, 1996, Crit. Rev. in Oncogenesis 7, 151-190). In addition, binding of single stranded DNA to RNA can result in nuclease-mediated degradation of the heteroduplex (Wu-Pong, supra). Backbone modified DNA chemistry, which have thus far been shown to act as substrates for RNase H are phosphorothioates, phosphorodithioates, borontrifluoridates, and 2'-arabino and 2'-fluoro arabino-containing oligonucleotides.

[00129] Antisense molecules may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described, e.g., in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell. Alternatively, a sense or an antisense oligonucleotide may be introduced into a cell

containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described, e.g., in WO 90/10448.

[00130] The term small interfering RNA ("siRNA") refers to small inhibitory RNA duplexes that induce the RNA interference (RNAi) pathway. (Elbashir, S. M. et al. Nature 411:494-498 (2001); Caplen, N. J. et al. Proc. Natl. Acad. Sci. USA 98:9742-9747 (2001); Harborth, J. et al. J Cell Sci. 114:4557-4565 (2001).) These molecules can vary in length (generally 18-30 base pairs) and contain varying degrees of complementarity to their target mRNA in the antisense strand. Some, but not all, siRNA have unpaired overhanging bases on the 5' or 3' end of the sense strand and/or the antisense strand. The term "siRNA" includes duplexes of two separate strands, as well as single strands that can form hairpin structures comprising a duplex region. As used herein, siRNA molecules are not limited to RNA molecules but further encompass chemically modified nucleotides and non-nucleotides. siRNA gene-targeting may be carried out by transient siRNA transfer into cells (achieved by such classic methods as liposome-mediated transfection, electroporation, or microinjection).

[00131] In an additional aspect of the present invention, the number of stem cells and/or CAR T-cells is increased by a factor of at least 2-fold. Preferably, the number of stem cells and/or CAR T-cells is increased by a factor of at least 2.5 fold, at least 3 fold, at least 3.5 fold, at least 4-fold, such as at least 5-fold, including at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold, or more. Surprisingly and unexpectedly such levels of stem cell and/or CAR T-cell expansion are achieved using the methods of the present invention.

[00132] As noted above, the methods of the present invention may be used to expand any population of stem cells. Preferably, the stem cells that may be

expanded according to the methods of the present invention may selected from hematopoietic stem cells (HSCs), hematopoietic stem and progenitor cells (HSPCs), endothelial progenitor cells (EPCs), mesenchymal stem cells (MSCs), cardiac stem cells (CSCs), neuronal stem cells (NSCs), and combinations thereof. According to one aspect, the stem cells are HSCs. According to yet another aspect, the stem cells are MSCs.

[00133] The methods of the present invention may also be capable of expanding stem cells such that the expanded cells have at least a 5-fold increase in total colony-forming units (CFU), such as an 8-fold, 10-fold, and even 15-fold or more increase. Further, the methods may be capable of providing an increase in CFU-granulocyte erythrocyte monocyte megakaryocyte (GEMM) colonies of at least 3.8-fold, such as at least 4-fold, 5-fold, and even at least 8-fold or more.

[00134] Another embodiment of the invention is a method for *ex vivo* expansion of a substantially undifferentiated stem cell population. This method comprises modulating a N^6-methyladenosine mRNA modification pathway in the undifferentiated stem cell population to expand the number of undifferentiated stem cells without significant differentiation of the stem cell population.

[00135] In this embodiment, a stem cell population is "substantially undifferentiated" if a sufficient number of cells in that population retain the ability to self-renew and can give rise to various differentiated cell types when transplanted into a recipient, for example, in the case of an HSC population, repopulating the HSC lineage when transplanted (or in the case of an MSC population, repopulating the MSC lineage when transplanted). As used herein, "without significant differentiation" means the expanded stem cell population has a sufficient number of cells that maintain a multi-lineage differentiation potential so that the full scope of a target stem

lineage may be regenerated upon transplantation of the expanded stem cell population into a recipient. Thus, e.g., in the case of an HSC population, the expanded HSC population, when transplanted into a recipient, is capable of regenerating the entire hematopoietic cell lineage. In the case of a MSC population, the expanded MSC population, when transplanted into a recipient, is capable of regenerating the entire mesenchymal cell lineage.

[00136] Another embodiment is a method for ex vivo expansion of a chimeric antigen receptor (CAR) T-cell population. This method comprises modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the CAR T-cell population to expand the number of CAR T-cells.

[00137] A further embodiment of the invention is a method for *ex vivo* expansion of an hematopoietic stem cell (HSC) population obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow. This method comprises modulating a N^6-methyladenosine mRNA modification pathway in the HSC population to expand the HSC population to a sufficient quantity while maintaining a multilineage differentiation potential in the HSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

[00138] A further embodiment of the invention is a method for *ex vivo* expansion of a mesenchymal stem cell (MSC) population obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow. This method comprises modulating a N^6-methyladenosine mRNA modification pathway in the MSC population to expand the MSC population to a sufficient quantity while maintaining a multilineage differentiation potential in the

MSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

[00139] A further embodiment of the invention is a method for ex vivo expansion of a chimeric antigen receptor (CAR) T-cell population prepared by modifying T-cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow. The method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the CAR T-cell population to expand the CAR T-cell population to a sufficient quantity which is sufficient for subsequent transplantation into a subject in need thereof.

[00140] As used herein, "obtained" from a tissue means any conventional method of harvesting or partitioning tissue from a donor. As noted previously, the tissue may be any tissue that contains a stem cell such as an HSC and/or MSC, and/or a T-cell that is capable of being modified with chimeric antigen receptors. Thus, for example, the tissue may be obtained from a blood sample, such as a peripheral or cord blood sample, or harvested from bone marrow. Methods for obtaining such samples are well known to the artisan. In the present invention, the samples may be fresh, i.e., obtained from the donor without freezing. Moreover, the samples may be further manipulated to remove extraneous or unwanted components prior to expansion. The samples may also be obtained from a preserved stock. For example, in the case of peripheral or cord blood, the samples may be withdrawn from a cryogenically or otherwise preserved bank of such blood. Such samples may be obtained from any suitable donor. Preferably, the donor is a mammal, for example, a primate, such as a human. Furthermore, the sample may be obtained from an autologous or allogeneic donor or source. Preferably, the sample is obtained from an autologous source.

[00141] In this method, "maintaining a multilineage differentiation potential" means that the expanded HSC and/or MSC population has the ability, when transplanted into a subject in need of such a transplant, to regenerate all the types of progenitor cells e.g., CMP, GMP, MEP, and CLP, and ultimately all the types of blood cells including, *e.g.*, red blood cells, B lymphocytes, T lymphocytes, natural killer cells, neutrophils, basophils, eosinophils, monocytes, macrophages, and platelets in the hematopoietic system.

[00142] In the present invention, that quantity of expanded HSCs and/or MSCs and/or CAR T-cells, which is "sufficient for subsequent transplantation" generally corresponds to that number of HSCs and/or MSCs and/or CAR T-cells, which would result in greater than about 1% engraftment after transplantation. This is one accepted measure of a successful transplant. In the present invention, any conventional method may be used to determine the % engraftment, including the one set forth in the Examples. Such a measure may be carried out with or without competitor cells, typically and preferably, without competitor cells. (Zhang, C.C., *et al.*, *Nat Med*, 12(2): 240-5, 2006. Zhang, C.C. and H.F. Lodish, *Blood*, 105(11): 4314-20, 2005).

[00143] In the above described *ex vivo* expansion methods, modulating the N^6-methyladenosine mRNA modification pathway may be achieved as previously set forth. Modulating the N^6-methyladenosine mRNA modification pathway may include introducing a mutation into the stem cells and/or CAR T-cells that results in modulation of a molecule in the m^6A mRNA modification pathway, or contacting the stem cells and/or CAR T-cells with a modulator of a molecule in the m^6A mRNA modification pathway selected from the group consisting of a small molecule, a

biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

[00144] In one aspect of the *ex vivo* expansion methods, the modulation of the m^6A mRNA modification pathway involves modulation of a molecule selected from the group consisting of m^6A mRNA modification readers, m^6A mRNA modification writers, m^6A mRNA modification erasers, and combinations thereof. Non-limiting examples of m^6A modification writers include methyltransferases that are capable of post-transcriptionally installing the m^6A modification in messenger RNA, and can include any selected from the group consisting of METTL3, METTL14, WTAP, KIAA1429 and combinations thereof. Non-limiting examples of m^6A modification erasers include demethylases that are capable of reversing the methylation, and can include any selected from the group consisting of FTI, ALKBH5 and combinations thereof. M^6A modification readers include proteins that are capable of selectively binding m^6A-methylated mRNA to exert regulatory functions through selective recognition of methylated mRNA. Suitable m^6A modification readers can include any selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, eIF3 and combinations thereof. According to one aspect, the m^6A modification readers comprise proteins of the YTH domain family of proteins, which includes Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2 and combinations thereof. (*see, e.g.,* Wang et al. *Nature*, 505(7481):117-120, 2014; Frayling et al. *Science*, 316: 889-894, 2007; Zheng et al. *Mol. Cell.*, 49: 18-29, 2012; Cao et al. *Open Biol.*, 6(4): 160003, 2016; Maity et al. *The FEBS Journal*, 283(9): 1607-1630, 2016).

[00145] In one aspect of the *ex vivo* methods, modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells and/or

CAR-T cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway. For example, the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, a m^6A mRNA eraser, and combinations thereof. In one aspect, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader, such as a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, HNRNPC, HNRNPA2B1, eIF3, and combinations thereof. In a preferred aspect, the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2. In yet another aspect, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser, such as a m^6A mRNA modification eraser selected from the group consisting of FTO, ALKBH5 and combinations thereof. In yet another aspect, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer, such as a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP, KIAA1429 and combinations thereof.

[00146] In one aspect of the *ex vivo* expansion methods, the mutation can be introduced by any of the methods previously disclosed herein. For example, the mutation can be introduced by exposing the stem cells and/or CAR T-cells to a Mx1-Cre targeting system (*see, e.g.,* Kuhn et al. *Science*, 269(5229): 1427-1429, 1995) that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway. In yet another aspect, a mutation is introduced that incorporates short hairpin RNA (shRNA) into the stem cells and/or CAR T-cells to reduce expression of a gene that expresses a molecule in the m^6A

mRNA modification pathway. For example, the shRNA may be introduced by exposing the stem cells and/or CAR-T cells to a vector to deliver shRNA, which may be a viral vector such as lentivirus (*see, e.g.,* Chira et al. *Oncotarget*, 6(31): 30675-30703, 2015). The shRNA may be capable of triggering gene silencing to regulate gene expression (*see, e.g.,* Paddison et al. *Genes Dev.*, 16(8): 948-958, 2002).

[00147] In these *ex vivo* expansion methods, according to one aspect, modulating of the m^6A mRNA modification pathway comprises down-regulating and/or inhibiting a member of the m^6A mRNA modification pathway, such as down-regulating and/or inhibiting a m^6A mRNA modification reader. As used herein, "down-regulating" means inhibiting or reducing the amount of or inhibiting or decreasing the activity of a member of the m^6A mRNA modification pathway. Such down-regulation may be accomplished using, e.g. antisense RNA, siRNA, antibodies, or small molecules. As another example, the m^6A mRNA modification reader may be down-regulated by contacting the stem cells and/or CAR T-cells with an inhibitor of an m^6A mRNA reader, to inhibit binding and/or recognizing of the m^6A modified mRNA by the m^6A mRNA reader. In one aspect, the m^6A mRNA modification reader that is down-regulated is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, eIF3 and combinations thereof. In a preferred aspect, the m^6A mRNA modification reader that is down-regulated is Ythdf2. The RNA decay role of Ythdf2 has been previously elucidated (*see, e.g.,* Wang et al. *Nature* 505(7481): 117-120, 2014). Inhibitors of the m^6A mRNA modification reader may be any selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484

(MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e (*see, e.g.* Helwak et al. *Cell*, 153(3): 654-655, 2013; Whisnant et al., *MBio* 4(2), 2013:e000193); (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p,

hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p (*see, e.g.,* Hafner et al. *Cell*, 141(1): 129-141, 2010; Helwak et al. *Cell*, 153(3): 654-655, 2013); (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-

519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262 (*see, e.g.* Helwak et al. *Cell*, 153(3): 654-655, 2013; Selbach et al. Nature, 455(7209): 58-63, 2008; Yang et al. *J Biol Chem.*, 292(9): 3614-3623, 2017); (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b,

hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296

(*see, e.g.,* Helwak et al. *Cell,* 153(3): 654-656, 2013; Selbach et al. *Nature*, 455 (7209):58-63, 2008; Baek et al, *Nature*, 455(7209):64-71, 2008; Leivonen et al. *Mol Cell Proteomics*, 10(7), 2011: M110.005322): (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t, hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262 (*see, e.g.* Helwak et al. *Cell,* 153(3): 654-655, 2013; Hafner et al. Cell, 141(1): 129-141, 2010; Kishore et al, Nat Methods, 8(7):559-64, 2011;

Memczak et al. *Nature*, 495(7441):333-8, 2013; Selbach et al. *Nature*, 455(7209):58-63, 2008; Chi et al. Nature. 460(7254):479-86, 2009).

[00148] In these *ex vivo* expansion methods, it is preferred that the stem cell is selected from HSCs, hematopoietic stem and progenitor cells (HSPCs), endothelial progenitor cells, (EPCs), mesenchymal stem cells (MSCs), cardiac stem cells (CSCs), neuronal stem cells (NSCs), and combinations thereof. According to certain aspects, the stem cell is an HSC. According to other aspects, the stem cell is a MSC. The *ex vivo* expansion methods can also use a population of cells comprising CAR T-cells. In these methods, the HSC and/or MSC is obtained from a mammalian, e.g., primate or human, tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, although any HSC and/or MSC-containing tissue may be used.

[00149] In another aspect of the method for *ex vivo* expansion of an hematopoietic stem cell (HSC) population, the expansion of the number of stem cells is by at least 2-fold, such as e.g., by at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, and including at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, or at least 20-fold or more.

[00150] In another aspect of the method for *ex vivo* expansion of a mesenchymal stem cell (MSC) population, the expansion of the number of stem cells is by at least 2-fold, such as e.g., by at least 2.5-fold, at least 3-fold, at least 3.5 fold, at least 4-fold, and including at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, or at least 20-fold or more.

[00151] In another aspect of the method for *ex vivo* expansion of CAR T-cell population, the expansion of the number of CAR T-cells is by at least 2-fold, such as e.g., by at least 2.5-fold, at least 3-fold, at least 3.5 fold, at least 4-fold, and including

at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, or at least 20-fold or more.

[00152] Yet another embodiment of the present invention is an expanded, substantially undifferentiated stem cell population made by a method of the present invention, such as, e.g., the method for *ex vivo* expansion of a substantially undifferentiated stem cell population or the method for *ex vivo* expansion of an hematopoietic stem cell (HSC) population.

[00153] Yet another embodiment of the present invention is an expanded, substantially undifferentiated stem cell population made by a method of the present invention, such as, e.g., the method for *ex vivo* expansion of a substantially undifferentiated stem cell population or the method for *ex vivo* expansion of an mesenchymal stem cell (MSC) population.

[00154] Yet another embodiment of the present invention is an expanded, CAR T-cell population made by a method of the present invention, such as, e.g., the method for *ex vivo* expansion of a CAR T-cell population.

[00155] An additional embodiment of the present invention is a method for *ex vivo* expansion of hematopoietic stem cells (HSCs) by at least 2-fold, wherein the expanded HSCs, are competent to reconstitute an HSC lineage upon transplantation into a mammalian subject in need thereof. This method comprises introducing a mutation into the stem cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of HSCs in a suitable culture medium.

[00156] An additional embodiment of the present invention is a method for *ex vivo* expansion of mesenchymal stem cells (MSCs) by at least 2-fold, wherein the

expanded MSCs, are competent to reconstitute a MSC lineage upon transplantation into a mammalian subject in need thereof. This method comprises introducing a mutation into the stem cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of HSCs in a suitable culture medium.

[00157] An additional embodiment of the present invention is a method for *ex vivo* expansion of chimeric antigen receptor (CAR) T-cells by at least 2-fold, wherein the expanded CAR T-cells are competent to treat a cancer and/or blood disorder upon transplantation into a mammalian subject in need thereof. This method comprises introducing a mutation into the CAR T-cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of CAR T-cells in a suitable culture medium.

[00158] In this aspect of the invention, "competent to reconstitute an HSC lineage" means that the expanded HSCs, when transplanted into a suitable mammalian subject, result in greater than 1% engraftment in the recipient, which engrafted cells are able to differentiate into the cell lineages necessary to have a normal functioning hematopoietic system. In this aspect of the invention, "competent to reconstitute a MSC lineage" means that the expanded MSCs, when transplanted into a suitable mammalian subject, result in greater than 1% engraftment in the recipient, which engrafted cells are able to differentiate into the cell lineages necessary to have a normal functioning hematopoietic system. In this aspect of the invention "competent to treat a cancer and/or blood disorder" means that the expanded CAR T-cells, when transplanted into a suitable mammalian subject, are capable of providing treatment of a cancer and/or blood disorder from which the mammalian subject is suffering, such as for example at least one of leukemia and

lymphoma. In this method, a "suitable culture medium", "fluid media" and "media" which are used interchangeably herein, mean physiologically balanced salt solutions that can maintain a stem cell population and/or CAR T-cell population for a required period of time, which solution may optionally be supplemented with suitable m^6A mRNA modification pathway modulators of the present invention. Such base culture media are well known in the arts. A non-limiting example of a suitable base culture medium for HSCs is StemSpan Media (Stem Cell Technologies; Cat. No. 09600), which is supplemented with 10ug/ml Heparin, 5X Penicillin/Streptomycin, 10 ng/ml recombinant mouse (rm) Stem Cell Factor, and 20 ng/ml rm-Thrombopoietin.

[00159] In one aspect of the invention, the *ex vivo* expansion of HSCs and/or MSCs and/or CAR T-cells by at least 2-fold can be performed by any of the methods that have been described herein. For example, the method may involve introducing a mutation that deletes, replaces or reduces expression of a gene expressing a m^6A mRNA modification reader, such as Ythdf2. Further, the mutation may be introduced by any of the methods described herein, such as by exposing the stem cells and/or CAR T-cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader. The mutation may also be introduced by incorporating shRNA into the stem cells and/or CAR-T cells to reduce expression of a gene that expresses a m^6A mRNA modification reader. Other methods of introducing a mutation, and mutations that target other m^6A mRNA modification readers that are described herein may also be provided.

[00160] In one aspect of this embodiment, the HSCs and/or MSCs and/or CAR T-cells are obtained from a mammalian tissue, preferably primate or human tissue, which is selected from cord blood, peripheral blood, and bone marrow. In this

embodiment, the number of HSCs and/or MSCs and/or CAR T-cells is expanded by a factor of at least 2-fold, such as at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, and including at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more.

[00161] Yet another embodiment of the present invention is a kit for expanding an hematopoietic stem cell (HSC) population, mesenchymal stem cell (MSC) population, and/or CAR T-cell population for subsequent transplantation into a subject in need thereof. The kit comprises a system for introducing a mutation into the HSC, MSC and/or CAR T-cell population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof. Preferably, in the kit, the system for introducing a mutation into the HSC, MSC and/or CAR-T cell population includes one or more reagents capable of introducing a mutation into the HSC, MSC and/or CAR-T cell population that results in deletion, replacement or reduced expression of a gene expressing Ythdf2. For example, the kit can include a system for introducing a mutation into the HSC, MSC and/or CAR-T cell population that comprises a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader. The kit can also include a system for introducing a mutation into the HSC, MSC and/or CAR T-cell population that comprises reagents for delivering a lentivirus that incorporates shRNA into the HSC, MSC and/or CAR T-cell population to reduce expression of a gene that expresses a m^6A mRNA modification reader. The kit may further comprise other systems/methods set forth herein for introducing the mutation to modulate a m^6A mRNA modification pathway, such as by deleting, replacing, or reducing expression of a gene expressing a m^6A mRNA modification reader, including Ythdf2. The kit

and the components therein may be packaged in any suitable manner for distribution and/or storage.

[00162] In yet another embodiment, a kit for expanding an hematopoietic stem cell population (HSC) population and/or mesenchymal stem cell (MSC) population and/or CAR-T cell population for subsequent transplantation into a subject in need thereof is provided. The kit comprises an inhibitor of a m^6A mRNA modification reader, and instructions for use thereof, where the inhibitor may be any of the inhibitors disclosed herein, such as, e.g., an inhibitor of Ythdf2.

[00163] In one aspect of this embodiment, the kits may be able to provide an expansion of the number of stem cells and/or CAR T-cells by a factor selected from the group consisting of at least 2-fold, at least 2.5 fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more.

[00164] A further embodiment of the present invention is a method for administering an hematopoietic stem cell (HSC) to a subject in need thereof. The method comprises (a) introducing, into a sample containing an HSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the HSCs to the subject. In this embodiment, the method of introducing the mutation, and the mutation targeted at the m^6A mRNA modification reader, are as previously disclosed, such as, for example, a mutation that results in deletion of a gene expressing Ythdf2, or a mutation that results in incorporation of shRNA into the HSC population that reduces expression of a gene expressing Ythdf2. Furthermore, the

HSCs may be obtained from any appropriate tissue such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00165] A further embodiment of the present invention is a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof. The method comprises (a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the MSCs to the subject. In this embodiment, the method of introducing the mutation, and the mutation targeted at the m^6A mRNA modification reader, are as previously disclosed, such as, for example, a mutation that results in deletion of a gene expressing Ythdf2, or a mutation that results in incorporation of shRNA into the MSC population that reduces expression of a gene expressing Ythdf2. Furthermore, the MSCs may be obtained from any appropriate tissue such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00166] A further embodiment of the present invention is a method for administering a chimeric antigen receptor (CAR) T-cell to a subject in need thereof. The method comprises (a) introducing, into a sample containing a CAR T-cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; and (c)

administering the CAR T-cells to the subject. In this embodiment, the method of introducing the mutation, and the mutation targeted at the m^6A mRNA modification reader, are as previously disclosed, such as, for example, a mutation that results in deletion of a gene expressing Ythdf2, or a mutation that results in incorporation of shRNA into the CAR T-cell population that reduces expression of a gene expressing Ythdf2. Furthermore, the CAR T-cells may be obtained from any appropriate tissue such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00167] A further embodiment of the present invention is a method for administering an hematopoietic stem cell (HSC) to a subject in need thereof. The method comprises: (a) culturing, in a suitable culture media, a sample containing an HSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the HSCs to the subject. In this method, the inhibitor is as previously disclosed, such as, e.g., an inhibitor of Ythdf2. Furthermore, the HSCs may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00168] A further embodiment of the present invention is a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof. The method comprises: (a) culturing, in a suitable culture media, a sample containing an MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a

number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the MSCs to the subject. In this method, the inhibitor is as previously disclosed, such as, e.g., an inhibitor of Ythdf2. Furthermore, the MSCs may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00169] A further embodiment of the present invention is a method for administering a chimeric antigen receptor (CAR) T-cell to a subject in need thereof. The method comprises: (a) culturing, in a suitable culture media, a sample containing an CAR T-cell population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the CAR T-cells to the subject. In this method, the inhibitor is as previously disclosed, such as, e.g., an inhibitor of Ythdf2. Furthermore, the CAR T-cells may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00170] An additional embodiment of the present invention is a method for reconstituting bone marrow in a subject in need thereof. The method comprises (a) introducing, into a sample containing an HSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient

to transplant into the subject; and (c) administering the HSCs to the subject. In this embodiment, the method of introducing the mutation, and the mutation targeted at the m^6A mRNA modification reader, are as previously disclosed, such as, for example, a mutation that results in deletion of a gene expressing Ythdf2, or a mutation that results in incorporation of shRNA into the HSC population that reduces expression of a gene expressing Ythdf2. Furthermore, the HSCs may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00171] An additional embodiment of the present invention is a method for reconstituting bone marrow in a subject in need thereof. The method comprises (a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; and (c) administering the MSCs to the subject. In this embodiment, the method of introducing the mutation, and the mutation targeted at the m^6A mRNA modification reader, are as previously disclosed, such as, for example, a mutation that results in deletion of a gene expressing Ythdf2, or a mutation that results in incorporation of shRNA into the MSC population that reduces expression of a gene expressing Ythdf2. Furthermore, the MSCs may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00172] An additional embodiment of the present invention is a method for treating cancer and/or a blood disorder in a subject in need thereof. The method comprises (a) introducing, into a sample containing a CAR T-cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader; (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; and (c) administering the CAR T-cells to the subject. In this embodiment, the method of introducing the mutation, and the mutation targeted at the m^6A mRNA modification reader, are as previously disclosed, such as, for example, a mutation that results in deletion of a gene expressing Ythdf2, or a mutation that results in incorporation of shRNA into the CAR T-cell population that reduces expression of a gene expressing Ythdf2. Furthermore, the CAR T-cells may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00173] In yet another embodiment, there is provided a method for reconstituting bone marrow in a subject in need thereof. This method comprises (a) culturing, in a suitable culture media, a sample containing an HSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the HSCs to the subject. In this method, the inhibitor is as previously disclosed, such as an inhibitor of Ythdf2. Furthermore, the HSCs may be obtained from any appropriate tissue, such as, e.g.,

a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00174] In yet another embodiment, there is provided another method for reconstituting bone marrow in a subject in need thereof. This method comprises (a) culturing, in a suitable culture media, a sample containing an MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the MSCs to the subject. In this method, the inhibitor is as previously disclosed, such as an inhibitor of Ythdf2. Furthermore, the MSCs may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00175] In these methods, "reconstituting bone marrow" means restoration of all or a portion of the bone marrow in a subject suffering from a disease in which normal bone marrow function has been compromised. Non-limiting examples of such diseases include blood disorders such as aplastic anemia, myelodysplastic syndromes (MDS), paroxysmal nocturnal hemoglobinuria (PNH), and blood cancers, such as leukemia. Thus, as used herein, "reconstituted" means that the transplanted HSCs and/or MSCs are able to successfully engraft in the host and differentiate into all the cell lineages typically found in or derived from bone marrow. Aspects of the methods herein may involve transplantation of HSCs and/or MSCs obtained from tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, to the subject, for the treatment of blood disorders such as leukemia and lymphoma.

[00176] In yet another embodiment, there is provided another method for treating cancer and/or a blood disorder in a subject in need thereof. This method comprises (a) culturing, in a suitable culture media, a sample containing a chimeric antigen receptor (CAR) T-cell population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; (b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and (c) administering the CAR T-cells to the subject. In this method, the inhibitor is as previously disclosed, such as an inhibitor of Ythdf2. Furthermore, the T-cells that are modified to prepare the CAR T-cells may be obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow, and the subject may be a mammal, such as a human.

[00177] In these methods, "treating cancer and/or a blood disorder in a subject" means eradicating cancer cells, alleviating symptoms, or otherwise reducing a disease state in a subject suffering from the cancer and/or blood disorder. Non-limiting examples of cancers and/or blood disorders include blood disorders such as aplastic anemia, myelodysplastic syndromes (MDS), paroxysmal nocturnal hemoglobinuria (PNH), and blood cancers, such as leukemia and lymphoma.

[00178] In these methods, "a period of time sufficient to expand the number of HSCs" means the minimum amount of time to expand the HSCs in culture to a point where there is a sufficient number of HSCs for one or more transplantations, and "a period of time sufficient to expand the number of MSCs" means the minimum amount of time to expand the MSCs in culture to a point where there is a sufficient number of MSCs for one or more transplantations. Similarly, "a period of time sufficient to expand the number of CAR T-cells" means the minimum amount of time

to expand the CAR T-cells in culture to a point where there is a sufficient number of CAR T-cells for one or more transplantations. Typically, such a period of time may be at least about 10 days in culture. Under certain circumstances, it may be desirable to expand the stem cell and/or CAR T-cell, e.g., HSC and/or MSC, population beyond what is required for a single transplantation. For example, it may be desirable to expand the stem cell and/or CAR T-cell, e.g., HSC and/or MSC, population to a number sufficient for multiple transplantations, such as e.g., from about 2 to about 100 transplantations. In these circumstances, the excess cells may be preserved for later use by any conventional method, such as e.g., by cryo-preservation.

[00179] As indicated previously, "a number sufficient to transplant" means the minimum number of stem cells, e.g., HSCs and/or MSCs and/or CAR T-cells, necessary to achieve greater than 1% engraftment in a recipient. "Administering the HSCs to the subject" means conventional methods for delivering HSCs to the subject, including but not limited to, delivering the HSCs surgically and/or intravenously. "Administering the MSCs to the subject" means conventional methods for delivering MSCs to the subject, including but not limited to, delivering the MSCs surgically and/or intravenously. "Administering the CAR T-cells to the subject" means conventional methods for delivering CAR T-cells to the subject, including but not limited to, delivering the MSCs surgically and/or intravenously. In these embodiments, the tissue the HSCs and/or MSCs and/or T-cells are obtained from, and the m^6A mRNA modification reader inhibitors are as previously disclosed.

[00180] An additional embodiment of the present invention is a method for expanding a population of hematopoietic stem cells (HSCs). This method comprises culturing a population of HSCs under conditions sufficient to result in an expansion of

the HSC population by at least 2-fold, wherein the expanded population of HSCs is suitable for transplantation into a mammal in need thereof. In this embodiment the "conditions sufficient to result in an expansion of the HSC population" are those conditions that can result in expansion of HSCs in culture by, e.g., at least 2-fold, such as, e.g., by at least 2.5-fold, at least 3-fold, at least 3.5 fold, at least 4-fold, at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more. "Suitable for transplantation into a mammal" means that the number and quality of HSCs is sufficient to support greater than 1% engraftment in a mammalian recipient, such as, e.g., a primate recipient, including an human recipient, in need thereof.

[00181] An additional embodiment of the present invention is a method for expanding a population of mesenchymal stem cells (MSCs). This method comprises culturing a population of MSCs under conditions sufficient to result in an expansion of the MSC population by at least 2-fold, wherein the expanded population of MSCs is suitable for transplantation into a mammal in need thereof. In this embodiment the "conditions sufficient to result in an expansion of the MSC population" are those conditions that can result in expansion of MSCs in culture by, e.g., at least 2-fold, such as, e.g., by at least 2.5-fold, at least 3-fold, at least 3.5 fold, at least 4-fold, at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more. "Suitable for transplantation into a mammal" means that the number and quality of MSCs is sufficient to support greater than 1% engraftment in a mammalian recipient, such as, e.g., a primate recipient, including an human recipient, in need thereof.

[00182] An additional embodiment of the present invention is a method for expanding a population of chimeric antigen receptor (CAR) T-cells. This method comprises culturing a population of CAR T-cells under conditions sufficient to result in an expansion of the CAR T-cell population by at least 2-fold, wherein the

expanded population of CAR T-cells is suitable for transplantation into a mammal in need thereof. In this embodiment the "conditions sufficient to result in an expansion of the CAR T-cell population" are those conditions that can result in expansion of CAR T-cells in culture by, e.g., at least 2-fold, such as, e.g., by at least 2.5-fold, at least 3-fold, at least 3.5 fold, at least 4-fold, at least 5-fold, at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more. "Suitable for transplantation into a mammal" means that the number and quality of CAR T-cells is sufficient to support greater than 1% engraftment in a mammalian recipient, such as, e.g., a primate recipient, including an human recipient, in need thereof.

[00183] Yet another embodiment of the present invention is a method for treating a subject in need of a bone marrow transplant, a peripheral blood transplant, or a cord blood transplant comprising administering to the subject a population of HSCs obtained by a method disclosed herein, particularly the methods for expanding a population of hematopoietic stem cells (HSCs). The subject may be a mammal, such as a human.

[00184] Yet another embodiment of the present invention is a method for treating a subject in need of a bone marrow transplant, a peripheral blood transplant, or a cord blood transplant comprising administering to the subject a population of MSCs obtained by a method disclosed herein, particularly the methods for expanding a population of mesenchymal stem cells (MSCs). The subject may be a mammal, such as a human.

[00185] Yet another embodiment of the present invention is a method for treating a subject suffering from cancer and/or a blood disorder, comprising administering to the subject a population of CAR T-cells obtained by a method

disclosed herein, particularly the methods for expanding a population of CAR T-cells. The subject may be a mammal, such as a human.

[00186] A further embodiment of the present invention is a method for expanding a population of hematopoietic stem cells (HSCs). The method comprises (a) obtaining from a mammal a tissue sample comprising an HSC population; (b) expanding, *in vitro*, the HSC population from the sample, wherein (i) the HSC population expands by at least 2-fold; and (ii) the expanded HSC population has at least a 5-fold increase in total colony forming units. In one aspect of this embodiment, the HSC population expands by at least 4-fold, such as e.g., at least 5-fold, including at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more. In another aspect of this embodiment, the mammal is a primate, including a human. Preferably, the human requires a peripheral blood transplant, a cord blood transplant, or a bone marrow transplant. In a further aspect, the tissue sample is obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

[00187] A further embodiment of the present invention is a method for expanding a population of mesenchylam stem cells (MSCs). The method comprises (a) obtaining from a mammal a tissue sample comprising a MSC population; (b) expanding, *in vitro*, the MSC population from the sample, wherein (i) the MSC population expands by at least 2-fold. In one aspect of this embodiment, the MSC population expands by at least 2.5-fold, such as at least 3-fold, at least 3.5 fold, at least 4-fold, such as e.g., at least 5-fold, including at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more. In another aspect of this embodiment, the mammal is a primate, including a human. Preferably, the human requires a peripheral blood transplant, a cord blood transplant, or a bone marrow transplant. In

a further aspect, the tissue sample is obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

[00188] A further embodiment of the present invention is a method for expanding a population of chimeric antigen receptor (CAR) T-cells. The method comprises (a) obtaining from a mammal a tissue sample comprising a T-cell population; (b) modifying the T-cell population with chimeric antigen receptors to provide CAR T-cell population; (c) expanding, *in vitro*, the CAR T-cell population from the sample, wherein (i) the CAR T-cell population expands by at least 2-fold. In one aspect of this embodiment, the CAR T-cell population expands by at least 2.5-fold, such as at least 3-fold, at least 3.5 fold, at least 4-fold, such as e.g., at least 5-fold, including at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more. In another aspect of this embodiment, the mammal is a primate, including a human. Preferably, the human is suffering from a cancer and/or a blood disorder. In a further aspect, the tissue sample is obtained from any appropriate tissue, such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

[00189] An additional embodiment of the present invention is a method for reconstituting an hematopoietic stem cell lineage in a recipient in need thereof. The method comprises (a) obtaining from a mammal a tissue sample comprising an HSC population; (b) expanding, in vitro, the HSC population from the sample, wherein: (i) the HSC population expands by at least 2-fold, such as for example, by at least 4-fold, including at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more, and (ii) the expanded HSC population has at least at 5-fold increase in total colony forming units; and (c) transplanting the expanded HSC population into a

subject in need thereof, such as a mammal, including a primate or human. In this embodiment, the human recipient requires a peripheral blood transplant, a cord blood transplant or a bone marrow transplant. Thus, in a further aspect, the tissue sample is obtained from any appropriate tissue such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow. The sample may be obtained from an autologous or allogeneic source. Preferably, the sample is obtained from an autologous source.

[00190] An additional embodiment of the present invention is a method for reconstituting a mesenchymal stem cell (MSC) lineage in a recipient in need thereof. The method comprises (a) obtaining from a mammal a tissue sample comprising a MSC population; (b) expanding, in vitro, the MSC population from the sample, wherein: (i) the MSC population expands by at least 2-fold, such as for example, by at least 4-fold, including at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more; and (c) transplanting the expanded MSC population into a subject in need thereof, such as a mammal, including a primate or human. In this embodiment, the human recipient requires a peripheral blood transplant, a cord blood transplant or a bone marrow transplant. Thus, in a further aspect, the tissue sample is obtained from any appropriate tissue such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow. The sample may be obtained from an autologous or allogeneic source. Preferably, the sample is obtained from an autologous source.

[00191] An additional embodiment of the present invention is a method for treating a subject suffering from cancer and/or a blood disorder. The method comprises (a) obtaining from a mammal a tissue sample comprising a T-cell population; (b) modifying the T-cell population with a chimeric antigen receptor

(CAR) to form a CAR T-cell population; (c) expanding, in vitro, the CAR T-cell population from the sample, wherein: (i) the CAR T-cell population expands by at least 2-fold, such as for example, by at least 4-fold, including at least 8-fold, at least 10-fold, at least 15-fold, at least 20-fold or more; and (c) transplanting the expanded CAR-T cell population into a subject in need thereof, such as a mammal, including a primate or human. In this embodiment, the human recipient may be suffering from, e.g., leukemia and/or lymphoma. Thus, in a further aspect, the tissue sample is obtained from any appropriate tissue such as, e.g., a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow. The sample may be obtained from an autologous or allogeneic source. Preferably, the sample is obtained from an autologous source.

[00192] In aspects of the present invention, it is preferred that the expanded HSC population comprises HSCs that have a phenotype selected from the group consisting of $CD34^-$ or $CD34^+/CD38^{-/low}/Thy\text{-}1^+/CD90^+/Kit^{-/lo}/Lin^-/CD133^+VEGFR2^+$, which are markers for the most primitive and long-term undifferentiated human HSCs; $CD150^+/CD48^-/CD244^-$, which is a marker for human HSCs and their progenitors; and/or $CD150^-/CD48^-/CD244^+$ and $CD150^-/CD48^+/CD244^+$, which are markers for non-self-renewing multipotent hematopoietic progenitors, and combinations thereof. (See, e.g., Mimeault, M., et al., Stem Cells: A Revolution in Therapeutics - Recent Advances in Stem Cell Biology and Their Therapeutic Applications in Regenerative Medicine and Cancer Therapies. Clin Pharmacol Ther., 82(3):252-64 (2007)). In aspects of the present invention, it is preferred that the expanded MSC population and/or MSC population subject to expansion, comprises MSCs that have a phenotype selected from the group consisting of N-cadherin+ and CD105+, and combinations thereof. That is, the MSC population of

any of the embodiments described herein can comprise at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs. In one embodiment, the MSC population comprises N-cadherin+ MSCs.

[00193] The exact proportions of HSCs and/or MSCs having these markers in the population is not critical, so long as the expanded HSC and/or MSC population as a whole is sufficient to result in at least 1% engraftment in a recipient.

[00194] In another embodiment, the invention is a method for expanding a hematopoietic stem cell population in a mammal in need of such expansion. This method comprises administering to the mammal a therapeutically effective amount of a modulator of a N^6-methyladenosine (m^6A) mRNA modification pathway, for a period of time sufficient to expand the HSC population by at least 2-fold with HSCs that possess the ability to reconstitute an hematopoietic lineage in the mammal.

[00195] In another embodiment, the invention is a method for expanding a mesenchymal stem cell population in a mammal in need of such expansion. This method comprises administering to the mammal a therapeutically effective amount of a modulator of a N^6-methyladenosine (m^6A) mRNA modification pathway, for a period of time sufficient to expand the MSC population by at least 2-fold with MSCs that possess the ability to reconstitute a mesenchymal lineage in the mammal.

[00196] In another embodiment, the invention is a method for expanding a chimeric antigen receptor (CAR) T-cell population in a mammal in need of such expansion. This method comprises administering to the mammal a therapeutically effective amount of a modulator of a N^6-methyladenosine (m^6A) mRNA modification pathway, for a period of time sufficient to expand the CAR T-cell population by at least 2-fold with CAR T-cells that possess the ability to treat cancer and/or a blood disorder in the mammal.

[00197] In these methods, the modulators may be as previously disclosed herein, and/or modulation may be performed by any method disclosed herein. For example, the modulator may comprise a system for introducing a mutation into the HSC and/or MSC and/or CAR T-cell population that deletes, replaces or reduces expression of a gene expressing a N^6-methyladenosine (m^6A) mRNA modification reader, such as Ythdf2. As yet another example, the modulator may comprise an inhibitor of a N6-methyladenosine (m6A) mRNA modification reader, such as an inhibitor of Ythdf2. The mammal in need of expansion may be a human.

[00198] In another embodiment, the invention includes a method of isolating mesenchymal stem cells (MSCs) from a biological sample, the method comprising contacting the biological sample having a population of MSCs with one or more N-cadherin antibodies. For example, according to certain aspects, the biological sample comprises a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow. Furthermore, in certain embodiments, the method of isolating the MSCs can further comprise one or more steps of expanding the population of MSCs from the biological sample, by modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the population of MSCs, to expand the number of mesenchymal stem cells, such as by any of the methods described herein. In one embodiment, the population of MSCs is expanded after isolating from the biological sample. In another embodiment, the population of MSCs in the biological sample is expanded before isolation of the MSCs from the biological sample. In one embodiment, the MSC population is expanded to a sufficient quantity while maintaining a multilineage differentiation potential in the MSC population, which is sufficient for subsequent transplantation into a subject in need thereof, such that the MSCs isolated by the method can be used for such transplantation. For example,

the isolated MSCs may be transplanted into a human subject. According to yet another embodiment, the MSCs may be further isolated from the biological sample by contacting with CD105 antibodies, either in addition to or as an alternative to the N-cadherin antibodies. In yet a further embodiment, the N-cadherin antibodies may be used to identify the MSCs in the biological sample, by contacting the biological sample with the N-cadherin antibodies and detecting those cells that bind to the N-cadherin antibodies.

[00199] In one embodiment, the method of isolating the MSCs comprises expanding the MSC population, by modulating the m^6A mRNA modification pathway by introducing a mutation into the stem cells that results in modulation of a molecule in the m^6A mRNA modification pathway or contacting the stem cell with a modulator of a molecule in the m^6A mRNA modification pathway selected from the group consisting of a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof, such as by any of the modulation methods described herein. For example, in one embodiment, modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway. In one embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, and a m^6A mRNA eraser. In yet another embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader. In one embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3. In

another embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2. In one embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser. In one embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser selected from the group consisting of FTO and ALKBH5. In another embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer. In one embodiment, the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP and KIAA1429.

[00200] In another embodiment, the method of isolating MSCs comprises expanding the population of MSCS by modulating the m^6A mRNA modification pathway, by exposing the stem cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway. In one embodiment, modulating the m^6A mRNA modification pathway comprises introducing a mutation that incorporates shRNA into the stem cells to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway. For example, in one embodiment, the shRNA is introduced by exposing the stem cells to a lentivirus to deliver the shRNA. According to yet another embodiment, modulating the m^6A mRNA modification pathway comprises down-regulating a m^6A mRNA modification reader. In one embodiment, the m^6A mRNA modification reader is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3. For example, in one embodiment, the m^6A mRNA modification reader comprises Ythdf2.

[00201] In one embodiment, the method of isolating MSCs further comprise expanding the population of MSCs by down-regulating the m^6A mRNA modification reader, by contacting the stem cells with an inhibitor of the m^6A mRNA modification reader that is any of those described herein, such as any of those selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e; (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-

mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p; (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185,

hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262; (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-

3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-

3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296: (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t, hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262.

[00202] According to one embodiment, the invention comprises an isolated population of mesenchymal stem cells made by any of the processes described

herein. For example, the invention in certain embodiments can comprise an expanded, isolated population of mesenchymal stem cells made by any of the expansion and/or isolation processes described herein.

[00203] In one embodiment, a kit for isolating a mesenchymal stem cell (MSC) population for subsequent transplantation into a subject in need thereof is provided. The kit comprises a system for contacting a biological sample comprising MSCs with one or more N-cadherin antibodies, and instructions for use thereof. In one embodiment, the kit further comprises a system for expanding the population of MSCs by introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof. In yet another embodiment, the system for introducing a mutation into the MSC population includes one or more reagents capable of introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing Ythdf2. In yet another embodiment, the system for introducing a mutation into the MSC population comprises a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader. In one embodiment, the system for introducing a mutation into the MSC population comprises reagents for delivering a lentivirus that incorporates shRNA into the MSC population to reduce expression of a gene that expresses a m^6A mRNA modification reader.

[00204] According to another embodiment of the invention, a method for administering a mesenchymal stem cell (MSC) to a subject in need thereof is provided. The method comprises isolating MSCs from a biological sample comprising a population of MSCs, by contacting the biological sample with one or more N-cadherin antibodies, and administering the isolated MSCs to the subject.

Furthermore, in one embodiment, the method further comprises introducing, into the biological sample containing the MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and culturing the biological sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject. In one embodiment, wherein the mutation results in deletion a gene expressing Ythdf2. In one embodiment, the mutation results in incorporation of shRNA into the HSC population that reduces expression of a gene expressing Ythdf2. According to yet another aspect, the MSCs are obtained from a biological sample comprising a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

[00205] According to yet another embodiment, a method for reconstituting bone marrow in a subject in need thereof is provided. The method comprises isolating mesenchymal stem cells (MSCs) from a biological sample comprising a population of MSCs, by contacting the biological sample with one or more N-cadherin antibodies, and administering the isolated MSCs to the subject. Furthermore, according to one aspect, the method further comprises introducing, into the biological sample containing the MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject. In one embodiment, the MSCs are obtained from a biological sample comprising a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

[00206] According to yet another embodiment, a method for treating a subject in need of a transplant, selected from the group consisting of a bone marrow transplant, a peripheral blood transplant and an umbilical cord blood transplant comprising administering to the subject a population of isolated MSCs obtained by any of the methods described herein. According to embodiment, the sample is from an autologous or allogeneic source. According to yet another embodiment, the sample is from an autologous source.

[00207] In the present invention, a "therapeutically effective amount" is an amount sufficient to effect beneficial or desired results. In terms of treatment of a mammal, a "therapeutically effective amount" of a modulator and/or expanded cells is an amount sufficient to treat, manage, palliate, ameliorate, or stabilize a condition, such as a bone marrow disease, in the mammal. A therapeutically effective amount can be administered in one or more doses.

[00208] The therapeutically effective amount is generally determined by a physician on a case-by-case basis and is within the skill of one in the art. Several factors are typically taken into account when determining an appropriate dosage. These factors include age, sex and weight of the subject, the condition being treated, the severity of the condition and the form of the drug being administered.

[00209] Effective dosage forms, modes of administration, and dosage amounts may be determined empirically, and making such determinations is within the skill of the art. It is understood by those skilled in the art that the dosage amount will vary with the route of administration, the rate of excretion, the duration of the treatment, the identity of any other drugs being administered, the age, size, and species of animal, and like factors well known in the arts of medicine and veterinary medicine. In general, a suitable dose of a modulator according to the invention will be that

amount of the modulator, which is the lowest dose effective to produce the desired effect. The effective dose of a modulator maybe administered as two, three, four, five, six or more sub-doses, administered separately at appropriate intervals throughout the day.

[00210] A modulator may be administered in any desired and effective manner: as pharmaceutical compositions for oral ingestion, or for parenteral or other administration in any appropriate manner such as intraperitoneal, subcutaneous, topical, intradermal, inhalation, intrapulmonary, rectal, vaginal, sublingual, intramuscular, intravenous, intraarterial, intrathecal, or intralymphatic. Further, a modulator of the present invention may be administered in conjunction with other treatments. A modulator of the present invention maybe encapsulated or otherwise protected against gastric or other secretions, if desired.

[00211] While it is possible for a modulator of the invention to be administered alone, it is preferable to administer the modulator as a pharmaceutical formulation (composition). Such pharmaceutical formulations typically comprise one or more modulators as an active ingredient in admixture with one or more pharmaceutically-acceptable carriers and, optionally, one or more other compounds, drugs, ingredients and/or materials. Regardless of the route of administration selected, the modulator of the present invention may be formulated into pharmaceutically-acceptable dosage forms by conventional methods known to those of skill in the art. *See*, *e.g.*, Remington's Pharmaceutical Sciences (Mack Publishing Co., Easton, Pa.).

[00212] Pharmaceutically acceptable carriers are well known in the art (*see*, *e.g.*, Remington's Pharmaceutical Sciences (Mack Publishing Co., Easton, Pa.) and The National Formulary (American Pharmaceutical Association, Washington, D.C.))

and include sugars (*e.g.*, lactose, sucrose, mannitol, and sorbitol), starches, cellulose preparations, calcium phosphates (*e.g.*, dicalcium phosphate, tricalcium phosphate and calcium hydrogen phosphate), sodium citrate, water, aqueous solutions (*e.g.*, saline, sodium chloride injection, Ringer's injection, dextrose injection, dextrose and sodium chloride injection, lactated Ringer's injection), alcohols (*e.g.*, ethyl alcohol, propyl alcohol, and benzyl alcohol), polyols (e.g., glycerol, propylene glycol, and polyethylene glycol), organic esters (*e.g.*, ethyl oleate and triglycerides), biodegradable polymers (*e.g.*, polylactide-polyglycolide, poly(orthoesters), and poly(anhydrides)), elastomeric matrices, liposomes, microspheres, oils (*e.g.*, corn, germ, olive, castor, sesame, cottonseed, and groundnut), cocoa butter, waxes (*e.g.*, suppository waxes), paraffins, silicones, talc, silicylate, *etc*. Each pharmaceutically acceptable carrier used in a pharmaceutical composition comprising a modulator of the invention must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the subject. Carriers suitable for a selected dosage form and intended route of administration are well known in the art, and acceptable carriers for a chosen dosage form and method of administration can be determined using ordinary skill in the art.

[00213] Pharmaceutical compositions comprising a modulator of the invention may, optionally, contain additional ingredients and/or materials commonly used in pharmaceutical compositions. These ingredients and materials are well known in the art and include (1) fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and silicic acid; (2) binders, such as carboxymethylcellulose, alginates, gelatin, polyvinyl pyrrolidone, hydroxypropylmethyl cellulose, sucrose and acacia; (3) humectants, such as glycerol; (4) disintegrating agents, such as agar-agar, calcium

carbonate, potato or tapioca starch, alginic acid, certain silicates, sodium starch glycolate, cross-linked sodium carboxymethyl cellulose and sodium carbonate; (5) solution retarding agents, such as paraffin; (6) absorption accelerators, such as quaternary ammonium compounds; (7) wetting agents, such as cetyl alcohol and glycerol monosterate; (8) absorbents, such as kaolin and bentonite clay; (9) lubricants, such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, and sodium lauryl sulfate; (10) suspending agents, such as ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth; (11) buffering agents; (12) excipients, such as lactose, milk sugars, polyethylene glycols, animal and vegetable fats, oils, waxes, paraffins, cocoa butter, starches, tragacanth, cellulose derivatives, polyethylene glycol, silicones, bentonites, silicic acid, talc, salicylate, zinc oxide, aluminum hydroxide, calcium silicates, and polyamide powder; (13) inert diluents, such as water or other solvents; (14) preservatives; (15) surface-active agents; (16) dispersing agents; (17) control-release or absorption-delaying agents, such as hydroxypropylmethyl cellulose, other polymer matrices, biodegradable polymers, liposomes, microspheres, aluminum monosterate, gelatin, and waxes; (18) opacifying agents; (19) adjuvants; (20) wetting agents; (21) emulsifying and suspending agents; (22), solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan; (23) propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane; (24) antioxidants; (25) agents which render the formulation

isotonic with the blood of the intended recipient, such as sugars and sodium chloride; (26) thickening agents; (27) coating materials, such as lecithin; and (28) sweetening, flavoring, coloring, perfuming and preservative agents. Each such ingredient or material must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the subject. Ingredients and materials suitable for a selected dosage form and intended route of administration are well known in the art, and acceptable ingredients and materials for a chosen dosage form and method of administration may be determined using ordinary skill in the art.

[00214] Pharmaceutical compositions suitable for oral administration may be in the form of capsules, cachets, pills, tablets, powders, granules, a solution or a suspension in an aqueous or non-aqueous liquid, an oil-in-water or water-in-oil liquid emulsion, an elixir or syrup, a pastille, a bolus, an electuary or a paste. These formulations may be prepared by methods known in the art, *e.g.*, by means of conventional pan-coating, mixing, granulation or lyophilization processes.

[00215] Solid dosage forms for oral administration (capsules, tablets, pills, dragees, powders, granules and the like) may be prepared by mixing the active ingredient(s) with one or more pharmaceutically-acceptable carriers and, optionally, one or more fillers, extenders, binders, humectants, disintegrating agents, solution retarding agents, absorption accelerators, wetting agents, absorbents, lubricants, and/or coloring agents. Solid compositions of a similar type maybe employed as fillers in soft and hard-filled gelatin capsules using a suitable excipient. A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using a suitable binder, lubricant, inert diluent, preservative, disintegrant, surface-active or dispersing agent. Molded

tablets may be made by molding in a suitable machine. The tablets, and other solid dosage forms, such as dragees, capsules, pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein. They may be sterilized by, for example, filtration through a bacteria-retaining filter. These compositions may also optionally contain opacifying agents and may be of a composition such that they release the active ingredient only, or preferentially, in a certain portion of the gastrointestinal tract, optionally, in a delayed manner. The active ingredient can also be in microencapsulated form.

[00216] Liquid dosage forms for oral administration include pharmaceutically-acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. The liquid dosage forms may contain suitable inert diluents commonly used in the art. Besides inert diluents, the oral compositions may also include adjuvants, such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, coloring, perfuming and preservative agents. Suspensions may contain suspending agents.

[00217] Pharmaceutical compositions for rectal or vaginal administration may be presented as a suppository, which may be prepared by mixing one or more active ingredient(s) with one or more suitable nonirritating carriers which are solid at room temperature, but liquid at body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active compound. Pharmaceutical compositions which are suitable for vaginal administration also include pessaries, tampons, creams, gels, pastes, foams or spray formulations containing such pharmaceutically-acceptable carriers as are known in the art to be appropriate.

[00218] Dosage forms for the topical or transdermal administration include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches, drops and inhalants. The active compound may be mixed under sterile conditions with a suitable pharmaceutically-acceptable carrier. The ointments, pastes, creams and gels may contain excipients. Powders and sprays may contain excipients and propellants.

[00219] Pharmaceutical compositions suitable for parenteral administrations comprise one or more modulator in combination with one or more pharmaceutically-acceptable sterile isotonic aqueous or non-aqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions just prior to use, which may contain suitable antioxidants, buffers, solutes which render the formulation isotonic with the blood of the intended recipient, or suspending or thickening agents. Proper fluidity can be maintained, for example, by the use of coating materials, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants. These compositions may also contain suitable adjuvants, such as wetting agents, emulsifying agents and dispersing agents. It may also be desirable to include isotonic agents. In addition, prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents which delay absorption.

[00220] In some cases, in order to prolong the effect of a drug containing a modulator of the present invention, it is desirable to slow its absorption from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material having poor water solubility.

[00221] The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form.

Alternatively, delayed absorption of a parenterally-administered drug may be accomplished by dissolving or suspending the drug in an oil vehicle. Injectable depot forms may be made by forming microencapsule matrices of the active ingredient in biodegradable polymers. Depending on the ratio of the active ingredient to polymer, and the nature of the particular polymer employed, the rate of active ingredient release can be controlled. Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions which are compatible with body tissue. The injectable materials can be sterilized for example, by filtration through a bacterial-retaining filter.

[00222] The formulations may be presented in unit-dose or multi-dose sealed containers, for example, ampules and vials, and may be stored in a lyophilized condition requiring only the addition of the sterile liquid carrier, for example water for injection, immediately prior to use. Extemporaneous injection solutions and suspensions may be prepared from sterile powders, granules and tablets of the type described above.

[00223] The following examples are provided to further illustrate the methods and compositions of the present invention. These examples are illustrative only and are not intended to limit the scope of the invention in any way.

Examples

[00224] The examples herein examine Ythdf2, a well-recognized m^6A reader promoting targeted mRNA decay (Wang et al. *Blood*, 505: 17-120, 2014), at least partly with the purpose of investigating its role in the context of HSC maintenance. Without being limited to any particular theory, it is believed that manipulation of Ythdf2 might potentially influence the life span of a great number m^6A-marked mRNAs, thus impacting adult HSC self-renewal versus differentiation and facilitating

HSC expansion. As shown in the examples below, Ythdf2 depletion specifically expands mouse and human HSCs without skewing lineage fate. Accordingly, it is believed that *Ythdf2* may play an essential role in regulating HSC self-renewal, and provide a novel approach to enhance hUCB HSCs *ex vivo* expansion, including in clinical applications.

[00225] The exmaples also show functional definition of the drug-resistant rHSC population, and a finding that rHSCs are maintained in the endosteal niche largely by N-cad$^+$ cells during homeostasis and under chemotherapeutic stress. It is further shown that N-cad$^+$ cells in endosteal zone are mesenchymal stem cells and contribute to rHSC maintenance.

EXAMPLE A

[00226] The following protocols were used in the "A" Examples below.

[00227] **Mice.** *Ythdf2* conditional KO mice were generated by Chuan He and Bin Shen group. Mice were housed in the animal facility at Stowers Institute for Medical Research (SIMR) and handled according to Institute and NIH guidelines. All procedures were approved by the IACUC of SIMR.

[00228] **Flow cytometry and HSPC sorting.** Mouse HSPCs, progenitors, and lineage cells were harvested from BM (femur and tibia) and spleen. Red blood cells were lysed using a 0.16 M ammonium chloride solution, and the cells were filtered with 70μm strainers to generate single cell suspensions. For mouse HSC identification, cells were stained with antibodies against Sca-1 (D7), c-Kit (2B8), CD34 (RAM34), Flk2 (A2F10), CD48 (HM48-1), CD150 (TC15-12F12.2), together with lineage cocktail including CD3 (145-2C11), CD4 (RM4-5), CD8 (53-6.7), Mac-1 (M1/70), Gr1 (RB6-8C5), CD45R (B220, RA3-6B2), IgM (Il-41) and Ter119 (TER-119). For progenitors and lineage cells, cells were stained with antibodies as previously described (Qian, P. et al. *Cell Stem Cell*, 18:214-228, 2016,

doi:10.1016/j.stem.2015.11.001). 7-aminoactinomycin D (7-AAD) (A1310, Life technologies) was used to exclude dead cells. Human cord blood samples were acquired from the St. Louis Cord Blood Bank. Mononuclear cells were isolated with Lymphoprep™ (StemCell technologies), followed by isolation of human $CD34^+$ cord blood cells by human CD34 MicroBead Kit UltraPure (Miltenyi Biotec). To quantify human HSPCs, cells were stained with antibodies against CD34 (581), CD38 (HIT2), CD45RA (HI100), CD90 (5E10), CD49f (GoH3), EPCR/CD201 (RCR-401). Cell sorting and analyses were performed on MoFlo (Dako), InFlux Cell Sorter (BD Biosciences), and/or MACSQuant (Miltenyi Biotec). Data analysis was performed using FlowJo software.

[00229] **Homing assay.** *In vivo* homing assays were performed as previously described (He et al. *Methods in Molecular Biology*, 1185: 279-284, 2014). Basically, whole bone marrow (WBM) cells from CD45.2 mice were labelled with 5 μM 5-(and -6)-carboxyfluorescein diacetate succinimidyl ester (CFDA SE) (Molecular Probes) at 37°C for 10 mins, washed three times, and 1×10^6 WBM were transplanted into lethally irradiated *ptprc* mice. After 18 hours, femurs and tibias were flushed, and CFDA SE+ cells were determined.

[00230] **Competitive reconstitution assay.** Competitive reconstitution assays were performed by intravenous transplantation of 2×10^5, 7.5×10^4 or 2.5×10^4 donor-derived WBM cells from *wt* or *Ythdf2* KO mice (CD45.2), together with 2×10^5 rescue cells (CD45.1) into groups of ten lethally irradiated (10 Gy) *ptprc* recipient mice. For secondary transplantation, primary transplant recipients were sacrificed. BM cells were dissected from femur and tibia, and then transplanted mouse-to-mouse at a dosage of 1×10^6 cells into irradiated secondary recipient mice. Baytril water was given to recipient mice three days before irradiation and continued for another two

weeks after irradiation. Primary and secondary CRU frequencies were measured using ELDA software (Hu et al. *Journal of Immunological Methods*, 347: 70-78, 2009), in which successful engraftment was defined as the presence of a distinct $CD45.2^+$ $CD45.1^-$ population ≥5% and ≥1% of total hematopoietic cells in peripheral blood, respectively (Purton et al. *Cell Stem Cell*, 1: 263-270, 2007). Also, the secondary transplantation recipient mice that died before 16 weeks post transplantation were counted for failed engraftment.

[00231] Cell cycle and apoptosis assays. Cell cycle analysis was performed with FITC mouse anti-human Ki67 set (BD Pharmingen) according to the manufacturer's instructions. Briefly, 5×10^6 BM cells were isolated and stained with HSC antibodies as described above. Cells were fixed by 4% paraformaldehyde at 4°C overnight or room temperature (RT) for 1 hour, and then permeabilized with 0.2% triton X-100 on ice for 15 mins. Cells were washed with PBS containing 2% FBS, and then were incubated with Ki-67 antibody at RT for 1 hour in the dark, and SYTOX Red (Invitrogen) at RT for another 5 mins, followed by flow cytometric analysis with InFlux Cell Sorter (BD Biosciences). For apoptosis analysis, Annexin V (Invitrogen) and SYTOX Red staining of 5×10^6 BM cells was performed according to the manufacturer's protocol.

[00232] m^6A RNA-IP-seq. Two replicates of 10^5 LT-HSC, ST-HSC (LSK $CD34^+$ $FLK2^-$) and MPP (LSK $CD34^+$ $FLK2^+$) from C57BL/6J mouse were sorted into TRIzol (Invitrogen), and total RNA was isolated according to the manufacturer's instructions. RNA was fragmented to ~100 nucleotide fragments with Ambion fragmentation reagent (2 mins incubation at 70°C). The samples were then subjected to Turbo DNase treatment (Ambion), followed by a phenol-chloroform extraction, and resuspension in 85μl of nuclease-free water, and 5μl was saved as input. Then, the

remaining 80µl RNA fragments were diluted into IPP buffer (150 mM NaCl, 0.1% NP-40, 10 mM Tris-HCl, pH 7.5). RNA was incubated with 25µl of protein-G magnetic beads, previously bound to 3µg of anti-m^6A plyclonal antibody (Synaptic Systems), for 3 hours at 4°C in IPP buffer. Beads were washed twice with 200µl IPP buffer, twice with 200µl low-salt buffer (50 mM NaCl, 0.1% NP-40, 10 mM Tris-HCl, pH 7.5) and twice with 200µl high-salt buffer (500 mM NaCl, 0.1% NP-40, 10 mM Tris-HCl, pH 7.5). Beads were then treated with 300µl Elution Buffer (5 mM Tris-HCL pH 7.5, 1 mM EDTA pH 8.0, 0.05% SDS, 4.2µl Proteinase K (20 mg/ml)) for 1.5 hours at 50°C, and RNA was recovered with phenol:chloroform extraction followed by ethanol precipitation. Three human $CD34^+$ umbilical cord blood cells were isolated as described above and isolated total RNA with TRIzol. RNA was fragmented to ~100 nucleotide fragments with Ambion fragmentation reagent (2 mins 50 secs incubation at 70°C). The samples were then subjected to Turbo DNase treatment (Ambion), followed by a phenol:chloroform extraction, and resuspension in 18µl of nuclease-free water, and 1µl was saved as input. m^6A RNA IP was performed with EpiMark® N6-Methyladenosine Enrichment Kit following manufacturer's instructions.

[00233] Following m^6A preparation of RNA, quality was assessed on Agilent 2100 Bioanalyzer, and 1 ng (mouse) or 10 ng (human) RNA was used to generate RNAseq libraries according to the manufacturer's directions for the SMARTer Stranded Total RNA-Seq Kit – Pico Input Mammalian (Takara Bio Inc) using 16 cycles (mouse) or 13 cycles (human) PCR2 amplification. The method uses random priming and a template switching oligo to generate complimentary DNA, followed by the ligation of barcoded adapters; ribosomal-derived cDNA is then removed through probe-directed enzyme cleavage and subsequent enrichment of un-cleaved fragments.

[00234] The protocol was modified to retain lower molecular weight sample fragments by using a 1.2x SPRI bead concentration for PCR1 cleanup. To remove dimerized adapters, libraries underwent 160-600 bp size selection with a Pippin Prep (Sage Science) 2% gel. The resulting libraries were checked for quality and quantity using the Bioanalyzer and Qubit Fluorometer (Life Technologies). Then equal molar libraries were pooled and requantified. For mouse m^6A-seq, libraries were sequenced as 50 bp single read on the Illumina HiSeq 2500 instrument using HiSeq Control Software 2.2.58. Following sequencing, Illumina Primary Analysis version RTA 1.18.64 and Secondary Analysis version bcl2fastq2 v2.18 were run to demultiplex reads for all libraries and generate FASTQ files. For human m^6A-seq, libraries were sequenced as 75 bp single read on the Illumina NextSeq instrument using NextSeq Control Software 2.1.2. Following sequencing, Illumina Primary Analysis version NextSeq RTA 2.4.11 and Secondary Analysis version bcl2fastq2 v2.18 were run to demultiplex reads for all libraries and generate FASTQ files.

[00235] **Plasmid construction and stable cell line generation.** Mouse Ythdf2 (mYthdf2) was cloned from commercial cDNA clone (ORIGENE # MC200730) into vector pcDNA5/FRT/Flag plasmid using primers listed: mYthdf2 ORF Clone BamhI F: 5'-CGC GGA TCC TCG GCC AGC AGC CTC TTG GA-3' and mYthdf2 ORF Clone NotI R: 5'-ATA AGA ATG CGG CCG CCT ATT TCC CAC GAC CTT GAC GT-3'. Then Flag-mYthdf2 was subcloned under EF1a promoter in pSicoR-EF1a-IRES-EGFP lentiviral construct (Gibson Assembly®, forward primer: 5'-GTC GAC GGT ACC GCG GGC CCA TGG ATT ACA AGG ATG ACG ACG-3' and reverse primer: 5'-GAG GGA GAG GGG CGG ATC CCC TAT TTC CCA CGA CCT TGA CGT-3'). Human Ythdf2 (hYthdf2) was cloned from plasmid provided by the Chuan He lab using primers indicated: Forward 5'-CGT TCG AAA TGT CGG CCA

GCA GCC TCT-3'; Reverse 5'-TCC CCC GGG TTA TTT CCC ACG ACC TT-3'. Then hYthdf2 was cloned into pSicoR-EF1a-IRES-EGFP constructs under EF1a promoter by BstBI and XmaI restriction digestions and ligation. To generate Flag-mYthdf2 HPC7 stable cell line, lentiviruses were generated by transfection of pSicoR-EF1a-Flag-mYthdf2-IRES-EGFP constructs together with the psPAX2 and pMD2.G plasmids at a ratio of 10:7.5:2.5 into 293T cells using calcium phosphate transfection. The virus particles were harvested 48, 72, and 96 hours post transfection, filtered by 0.45 micrometers filter unit (Millipore), and then centrifuged at 18,000 RPM, 4°C for 2 hours. HPC7 cells were infected with recombinant lentivirus-transducing units in the presence of 4μg/mL polybrene (Sigma). 48 hours after infection, GFP^+ cells were sorted and cultured for experiments.

[00236] irCLIP-seq and data analysis. For irCLIP-seq, the procedure was modified from the previously reported methods (Zarneger et al. *Nature Methods*, 13: 489-492, 2016); Simsek et al. *Cell*, 169: 1051-1065 e1018, 2017). In brief, irCLIP was performed on ~3×10^8 Flag-Ythdf2 HPC7 cells by UV crosslinking cells at 0.4J/cm^2 for 3 times. Whole-cell lysates were generated in lysis buffer (150mM KCl, 10mM HEPES pH 7.6, 2mM EDTA, 0.5% NP-40, 0.5mM DTT, 1:100 protease inhibitor cocktail, 400U/ml RNase inhibitor; 1ml cell pellet and 2ml lysis buffer). Pipetted up and down several times, and then the mRNP lysate was incubated on ice for 5 mins and shock-frozen at -80°C with liquid nitrogen. The mRNP lysate was thawed on ice and centrifuged at 15,000g for 15 mins to clear the lysate. Flag-Ythdf2 was isolated with 30μl of protein-G magnetic beads per 1ml lysate, previously bound to 2μg of anti-Flag monoclonal antibody (Sigma) for 2 hours at 4°C on rotation. The beads were collected, washed eight times with 1ml ice-cold NT2 buffer (200mM NaCl, 50mM HEPES pH 7.6, 2mM EDTA, 0.05% NP-40, 0.5mM DTT, 200U/ml

RNase inhibitor) and one time with 200µl irCLIP NT2 buffer (50mM Tris, pH 7.5; 150mM NaCl; 1mM $MgCl_2$; 0.0005% NP-40). mRNP complex was digested with RNase 1 (Thermo Fisher #AM2294) at 0.4U/µl in irCLIP NT2 buffer (aqueous volume of 30µl and supplemented with 6 µl of PEG400 (16.7% final)). The nuclease reaction was incubated at 30°C for 15 mins in an Eppendorf Thermomixer, 15 s 1,400 r.p.m., 90 s rest. Nuclease digestions were stopped by addition of 0.5mL of ice-cold high-stringency buffer (20mM Tris, pH 7.5; 120mM NaCl; 25mM KCl; 5mM EDTA; 1% Trition-X100; 1% Na-deoxycholate). Immunoprecipitates were then quickly rinsed with 0.25mL then with 0.05mL of ice-cold irCLIP NT2 buffer. The irCLIP adaptor ligation and library construction followed previously reported protocol (Zarneger et al. *Nature Methods*, 13: 489-492, 2016).

[00237] Data were demultiplexed using FAST-iCLIP version 0.9.3 and aligned to mouse genome mm10 from UCSC using STAR (2.4.2a) with parameters "--outFilterScoreMinOverLread 0 --outFilterMatchNminOverLread 0 --outFilterMatchNmin 0". RPM-normalized genome browser tracks were created in R (3.4.1) and plotted using the Gviz package (1.20.0). Enriched motifs were identified by taking midpoints of each binding site found in all three replicates, adding 20 bases up and downstream, and running MEME (4.11.1) with parameters "-dna -mod zoops -revcomp -minw 5 -maxw 10 -nmotifs 10 -maxsize 1000000". After motifs were identified, we ran tomtom (4.11.1) against transfac (1-2017) to identify known binding sites. GO enrichment analysis was performed using a hypergeometric test in R. GO terms were considered enriched if they had a BH-adjusted p-value less than 0.05. Selected terms of interest are shown in the bar plot. Bars in the bar plot indicate percentage of genes in the list being tested having the term divided by the percentage of genes in the genome having the term. Peaks found by FAST-iCLIP in

all three replicates were assigned to various features in the genome. Promoters were defined as upstream 150 bases from the TSS. "trans_stop" was defined as upstream and downstream 200 bases from the transcript start site.

[00238] Cord blood transduction. Cord blood transduction was conducted as described previously (Rentas, S. et al. *Nature*, 532:508-511, 2016, doi:10.1038/nature17665). Briefly, fresh $CD34^+$ cord blood cells or flow-sorted $CD34^+$ $CD38^-$ cells were prestimulated for 12-18h in StemSpan medium (StemCell Technologies) supplemented with growth factors interleukin 6(IL-6; 20ng/ml, Peprotech), stem cell factor (SCF; 100ng/ml, Peprotech), Flt3 ligand (FLT3-L; 100ng/ml, Peprotech) and thrombopoietin (TPO; 20ng/ml, Peprotech). Lentiviruses were then added in the same medium at a multiplicity of infection (MOI) of 50-200 for 24 hours. Cells were then given 2 days after transduction before *in vitro* or *in vivo* assays. Human YTHDF2 was targeted for knockdown by shRNA targeting 5'-AAGGACGTTCCCAATAGCCAA-3' near the N terminus of CDS, as used in a previous report (Wang, X. *et al. Nature* 505:117-120, 2014, doi:10.1038/nature12730). Scramble shRNA (seed sequence 5'-GCGCGATAGCGCTAATAAT-3') were used as control.

[00239] Clonogenic progenitor assays. Flow-sorted GFP^+ cord blood cells from day 10 cultured transduced cells (12,000 per ml) were resuspended in semi-solid methylcellulose medium (Methocult H4034; StemCell Technologies). Colony counts were carried out after 14 days of incubation.

[00240] Human umbilical cord blood HSPC culture. 2 days after transduction, human cord blood $CD34^+$ or $CD34^+$ $CD38^-$ cells were collected and the GFP^+ percentage was determined by flow cytometry. To ensure that equal numbers of GFP^+ cells were cultured before expansion, identically cultured GFP^- cells were

added to the one with higher GFP^+ percentage to match the % GFP^+ between control and hYthdf2 KD. Then cells were seeded at a density of 10^5 per ml in StemSpan medium (StemCell Technologies) supplemented with growth factors IL-6 (20ng/ml), SCF (100ng/ml), FLT3-L (100ng/ml), TPO (20ng/ml) and CHIR99021 (250 nM) (Stemgent) (Perry et al. *Genes and Development*, 25: 1928-1942, 2011).

[00241] Human HSC xenotransplantation. For human cord blood HSC *ex vivo* expansion analysis, 10^5 sorted $CD34^+$ $CD38^-$ cells were transduced with human *YTHDF2* shRNA or control shRNA for 3 days and then analyzed for transduction efficiency (%$GFP^{-/+}$) and stem cell markers. On day 10, cultured cells were collected for stem cell marker analysis. For hUBC HSC primary LDA assay, $CD34^+$ cells were enriched as described above and transduced with human *YTHDF2* shRNA or control shRNA at 50 MOI. Media were changed at 24 hours post infection. Equal number of GFP^+ cells were sorted out from control or *YTHDF2* KD cells on 3 days post infection and cultured overnight. Three doses, 50K, 20K and 10K, of sorted GFP^+ cells were transplanted into sublethally irradiated (3.25Gy) NSG mice, respectively. The cut-off for HSC engraftment was an exhibition of more than 1% human $CD45^+$ GFP^+ cells out of total $CD45^+$ cells in BM of primary transplantation recipients. For hUCB HSC secondary LDA assay, BM cells from highest two doses primary recipients were collected and mixed together at 10 weeks post transplantation. Three doses, 1.2×10^7, 8×10^6, 4×10^6, of BM cells were transplanted into sublethally irradiated (3.25Gy) NSG mice, respectively. The cut-off for HSC engraftment was an exhibition of more than 0.2% human $CD45^+$ GFP^+ cells out of total $CD45^+$ cells in BM of secondary transplantation recipients. HSC frequency was assessed using ELDA software (Hu et al. *Journal of Immunological Methods*, 347: 70-78, 2009). For all

human cord blood xenotransplantation experiments, female NSG mice aged 6-8 weeks were used.

[00242] m^{6}A-seq data analysis. Human and mouse m^{6}A-seq data were aligned to the transcriptome of hg19 and mm10. In order to identify m^{6}A peaks, hg19 and mm10 transcriptome was divided into 25 nucleotide-wide tiles. The number of reads in the m^{6}A IP and non-IP (control) sample was counted in each tile, and p value was calculated with Fisher exact test and adjusted for multiple testing. Tiles with significant m^{6}A signal enrichment (adjust-Pval <= 0.05) were merged into bigger regions. Regions smaller than 100 bp were discarded, and regions over 200 bp were divided into 100 to 200 bp sub-regions; m^{6}A signal over control was calculated at each region; and regions with at least 2-fold enrichment in all replicates were identified as m^{6}A peaks. m^{6}A peaks distribution and m^{6}A marked genes were determined by overlapping all m^{6}A peaks with hg19 and mm10 RefGene annotation. m^{6}A marked genes were identified by overlapping m^{6}A peaks with hg19 RefGene. To filter for transcription factors, genes marked by m^{6}A in all three samples were compared against human transcription factor database http://fantom.gsc.riken.jp/5/sstar/Browse_Transcription_Factors_hg19. GO term analysis was then performed using R package enrich GO. m^{6}A marked human transcription factors were used as searching list, and all the expressed genes were used as background. Hemopoiesis related BP terms with significant enrichment were used to generate Figure 3C.

[00243] RNA-seq. Human cord blood CD34$^+$ cells were transduced with control or human *YTHDF2* KD lentivirus and sorted out for GFP$^+$ CD34$^+$ 10 days later. Three replicates of 12,000 GFP$^+$ CD34$^+$ cells were sorted for each group and were used to extract total RNA. Four nanograms of high quality total RNA was used

for cDNA synthesis and library preparation according to the manufacturer's directions with the SMART-Seq v4 Ultra Low Input RNA Kit for Sequencing (Takara, 634891) and Nextera XT (Illumina, FC-131-1096). Resulting short fragment libraries were checked for quality and quantity using an Agilent 2100 Bioanalyzer and Invitrogen Qubit Fluorometer. Equal molar libraries were pooled, requantified, and sequenced as 75 base pair single reads on a High Output flow cell on the Illumina NextSeq 500 instrument. Following sequencing, Illumina Primary Analysis version NextSeq RTA 2.4.11 and Secondary Analysis version bcl2fastq2 2.18 were run to demultiplex reads for all libraries and generate FASTQ files.

[00244] For RNA-seq analysis, reads were aligned to UCSC genome hg38 with Tophat version 2.0.13 with default parameters, using Ensembl 87 gene models. Read counts were generated using HTSeq-count with -m intersection-nonempty. Reads were also aligned to ERCC control sequences and counts tabulated. A scaling factor was calculated based on the median of the ERCC counts for each sample and used for normalization. Differentially expressed genes were found using the edgeR package (3.18.1) in R (3.4.1). Differentially expressed genes were required to have a BH-adjusted p-value < .05 and a 2-fold change in expression.

[00245] **RNA stability assay.** 15,000 sorted LT-, ST-HSCs and MPPs were cultured in StemSpan SFEM medium (Stem Cell Technologies) supplemented with 10μg/mL heparin (Sigma), 0.5× penicillin/streptomycin (Sigma), 10ng/mL recombinant mouse (rm) SCF (Biovision, Inc.), and 20ng/mL Tpo (Cell Sciences, Inc.) (Perry et al. *Genes and Development*, 25: 1928-1942 (2011)) at 37^{0}C 5% CO_2 5% O_2. Sorted cells were treated with 5μM actinomycin D (Sigma) for inhibition of mRNA transcription. Cells were harvested at 0 hour or 4 hours post treatment, and total RNA was extracted and used for RNA-seq.

[00246] **m^6A RNA methylation quantification**.

[00247] Mouse BM Lineage negative cells from *wt* and *Ythdf2* KO mice *were* enriched with mouse Lineage Cell Depletion Kit (Miltenyi Biotec), followed by total RNA extraction with TRIzol (Invitrogen). The quantification of m^6A RNA methylation in Lin^- cells were performed with m^6A RNA Methylation Quantification Kit (Abcam ab185912) following manufacturer's protocol. 200ng total RNA were used per replicates for either group.

[00248] **qPCR analysis.**

[00249] 10^5 LSK cells were sorted from *wt* and *Ythdf2* KO mice. Total RNA were extracted with TRIzol (Invitrogen). cDNA synthesis was conducted with High-Capacity RNA-to-cDNA™ Kit (Thermo) following manufacturer's protocol. qPCR primers used are listed in Table S5, qPCR primers used to verify the expressional levels of transcription factors in *wt* and *Ythdf2* KO HSPCs.

[00250] **Western blot and intracellular staining.** To validate the KO or KD efficiency in *Ythdf2* KO mouse model or hUCB, 33,000 $cKit^+$ cells or 120,000 GFP^+ cells were sorted from BM or transfected hUCB samples, respectively. Hela cells transduced to overexpress human YTHDF2 were used validate overexpression efficiency as shown in Fig. 14B. Immunoblotting was performed with anti-YTHDF2 rabbit polyclonal antibody (MBL, RN123PW) and β-actin mouse monoclonal antibody (NOVUS, NB600-501). Secondary antibodies used were IRDye 800CW Goat anti-Mouse IgG and IRDye 800CW Goat anti-Rabbit IgG antibodies (LI-COR). For intracellular staining, BM cells from *wt* and *Ythdf2* KO mice were stained with HSC markers as above, then fixed with the Cytofix/Cytoperm kit (BD Biosciences) according to the manufacturer's instructions. Fixed and permeabilized cells were immunostained with anti YTHDF2 antibody (MBL RN123PW), anti TAL1 antibody

(Santacruz sc-393287), anti GATA2 antibody (Santacruz sc-267), anti RUNX1 antibody (Santacruz sc-365644), anti STAT5 antibody(Santacruz sc-74442) and detected by Alexa-488 donkey anti-rabbit IgG antibody (Invitrogen).

[00251] Single cell immunostaining. 10,000 LSKs from *wt* and *Ythdf2* KO mice were sorted onto Poly-L-lysine coating slides, which were placed in a moisture chamber and incubated at 4^0C for 30 mins to allow cells settling onto the slides. Cells were fixed with chilled methanol at RT for 10 mins, blocked with universal blocking reagent (BioGenex) at RT for 30 mins, and stained with mouse TAL1 antibody (Santa Cruz, SC393287) or mouse IgG control (Abcam) at 4°C overnight. Cells were then stained with Alexa Fluor 488 donkey anti-mouse IgG (Thermo Fisher Scientific) at 4°C for 30 mins. Images were taken on a PerkinElmer Ultraview spinning disk system with Yokagawa CS-X1 disk. All emission was collected onto a C9100-23 Hamamatsu EM-CCD using Velocity software (PerkinElmer). For Z-stacks, the step size was set at 400nm. Staining intensity per image was quantified by ImageJ program.

[00252] FISH in conjugation with fluorescent immunostaining. Sorted LSKs were spun onto microscope glass slide (Fisher Scientific Cat. No. 12-544-4) using a Cytospin™ 4 Cytocentrifuge at 800 rpm for 1 min with medium acceleration (Thermo Scientific, cat. no. A78300003), followed by an immediate immersion into 4% PFA (diluted from 16% (wt/vol) aqueous solution, Electron Microscopy Sciences, cat. no. 15710). Cells were fixed at RT (25 ± 2 °C) for 30 mins. RNA in situ hybridization was performed using RNAscope multiplex fluorescent detection kit according to the manufacturer's instructions (Advanced Cell Diagnostics) with a couple of modifications: Antigen retrieval was unnecessary, and digestion was performed with 1:15 diluted proteinase III solution for 10 mins at RT. RNAscope

probes targeting mouse *Tal1* and *Gata2* were designed and produced by ACDbio. After the in situ hybridization was completed, slides were rinsed twice with PBST and directly processed with background blocking (Background buster solution, Innovex, cat. no. NB306) and primary antibody incubation. Anti-YTHDF2 (MBL, 1: 500) and anti-Dcp1α (Santa Cruz, SC100706, 1:200) antibodies were diluted with antibody diluent reagent buffer (Life technologies, cat. no. 003118) and incubated at 4°C overnight. Donkey anti- rabbit Alexa Fluor 488 (Invitrogen, 1:500) and donkey anti-mouse Alexa Fluor 633 (Invitrogen, 1:500) were used for protein target multiplexing.

EXAMPLE A-1

[00253] ***Ythdf2* KO leads to increase in phenotypic HSCs in primary mice.**

[00254] To investigate the effects of *Ythdf2* on phenotypic HSCs, Crispr-Cas9 technology was utilized to generate *Ythdf2*$^{f/f}$ conditional knockout mice, and then crossed with *Mx1-Cre* mice to specifically reduce *Ythdf2* expression in hematopoietic cells (hereafter *Ythdf2* KO mice) (Fig. 1A and B). BM HSPCs showed no discernible difference at the absence of pI:pC (Figure 7A). Four weeks after pI:pC injections, a significant increase was observed in both frequency and absolute number of long-term HSCs (Lin$^-$ Sca1$^+$ cKit$^+$ (LSK) CD34$^-$ Flk2$^-$; LT-HSCs) and short-term HSCs (LSK CD34$^+$ Flk2$^-$; ST-HSCs), but not multipotent progenitors (LSK CD34$^+$ Flk2$^+$; MPPs) in *Ythdf2* KO mice compared to littermate *wild type (wt)* mice (Fig. 1C to 1E). It was found that the frequency and absolute cell number of Long Term HSCs (LT-HSCs) and ST-HSCs increased by over 2-fold while MPP exhibited milder response (Figure 1C and 1E). Although *Ythdf2* KO led to increased BM cellularity, the absolute number of committed progenitors, including common myeloid progenitors (CMPs), granulocyte-macrophage progenitors (GMPs), megakaryocyte-erythrocyte progenitors (MEPs) and common lymphoid progenitors (CLPs), as well as mature lineage cells, erythrocytes, myeloid cells, B cells and T cells, showed no significant

difference between *Ythdf2* KO and *wt* mice (Fig. 1F to H). Cell cycle analysis revealed no discernible change of quiescence in HSCs or MPPs after *Ythdf2* KO (Fig. 7B). Notably, the percentage of apoptotic cells in *Ythdf2* KO LT-, ST-HSCs and MPPs significantly reduced compared to *wt* controls (Fig. 7C). To further identify any potential HSC defects in *Ythdf2* KO mice, the number of HSCs, committed progenitors, and mature lineages in the spleen were examined, and no significant differences were found between *wt* and *Ythdf2* KO mice (Figs. 7D to 7H). In summary, *Ythdf2* KO in primary mice specifically increases HSC numbers with no bias or defects in either progenitor or lineage cells.

EXAMPLE A-2

[00255] ***Ythdf2* KO expands functional HSCs in mice.**

[00256] To determine whether *Ythdf2* KO expands functional HSCs, a short-term homing assay was initially perfomed by transplanting 1×10^6 carboxyfluorescein diacetate succinimidyl ester (CFDA SE)-labelled BM cells from KO mice or their control littermates into lethally irradiated recipient mice, and no significant difference was found in their homing capacity between mutant and *wt* controls (Fig. 7I). Limited dilution, competitive repopulation unit assay (LDA) was then executed by transplanting 2×10^5, 7.5×10^4 or 2.5×10^4 donor BM cells (CD45.2), together with 2×10^5 recipient BM cells derived from the *ptprc* mutant strain (CD45.1), into lethally irradiated recipient mice (Fig. 2A). Consistent with an increased number of phenotypic HSCs in *Ythdf2* KO mice, it was found that competitive repopulating units (CRUs) increased 2.2-fold in *Ythdf2* KO HSCs compared to controls (Fig. 2B). In the 2×10^5 group, compared to controls, and a significant increase was observed in the overall repopulation rate from *Ythdf2* KO donor cells at 16 weeks post

transplantation (Fig. 2C). Moreover, recipients of *Ythdf2* KO BM cells, compared to that of controls, exhibited markedly higher frequency and absolute number of donor derived LT-HSCs and ST-HSCs, but not MPPs in BM (Fig. 2D and 2E). Furthermore, it was found that donor derived committed progenitors and mature lineages in BM from transplantation recipients of mutant and *wt* cells showed no significant changes (Fig. 2F and 2G). To determine the long-term repopulation ability of HSCs from *Ythdf2* KO mice, the secondary transplantation with BM cells derived from primary recipients was conducted. Notably, it was found that compared to controls, CRUs from *Ythdf2* KO cells revealed a 3.5-fold increase (Fig. 2H) and exhibited no signs of leukemia in both BM and spleen at 16 weeks after secondary transplantation (Figs. 9A to 9F). Furthermore, in Figs. 2I and 2J, a limiting dilution assay was conducted by transplanting total bone marrow (BM) from WT or Ythdf2 KO mice with 3 different dosages. Four weeks post transplantation, it was observed that the engraftment of donor cells increased in the mice transplanted with 200,000 Ythdf2 KO BM cells, as compared to that with WT BM cells. Furthermore, this increase did not generate lineage bias in the transplantation recipients.

[00257] We also investigated the long-term effect of *Ythdf2* KO on hematopoiesis under homeostasis condition by examining the stem cells, progenitor cells, and lineages in both BM and spleen at over 5 months post pI:pC injections (Fig. 9A). Although we observed a modest increase in LT-HSCs in BM from *Ythdf2* KO mice compared to that of controls (Fig. 9C), there were no discernible differences between *Ythdf2* KO and control mice in progenitors and lineage cells from either BM or spleen (Figs. 9D to 9J). These observations indicate that long-term effect of *Ythdf2* KO *in vivo* neither skews lineage differentiation nor facilitates aberrant proliferation, which is in line with previous reports that *Ythdf2* is not required for

leukemogenesis. To verify the frequency of functional HSCs in the BM at 5 moths post pI:pC induction, we transplanted 7.5 × 10^4 BM cells from *wt* and *Ythdf2* KO mice with competent cells into lethally irradiated recipients. We found that *Ythdf2* KO led to significantly higher engraftment in recipients comparing to *wt* controls, suggesting that *Ythdf2* KO has long-term capability on mouse HSC expansion *in vivo* (Fig. 9K). Taken together, these data reveal that *Ythdf2* KO results in specific and significant mouse HSC expansion *in vivo* without affecting lineage commitment.

EXAMPLE A-3

[00258] Ythdf2 regulates HSC self-renewal gene expression by m^6A-mediated mRNA decay.

[00259] To explore the underlying mechanisms of how *Ythdf2* KO expands HSCs, mapping was performed of the m^6A methylome by methylated RNA immunoprecipitation combined with high-throughput sequencing (MeRIP-seq or m^6A-seq) in LT-HSCs, ST-HSCs, and MPPs sorted from adult C57BL/6J mice (Meyer et al. *Cell*, 149: 1635-1646, 2012; Schwartz et al. *Cell*, 155: 1409-1421, 2013; Dominissini et al. *Nature*, 485: 201-206, 2012). m^6A peaks were selected by identifying significantly enriched overlapping peaks from two independent replicates. Consistent with previous studies (Meyer et al. *Cell*, 149: 1635-1646, 2012); Dominissini et al. *Nature*, 485: 201-206, 2012), it was found that m^6A peaks were abundant in mRNA open reading frame (ORF), in 3' untranslated regions (UTRs), and around the stop codon in all three HSPC populations. Transcripts of moderately expressed genes were more likely to be methylated (Figs. 10A to 10C). Intriguingly, it was found that m^6A modifications were enriched in the mRNAs of transcription factors, such as *Gata2*, *Etv6, Stat5* and *Tal1,* which have been documented to be

critical for HSC self-renewal and stem cell state maintenance (Wang et al. *Blood*, 113: 4856-5865, 2009; Ebina et al. *The EMBO Journal*, 34: 694-709, 2015; Orkin et al. *Cell*, 132: 631-644, 2008: de Pater et al. *The Journal of Experimental Medicine*, 210: 2843-2850, 2013; Hock et al. *Genes and Development*, 18: 2336-2341, 2004; Lim et al. *The Journal of Clinical Investigation* 122: 3705-3717, 2012; Reynaud et al. *Blood*, 106: 2318-2328, 2005; and Kato et al. *The Journal of Experimental Medicine*, 202: 169-179, 2005), suggesting the m^6A modification could play critical roles in the regulation of HSCs (Table S1, Key transcription factors critical for HSC self-renewal and maintenance are labeled by m^6A in HSPCs). Given the accumulating evidence that m^6A mRNA methylation regulates stem cell fate determination by facilitating the decay of mRNAs coding for transcription factors and genes in key signaling pathways involved in self-renewal and differentiation (Batista et al. *Cell Stem Cell*, 15: 707-719, 2014; (Geula et al. *Science* 347: 1001-1006, 2015; Yoon et al. *Cell*, 2017; Zhang et al. *Nature*, 549: 273-276, 2017; Zhao et al. *Nature*, 542: 475-478, 2017; Li et al. *Cancer Cell*, 31: 127-141, 2017; Li et al. *Nature*, 548: 338-342, 2017) the mRNA degradation rates were next measured in LT-, ST-HSCs, and MPPs by monitoring mRNA levels after transcription inhibition with actinomycin D. It was found that degradation rates of methylated mRNAs were significantly faster than unmethylated mRNAs in ST-HSCs, and MPPs (Fig. 10D). As Ythdf2 is a well-recognized m^6A "reader" that mediates mRNA decay (Wang et al. *Nature*, 505: 117-120, 2014), the targets of Ythdf2 were further determined by performing infrared UV-crosslinking immunoprecipitation sequencing (irCLIP-seq) in the mouse multipotent hematopoietic precursor cell line HPC-7 (Pinto do et al. *The EMBO Journal*, 17: 5744-5756, 1998; Zarnegar et al. *Nature Methods*, 13: 489-492, 2016) (Fig. 3A; Figs. 11A to 11C). The results showed that 57.8% of Ythdf2 target mRNAs contained m^6A

peaks (Fig. 11D). Ythdf2 binding sites were enriched with the conserved m^6A motif and exhibited the characteristic of m^6A distribution features (Fig. 3B and 3C). Gene ontology (GO) analysis of Ythdf2 target transcripts revealed enrichment of genes related to hematopoietic or lymphoid organ development, suggesting the involvement of Ythdf2 in the regulation of hematopoiesis (Fig. 3D). Notably, it was found that Ythdf2 bound to transcription factor mRNAs, such as that of *Tal1* and *Gata2*, on sites largely overlapping with m^6A peaks (Fig. 3E; Fig. 5E and Table S2, Ythdf2 targeted mRNAs from three irCLIP-seq replicates). Significant change was not observed in the total RNA mass in LSK $Flk2^-$ cells from *wt* and *Ythdf2* KO mice. Though m^6A modification only constitute 0.1-0.4% of adenosine nucleotide in mammal cells, it was found that *Ythdf2* KO led to increased level of m^6A content in total RNA from BM Lin^- cells, suggesting that Ythdf2 specifically regulates the stability of m^6A-marked mRNAs (Figs. 12A and 12B). Consistently, qPCR analysis of total mRNA revealed increased levels of *Tal1*, *Gata2*, *Runx1* and *Stat5a*, whose mRNAs have shown to be modified by m^6A, in *Ythdf2* KO LSK cells compared to *wt* controls (Fig. 3F). Single cell immunofluorescence staining and intracellular flow cytometry further revealed that *Ythdf2* KO HSPCs exhibited significant increases in the intensities of m_6A-labeled transcription factors involved in stem cell self-renewal, such as TAL1, GATA2, RUNX1 and STAT5, indicative of a suppressive role of Ythdf2 in HSC self-renewal (Fig. 3G; Fig. 12C). A previous study has shown that Ythdf2 regulates RNA metabolism through localizing the bound mRNAs to mRNA decay sites (Wang et al. *Nature*, 505: 117-120, 2014). To further explore the mechanism of Ythdf2 in regulating HSC self-renewal, fluorescence in situ hybridization (FISH) was performed of *Tal1* mRNA and fluorescence immunostaining of Ythdf2 and Dcp1a, a marker of mRNA decay sites (Sheth et al. *Science*, 30:805-

808, 2003; Kedersha et al. *Methods in Enzymology*, 431: 61-81, 2007), and their relative spatial distribution was analyzed in sorted *wt* and *Ythdf2* KO HSPCs. Co-localization of *Tal1* mRNA, Dcp1a and Ythdf2 was observed in *wt* cells while substantially reduced in *Ythdf2* KO controls (Figs. 3H and 3I). Furthermore, similar observation was confirmed by co-staining *Gata2* mRNA FISH with Ythdf2 and Dcp1a in *wt* or *Ythdf2* KO HSPCs (Figs 12D and 12E). To determine whether the increased transcription factors, such as *Tal1*, expression accounts for the HSC expansion in *Ythdf2* KO mice, rescue experiments were performed using short hairpin (sh) RNA-mediated *Tal1* knock down (KD) in *wt* and *Ythdf2* KO LSK cells, followed by transplanting into lethally irradiated recipients. Depletion of *Tal1* in HSPCs significantly impaired the reconstitution capacity of *wt* cells as reported previously and also rescued the increased engraftment of *Ythdf2* KO cells (Fig. 12F). Overall, these data indicate that Ythdf2 regulates HSC self-renewal by enabling the degradation of mRNAs encoding transcription factors essential for stem-cell renewal.

EXAMPLE A-4

[00260] Dissecting the role of Ythdf2 in human UCB HSPCs by m^6A-seq and RNA-seq.

[00261] The limited number of HSCs in a single human umbilical cord blood unit has been an obstacle for clinical applications, such as HSC transplantation (Walasek et al. *Annals of the New York Academy of Sciences*, 1266: 138-150, 2012). The observation that *Ythdf2* KO resulted in an increase of phenotypic and functional mouse HSCs prompted a test whether *YTHDF2* knockdown (KD) could facilitate human UCB HSC expansion. First, m^6A-seq with $CD34^+$ cells isolated from 3 individual hUCB samples was performed (Fig. 13A). m^6A modifications

predominantly occurred in mRNAs (~95%), preferential in mRNA ORF regions, 3'UTRs, and near the stop codon, as expected (~90%) (Figs. 4A and 4B; Fig. 13B). m^6A landscapes in mouse and hUCB HSPCs were compared, and it was found that 2,239 genes were commonly m^6A tagged (Fig. 4C). These commonly m^6A-tagged transcripts were enriched for genes related to hematopoiesis and stem cell maintenance (Fig. 4D). Due to the enrichment of m^6A labeling in the mRNAs of transcription factors responsible for mouse HSC self-renewal, the m^6A-marked transcription factor transcripts in hUCB $CD34^+$ cells were next characterized by performing GO term analysis. Among the 722 identified m^6A-labeled transcription factor mRNAs, major GO terms were related to cell fate commitment and stem cell maintenance (Fig. 13C). For example, *HOXB4*, overexpression of which has been reported to expand human and mouse HSCs *ex vivo* (Amsellem et al. *Nature Medicine*, 9: 1423-1427, 2003; Antonchuck et al. *Cell*, 109: 39-45, 2002), was marked by m^6A in hUCB $CD34^+$ cells (Fig. 4E). Other transcription factors required for HSC self-renewal and critical to induce HSCs from other cell types (Ebina et al. *The EMBO Journal*, 34: 694-709, 2015; Galan-Caridad et al. *Cell*, 129: 345-357, 2007, such as *Zfx, RUNX1* and *FOSB,* were also m^6A-tagged in hUCB $CD34^+$ cells (Figs. 13F and 13G and see also Supplementary Table S3 of article "Supression of m6A Reader Ythdf2 Prmotd Hematopoeitic Stem Cell Expansion" by Li et al, *Cell Research* 28, 904-917 (2018), which article (and including the Supplementary Tables thereof) is hereby incorporated by reference herein in its entirety, Genes marked by m^6A in human UCB $CD34^+$ HSPCs from individual samples). To further dissect the role of YTHDF2 in hUCB HSPCs, RNA-seq was performed with control or *YTHDF2* KD hUCB $CD34^+$ cells (Fig. 4F; Figs. 13D and 13E). Remarkably, transcripts marked by m^6A, including *HOXB4* and other HSC self-renewal related transcription factors,

showed significant increases of input mRNA reads in the *YTHDF2* KD cells compared to the control, without noticeable changes for non-m^6A labelled genes (Figs. 4G to 4I; Figs. 13F and 13G). These results support the role of YTHDF2 in regulating hUCB HSC self-renewal through RNA degradation.

EXAMPLE A-5

[00262] Expansion of hUCB HSCs by *YTHDF2* KD.

[00263] To further explore whether suppression of YTHDF2 can expand human HSCs, short hairpin (sh) RNA-induced *YTHDF2* KD in hUCB HSPCs was performed as above (Fig. 4F). After 7 days *ex vivo* culture, lentiviral knockdown of YTHDF2 resulted in an average 14.3-fold and 13.6-fold increase, respectively, in the frequency and absolute number of $CD34^+$ $CD38^-$ $CD45RA^-$ $EPCR^+$ phenotypic HSCs and a 5.1-fold increase in CFUs relative to control cells, especially the most primitive CFU-granulocyte erythrocyte monocyte megakaryocyte (GEMM) colony type and burst forming unit-erythroid (BFU-E), reflecting higher expression level of key transcription factors for hematopoiesis, such as *TAL1*, in *YTHDF2* KD hUCB cells (Figs. 5A to 5D; Figure 14A). Interestingly, the apoptotic rate was significantly reduced in *YTHDF2* KD hUCB HSPCs compared to control cells, similar to the trend of HSCs in *Ythdf2* KO mouse (Fig. 5E). Also, Fig 5F shows that the Ythdf2 knockdown (KD) HSCs exhibited up to a 10-fold increase compared to control HSCs 10 days post transduction. Next, the effect of overexpression (OE) *YTHDF2* on HSPC function was explored. Overexpression of *YTHDF2* reduced clonogenic potential of hUCB HSPCs by 2.2 fold, suggesting YTHDF2 negatively regulates HSC maintenance *ex vivo* (Figs. 14B and 14C).

[00264] To determine whether *YTHDF2* KD can expand human HSCs *in vivo,* LDA was performed by transplanting GFP^+ cells sorted from hUCB $CD34^+$ cells

infected with control and *YTHDF2* shRNA at day 4 post infection (Fig. 6A). At 10 weeks post transplantation, we analyzed BM cells were analyzed from recipient NOD/SCID *Il2rg*^{null} (NSG) mice and measured the functional HSC frequency after *in vivo* expansion. Notably, compared to control group, recipients of *YTHDF2* KD cells displayed a 9-fold increase in human hematopoietic cell (hCD45^{+} GFP^{+}) engraftment in BM without changes in the proportions of each lineage (Figs. 6B and 6CH; Figs. 15A and 15B). *YTHDF2* KD significantly increased the percentage of myeloid, megakaryocyte and erythrocyte in the BM of primary recipients (Figs 15C). Accordingly, it was found that the HSC frequency in *YTHDF2* KD cells was increased 4.4-fold relative to that in control cells (Fig. 6D). It was confirmed the long-term capability of *YTHDF2* KD hUCB cells to be reconstituted and undergo self-renewal; 12 weeks after transplantation of BM from primary recipients into sublethally irradiated secondary NSG recipient mice, human hematopoietic cell chimerism in BM were higher in the *YTHDF2* KD group, as compared to that in the control group (Figs. 6E, 6F; Fig. 15D). CRUs from *YTHDF2* KD cells revealed an 8-fold increase relative to that in control cells (Fig. 6G). These data demonstrate that *YTHDF2* KD remarkably facilitates the expansion of both phenotypic and functional hUCB HSCs *ex vivo.*

EXAMPLE A-6

[00265] The examples herein demonstrate that conditional deletion of Ythdf2, m6A reader, lead to expansion of phenotypic and functional HSCs without lineage bias. To investigate if there is concomitant increase in mesenchymal stem cells *in vivo*, Ytdhf2$^{f/f}$ mice were crossed with Mx1-Cre mice to conditionally delete Ythdf2 expression from mesenchymal cells. Nine-months post pI:pc injection bone marrow cells were isolated from Ythdf2^{KO} and their wild type littermates. Single-cell

suspension of total bone marrow cells were immuno-stained with flow antibodies. Hematopoietic (CD45, Ter119) and endothelial cells (CD31) were excluded using specific markers. Mesenchymal stem cell present within the total bone marrow stromal cells were further purified by inclusion of N-Cadherin and CD105 antibodies. Mesenchymal stem cells marking both N-Cadherin$^+$ and CD105$^+$ were quantitated. Conditional deletion of Ythdf2 led to 3.6-fold expansion in frequency of mesenchymal stem cells (Fig. 16). Our study clearly demonstrates that loss of Ythdf2 can expand bone marrow mesenchymal stem cells *in vivo*.

[00266] Discussion

[00267] Although recent studies explore the biological functions of mRNA m^{6}A modifications (Zheng et al. *Molecular Cell*, 49: 18-29, 2013; Zhou et al. *Nature*, 526: 591-594, 2015; Alarcon et al. *Cell*, 162: 1299-1308, 2015; Zhang et al. *Cancer Cell*, 31: 591-606 e596, 2017; Lence et al. *Nature*, 540: 242-247, 2016; Haussmann et al. *Nature*, 540: 301-302, 2016; Chen et al. *Cell Stem Cell*, 16: 289-301, 2015; Alarcon et al. *Nature*, 519: 482-485, 2015; Xiao et al. *Molecular Cell*, 61: 507-519, 2016; Wojtas et al. *Molecular Cell*, 68: 374-387 e312, 2017; Ivanovna et al. *Molecular Cell*, 67: 1059-1067 e1054, 2017; Fustin et al. *Cell*, 155: 793-806, 2013; Slobodin et al. *Cell*, 169: 326-337 e312, 2017; Schwartz et al. *Cell*, 159: 148-162, 2014; Pendleton et al. *Cell*, 169: 824-835 e814, 2017; Shi et al. *Cell Research*, 27: 315-328, 2017; Huang et al. *Nature Cell Biology*, 20: 285-295, 2018; Bertero et al. *Nature*, 2018; Liu et al. *Nature*, 518: 560-564, 2015), embodiments herein identify Ythdf2 as an important regulator of human and mouse HSC self-renewal by coupling the post-transcriptional m^{6}A modification to the degradation of mRNAs encoding key transcription factors for self-renewal. Repression of Ythdf2 in mouse HSPCs and hUCB HSCs can lead to increased expression of multiple key TFs critical for self-

renewal, thereby facilitating *ex vivo* expansion of both phenotypic and functional HSCs without noticeable lineage bias and leukemia potential. In addition, stem cell niches, to some extent, may contribute to Ythdf2 suppression-mediated mouse HSC expansion as *Mx1-cre* can be activated in mesenchyme stromal cells. It would be intriguing to study the function of *Ythdf2* on mesenchymal stem cells (MSCs) and how repression of Ythdf2 in both HSCs and MSCs may synergistically expand HSCs *in vivo*.

[00268] Given the broad and complicated impact of m^6A writer complex *Mettl3* and *Mettl14* on mRNA splicing, translation, and pri-miRNA processing (Barbieri et al. *Nature*,, 2017; Alarcon et al. *Nature*, 519: 482-485, 2015; Liu et al. *Nature*, 518: 560-564, 2015), *Mettl3* or *Mettl14* depletion results in distinct outcomes in normal stem cells and leukemia. Recent studies have demonstrated that *Mettl3* and *Mettl14* play essential roles in leukemia development and leukemia stem cell maintenance (Vu et al. *Nature Medicine*, 2017; Barbieri et al. *Nature*, 2017; Weng et al. *Cell Stem Cell*, 22: 191-205 e199, 2018). In contrast, Ythdf2 is believed to be mainly involved in m^6A-mediated mRNA decay (Batista et al. *Cell Stem Cell*, 15: 707-719, 2014; Yoon et al. *Cell*, 2017; Zhang et al. *Nature*, 549: 273-276, 2017; Wang et al. *Nature*, 505: 117-120, 2014). According to certain embodiments herein, it is believed that manipulating *Ythdf2* may extend the half-life of specific m^6A-marked mRNAs encoding TFs critical for stem cell self-renewal without affecting other aspects of mRNA processing. The Examples herein show that *Ythdf2* depletion in HSCs neither skews the lineage commitment nor induces hematological malignancies, reducing the risk of leukemogenesis with expanded HSCs. Furthermore, stem cell self-renewal is a complexed process comprised of cell division, survival, prevention of differentiation and stemness retention. The observation that *Ythdf2*-deficient HSCs

exhibited lower apoptotic rate indicates embodiments of methods herein also benefit another feature of stem cell self-renewal.

[00269] A major limitation in using hUCB HSC transplantation is the insufficient number of HSCs in one hUCB unit. Albeit previous studies have revealed that Dlk1, SR1, Musashi2 and UM171 can expand hUCB HSCs by targeting Notch, AHR signaling or other unknown pathway (Boitano et al. *Science*, 329: 1345-1348, 2010; Fares et al. *Science*, 345: 1509-1512, 2014; Rentas et al. *Nature*, 532: 508-511, 2016; Chou et al. *Experimental Hematologyl,* 41: 479-490 e474, 2013). Accordingly, embodiments herein provide a novel and potent way to target multiple key TFs critical for HSC self-renewal and to enhance the expansion of HSCs. For example, reducing Ythdf2 level and function during *in vitro* culture via small chemicals or AAV-mediated KD may allow the Ythdf2 level and function to restore after transplantation *in vivo*, and thus not affect normal HSC maintenance and function in human patients. Furthermore, in certain embodiments, methods described herein may be combined with other methods to facilitate the expansion of not only human HSCs, but also other stem cells, rendering an approach for stem cell-based therapies.

EXAMPLE B

[00270] The following protocols were used in the "B" Examples below.

[00271] **Animals.** C57BL/6-Gt(ROSA)26Sortm1(HBEGF)Awai/J(iDTR), B6.Cg-Gt(ROSA)26Sortm14(CAG-tdTomato)Hze/J(R26RtdT), Tg(Cspg4-DsRed.T1)1Akik/J, Cxcl12tm2.1Sjm/J, Kitltm2.1Sjm/J ($SCF^{f/f}$), Cxcl12tm1.1Sjm/J ($CXCL12^{f/f}$) mice were obtained from the Jackson Laboratory. *N-cad-CreER^T*, and *N-cad-TdT* mice were generated by Applied StemCell, Inc. To induce *N-cad-CreER^T; R26-tdT* mouse, tamoxifen (Sigma) was injected intraperitoneally at 2mg per injection for 3 days. To induce *N-cad-CreER^T; R26-tdT* at embryonic stage, a single

dose of 1.5mg of TMX was injected intraperitoneally (IP) into the E12.5 pregnant dam. Cesarean section was performed at E19.5 and the neonatal mice were transferred to foster mice. To induce N-Cad^{+} cells ablation in *N-cad-CreER^{T};iDTR* mice, DT (Sigma) was injected intraperitoneally every other day at a dose of 50ng per g body as indicated. 5FU (Sigma-Aldrich) was injected once in the tail vein at 150μg per g body weight. After 5FU injection, mice were analyzed as described in the text. All mouse strains used in this study had a C57BL/6J genetic background. Animals were randomly included in the experiments according to genotyping results. Animal experiments were conducted in a blinded fashion with respect to the investigator. The numbers of animals used per experiment are stated in the figure legends. All mice used in this study were housed in the animal facility at the Stowers Institute for Medical Research (SIMR) and were handled according to SIMR and National Institutes of Health (NIH) guidelines. All procedures were approved by the Institutional Animal Care and Use Committee (IACUC) of the SIMR.

[00272] **Flow cytometry.** For phenotype analysis, hematopoietic cells were harvested from bone marrow (femur and tibia). Red blood cells were lysed using a 0.16 M ammonium chloride solution. For cell surface phenotyping, a lineage cocktail (Lin, phycoerythrin (PE)-Cy5) was used, including anti-CD3 (145-2C11), anti-CD4 (RM4-5), anti-CD8 (53-6.7), anti-Mac-1 (M1/70), anti-Gr1 (RB6-8C5), anti-B220 (RA3-6B2), anti-IgM (II/41) and anti-TER119 (TER-119) (100 ng antibody cocktail per million bone marrow cells, eBioscience). Monoclonal antibodies to SCA1 (D7, eBioscience), c-KIT (2B8, eBioscience), FLK2 (A2F10, eBioscience), CD34 (RAM34, eBioscience), CD48 (HM48-1, eBioscience), CD150 (TC15-12F12.2, BioLegend) and CD49b (HMα2, Biolegend) (all used as 50 ng per million bone marrow cells) were also used where indicated. For lineage analysis of peripheral blood,

monoclonal antibodies to CD45.1 (A20, eBioscience), CD45.2 (104, eBioscience), CD3, B220, Mac-1 and Gr1 were used. 7-aminoactinomycin D (7-AAD) (A1310, Life technologies) was used to exclude dead cells. For stromal niche cell analysis, CD45 (30-F11, eBioscience), CD31 (390, eBioscience), PDGFRα-biotin (APB5, eBioscience), LepR-Bio (R&D), CD51 (clone RM7-V, Biolegend). Samples stained with biotin conjugated antibodies were washed with staining medium, then incubated with streptavidin brilliant violet 421TM (Biolegend, 1:500). Cell sorting and analysis were performed using MoFlo (Dako), InFlux Cell Sorter (BD Biosciences), MACSQuant (Miltenyi Biotec) or CyAn ADP (Dako) instruments. Data analysis was performed using FlowJo software.

[00273] Whole-mount sternum HSC immunostaining. Sternal bones were collected and transected with a surgical blade into 3-4 fragments. The fragments were bisected sagittally to expose bone marrow cavity, fixed in 4% PFA. blocked/permeabilized in PBS containing 20% normal goat serum and 0.5% Triton X100, and stained with primary antibodies for 3 days. The tissues were incubated with secondary antibodies for 2 hours (Bruns et al., 2014; Kunisaki et al., 2013). Fluorescence imaging was performed on a spinning-disk confocal microscope (UltraVIEW; PerkinElmer), including an inverted microscope (Axiovert 200 M; Carl Zeiss Microimaging, Jena, Germany), attached to a spinning-disk confocal system (CSU-X1; Yokogawa Corporation of America) and Orca-R2 camera (Hamamatsu) with Volocity acquisition software (PerkinElmer) and a 20x/0.8 Plan-Apochromat objective (Carl Zeiss). Images were collected as a series of optical sections, with a step size of 4 μm. Images were collected in a tile pattern (overlap 10%) sufficient to cover the entire sample. Channels were collected sequentially. (Blue dye) was excited using 405 nm light (50 mW diode laser, OEM) and (red dye) was excited

using 561 nm light (50 mW solid state laser, OEM), and each was collected using a multibandpass emission filter with 415nm-775nm 580nm-650nm bands. (Green dye) was excited using 488 nm light (50 mW solid state laser, OEM) and collected using a multibandpass emission filter of 500nm-550nm, and (far red dye) was excited using 640 nm light (50 mW solid state laser, OEM) and collected using a multibandpass emission filter with 455nm-515nm and 660nm-750nm. Exposure times and laser powers were adjusted to compensate for variations in staining.

[00274] Second Harmonic Generation (SHG) imaging was performed immediately following fluorescence imaging. SHG images were collected on a LSM-780 laser scanning confocal microscope (Carl Zeiss) equipped with a QUASAR detection unit, a 10x 0.45 Plan-Apochromat objective (Carl Zeiss), and Zen 2012 acquisition software (v8.1.3, Carl Zeiss). Images were collected as a series of optical sections, with a step size of 8 μm and a pixel size (1.32 μm/pixel) an integer multiple of four times the fluorescence pixel size. SHG images were taken with a laser light wavelength of 900 nm and collected at 371-420 nm. As a reference for image alignment, images of Cd150-PE were taken using the 561nm line of a DPSS laser (Melles Griot) and collected at 566-735 nm concurrently with the SHG images. Images were collected in a tile pattern (no overlap) sufficient to cover the entire sample. Tiles were stitched into a complete 3D image using Zen software.

[00275] Images were analyzed using Fiji software (1.51g National Institutes of Health). To align SHG and fluorescence images, fluorescence images were first background subtracted, and image tiles were stitched into a complete 3D image using the Grid/Collection stitching plugin (reference http://bioinformatics.oxfordjournals.org/content/25/11/1463.abstract). Given that the transfer of the sample from the fluorescence microscope to the SHG microscope

involved a small amount of sample rotation, it was necessary to realign the SHG and fluorescence images in 3 dimensions. Alignment of SHG and fluorescence image sets was carried out using a custom plugin available at http://research.stowers.org/imagejplugins. Firstly, a minimum of 8 common landmarks were identified by visual inspection of both the SHG and fluorescence data sets. Next the Kabsch algorithm was used to find the best scaled rotation to transform the fluorescence coordinates to the SHG image coordinates. Finally, each 3D voxel in the fluorescence image was transformed to the corresponding SHG position and trilinear interpolation was used the find the SHG intensity at that position to create the realigned composite image.

[00276] Image analysis was conducted by researchers unfamiliar with the hypotheses of the study. HSCs were identified by eye. Cells were considered negative for staining if the shape of the cell could not be discerned by eye, or if the shape of the cell formed a dark region in a field of positive signal. Distance measurements to niche components were made using Fiji and Microsoft Excel software. The locations of the HSC and nearest point of each of the three niche components were marked using point ROIs in Fiji and locations were transferred to excel, where distances in 3D were then calculated using the 3D Pythagorean Theorem. To calculate distances for randomly distributed HSCs, random point ROIs were generated using a custom plugin in FIJI in the same images analyzed for observed HSCs. The randomly generated points were considered simulated HSCs if they appeared in a reasonable HSC location (as assessed by the presence of Lin+ cells in the surrounding regions). Niche distance measurements for simulated HSCs were then made in the same manner as for observed HSCs.

[00277] The statistical significance of differences in the distribution of distances was assessed by Kolmogorov-Smirnov analysis using Origin software. Statistical significance of changes in percentages of HSCs at 5 μm were assessed using a Student's T test in Microsoft Excel. Changes were considered significant if $P < 0.05$.

[00278] Final images shown in figures are maximum projections that have been background subtracted and contrast adjusted for clarity.

[00279] **Transplantation and Repopulation assay.** 100 sorted pHSCs or rHSC cells together with 1.0×10^5 CD45.1 rescue bone marrow cells were transplanted into lethally irradiated (10 Gy) CD45.1 recipients. 2.0×10^5 CD45.2 BM cells from *N-cad-CreER^T;iDTR* and control mice together with 2.0×10^5 CD45.1 rescue bone marrow cells were transplanted into lethally irradiated (10 Gy) CD45.1 recipients. Every 4 weeks post transplantation, peripheral blood was collected from the submandibular vein. Hematopoietic repopulation was measured from donor-derived blood cells (CD45.2).

[00280] **RNA sequencing and analysis.** cDNA was generated from 1000 purified cells using SMARTer Ultra Low Input RNA kit (Clonetech) and library was generated by the Nextera XT DNA Library Preparation Kit (Illumina), followed by sequencing on an Illumina HiSeq2500 for 50bp single reads. Raw reads were demultiplexed into Fastq format allowing up to one mismatch using Illumina bcl2fastq2 v2.18. Reads were aligned to UCSC genome mm10 with TopHat v2.0.13, default parameters. FPKM values were generated using Cufflinks v2.2.1 with "-u –max-bundle-frags 100000000". Read counts were generated using HTSeq-count with "-m intersection-nonempty". Three or four replicates were sequenced for each population. Data are accessible at NCBI GEO: GSE104887

[00281] **CFU-F assay and *in vitro* differentiation.** Cells were sorted directly into culture at a 96-well plate. The cultures were incubated at 37°C in a humidified atmosphere with 5% O_2 and 10% CO_2 for 7-10 days. Colonies were stained by CellTracker™ Green CMFDA (Life technologies) and image was acquired by Celigo Imaging Cytometer (Nexcelom). For *in vitro* differentiation, clonally expanded Ncad-CreER^T driven Tomato$^+$ BM/Bone stromal cells were isolated from CFU-F cultures by digesting with 0.25% Trypsin/EDTA, split into 3 aliquots, and seeded into separate cultures permissive for differentiation: StemPro Osteogenesis kit Gibco A10072-01, Adipogenesis kit A10070-01 and Chondrogenesis differentiation kit A10071-01. The osteoblastic differentiation was assessed by VECTOR Red Alkaline Phosphatase; the adipogenic differentiation was detected by Oil Red O (Sigma); and the chondrogenic differentiation was detected by Toluidine blue (Sigma, 0.1g T Blue/100mL distilled water).

[00282] **Bone sectioning, immunostaining and imaging.**

[00283] Freshly isolated femurs were fixed in 4% paraformaldehyde overnight, followed by 1 to 3 days decalcification in 10% EDTA. For paraffin section, bone samples were processed with Sakura Tissue Tek VIP 5 Tissue Processor (Sakura America, Torrance, CA), and paraffin sections were cut in 5 um thickness. Sections were deparaffinized with xylene, followed by Alcian Blue/Hematoxylin/Orange G staining. For frozen section, bone samples were processed with the CryoJane tape-transfer system. Sections were blocked with Power Block™ Universal Blocking Reagent for 30 minutes to 1 hour and then stained overnight with rabbit-anti-Aggrecan (Millipore, 1:300), rabbit-anti-Perilipin (Cell Signaling, 1:300) and goat-anti-Osteopontin (R&D, 1:300). Donkey-anti-goat Alexa Fluor 488 and Donkey-anti-goat Alexa Fluor 647 were used as secondary antibodies (all from Invitrogen, 1:300).

Antibodies were diluted with Antibody Diluent Solution (Invitrogen 00-3218). Slides were mounted with FLUORO-GEL (Electron Microscopy Science 1798510), and images were acquired with an Olympus slide scanner.

[00284] Femoral groove surgery. Mice were anesthetized with 2.5% isoflurane, and buprenorphine was administered for analgesia. The skin of the right leg was shaved and scrubbed with alcohol and iodine. A small incision was made in the skin, lateral to the knee joint. After sliding the skin medially for visualization, an internal incision was made medial to the patella, extending into the quadriceps muscle and along the patella tendon to release the tissue. The patella was subluxated laterally, and the distal femur was exposed. The subchondral bone was perforated using a microsaw to penetrate the articular cartilage at the knee joint. The extensor mechanism (quadriceps, patella tendon and patella) was returned to its original anatomical location. The internal incision was sutured with absorbable suture, and the skin sutured with non-absorbable suture.

[00285] Statistics.

[00286] Values are shown as the mean ± s.e.m. All statistical analyses were generated using GraphPad Prism 5 (GraphPad Software). Student's t test was used for comparisons between two groups. Statistical significance was defined as $p < 0.05$.

EXAMPLE B-1

[00287] Functionally distinguished reserve and primed HSCs in mouse bone marrow. To explore the reserve HSC (hereafter rHSC(s)) subpopulation, a cell surface marker was adapted, CD49b (Integrin α2), which can distinguish intermediate-term from permanently long-term HSCs (LT-HSCs) (Benveniste et al., 2010; Qian et al., 2015; Wagers and Weissman, 2005; Yang et al., 2005). Intriguingly, it was found a $CD48^{-}$ $CD49b^{-}$subpopulation which exists only in

conventional LT-HSCs ($CD34^-Flk2^-Lineage^-$ $Sca\text{-}1^+c\text{-}Kit^+$ (LSK) cells) but not in short-term HSCs (ST-HSCs; $CD34^+FLK2^-LSK$) or multipotent progenitor cells (MPPs; $CD34^+FLK2^+LSK$). It was proposed that the $CD48^-$ $CD49b^-$ LT-HSCs subpopulation enriches rHSCs and that the $CD48^-CD49b^+$ LT-HSCs subpopulation enriches primed HSCs (hereafter pHSC(s)) (Fig. 17A) and tested with a repopulation assay. It was found that both rHSCs and pHSCs supported hematopoiesis in lethally irradiated mice for up to 40 weeks after transplantation without significant difference (Fig. 17B), consistent with a previous report (Benveniste et al., 2010). However, transplanted pHSCs had very low efficiency in generating rHSCs (95.4% reduction) as well as ST-HSCs and MPPs (~78% reduction for both populations) in recipients compared to transplanted rHSCs, suggesting that rHSCs hierarchically precede pHSCs (Fig. 17C). Using the Scl-tTA-induced H2B-GFP label-retaining model, it was found that rHSCs significantly enriched more H2B-GFP^{high} cells compared to pHSCs (P=0.0039), indicating that rHSCs have slower cell cycle compared to pHSCs (Fig. 17D). Molecularly, it was found that rHSCs had higher expression of *Gadd45g*, *Cdkn1c (encoding p57),* and *Foxo1* that are all involved in maintaining G_0 phase of HSCs, and lower expression of cell cycle activators such as *Myc, Pcna, Ccng2,* and *Cdk4*. There was no difference in Ki67 expression between rHSCs and pHSCs, indicating that Ki67 expression alone is insufficient to distinguish the two HSC subpopulations (Fig.17E).

[00288] Because the functional definition for rHSC is drug-resistance, rHSCs or pHSCs were transplanted into recipient mice and the mice were challenged with 5FU at 4 weeks post transplantation. As shown in Figure 17F, rHSCs were insensitive to 5FU treatment; however, pHSCs dramatically reduced their reconstitution ability (44% reduction at 20 weeks post transplantation). Taken

together, the data indicated that $CD48^{-}CD49b^{-}$ LT-HSC indeed enriched rHSCs that were resistant to chemotherapeutic treatment, whereas $CD48^{-}CD49b^{+}$ LT-HSC enriched pHSCs that were sensitive to chemotherapy; furthermore, the former gave rise to the latter but not vice versa in the transplantation assay.

[00289] The direct consequences of acute 5FU challenge on rHSCs and pHSCs were further analyzed. As shown in Fig. 17G, at 3 days post 5FU, around 92% of pHSCs were eliminated and only rHSCs survived, suggesting that rHSCs must have specifically turned on their DNA repair system to overcome the chemotherapeutic stress. To test this hypothesis, the transcriptome profiling of DNA damage response genes in rHSCs, pHSCs and rHSCs post 5FU treatment was analyzed. It was observed that rHSCs maintained a lower expression of genes involving the DNA damage repair system compared to pHSCs during homeostasis (Fig. 17H), but that most DNA repair pathways, such as DNA mismatch repair (MMR), nucleotide excision repair (NER), base excision repair (BER), and homologous recombination, (HR) were significantly activated in rHSCs under 5FU challenge (Fig. 17I). Furthermore, in parallel, a great number of stress response genes (Rodina et al., 2016), which primarily belong to Hsp90 and Hsp70 family, were also upregulated (1.8 ± 0.17-fold and 1.4 ± 0.1-fold respectively) (Fig. 17J), which partially explained how rHSCs survived and reconstituted the hematopoietic system under chemotherapeutic stress.

[00290] Taken together, the coexistence of pHSCs and rHSCs were functionally demonstrated in BM. Even with their quiescent state and active DNA-repairing pathways, pHSCs were still sensitive to chemotherapy, whereas rHSCs activated their DNA damage repair and stress response genes to survive

chemotherapeutic stress and give rise to pHSCs; thus, rHSCs play a critical role in supporting hematopoietic regeneration under severe stress.

Example B-2

[00291] Drug-resistant rHSCs predominantly localize in the endosteal region of bone marrow

[00292] Whether extrinsic mechanisms from the BM niche contributed to rHSC maintenance during hemostasis and under chemotherapeutic stress was further examined. To this end, whole mount HSC staining was performed, which simultaneously detected the relative distribution of rHSCs and pHSCs to bones (achieved by second-harmonic generation, SHG), megakaryocytes (MKs) or vessels within ~75μm thickness bone cavity (Fig. 18A-B). Our quantification data showed that 43.4% rHSCs and 31.0 % pHSCs were located within 10μm distance from vessels, and that 22.6% rHSCs and 24.6% pHSCs were located within 10μm from MKs (Fig. 18C-D), consistent with previous reports that the bulk of the HSC population resides in perivascular and sinusoid zones (Acar et al., 2015; Bruns et al., 2014; Chen et al., 2016; Zhao et al., 2014). Interestingly, it was noticed that 16.4% rHSCs compared to only 3.69% pHSCs located within 10μm from the bone surface (Fig. 2E). These data showed that both rHSCs and pHSCs were unbiasedly distributed to vessels and MKs, but that rHSCs were located significantly closer to endosteal bone surface compared to pHSCs (P=0.00182).

[00293] To test whether the endosteal region preserved rHSCs during chemotherapeutic stress, the distribution of rHSCs was examined at day 3 post 5FU treatment when pHSCs were eliminated (Fig. 18B). Interestingly, we found that ~55% of surviving rHSCs were preserved by the endosteal niche upon acute 5FU stress, which is a ~3.5-fold enrichment compared to homeostasis (Fig. 18E). However, there

was no significant difference in frequency of surviving rHSCs observed near vessels or MKs (Fig. 18C-D). Consistently, it was observed that only 4.24% of pHSCs survived acute 5FU stress as shown in Figure 17G. Next, the dynamic process of BM damage and the subsequent recovery after 5FU stress was studied by examining the BrdU-labeled surviving and proliferation cells. It was noticed that at day 2 post 5FU treatment, there was a large loss of the BrdU-labeled cells, indicating an active apoptosis induced by 5FU. At day 3 post 5FU treatment, it was observed that surviving $BrdU^+$ cells (mostly single cells) were mainly detected adjacent to bone lining cells in the endosteal region (Fig. 24A-D). At day 3.5, it was observed that pairs of $BrdU^+$ cells appeared at the endosteal surface, indicating activation and division of surviving cells. Starting and continuing at days 4 and 5, the number of proliferating cells gradually increased, and these cells were very often detected as clusters close to either vessels or potential adipocyte structures (~55% at day 4 and ~65% at day 6) (Fig. 24E-I). This observation suggested that bone surface was the niche where cells post 5FU initially survived. These cells were then activated and gave rise to daughter cells, the latter of which underwent expansion mainly in vessels or adjacent to megakaryocytes (Zhao et al., 2014). It was further confirmed that surviving 5FU-rHSCs were indeed detected often as single cells adjacent to the bone surface, and proliferating HSCs often associated with MKs or near the vessels. Surviving rHSCs (green, CD150+ Lin- CD49b-) at day 3 post 5FU treatment were often detected as single cells adjacent to the bone surface (white, SHG), and proliferating HSCs were often associated with MKs (CD150+ Lin+) or near the vessels (red, CD31+) (Fig. 29).

[00294] $N\text{-}cad^+$ pre-osteoblastic cells in bone surface have been found resistant, whereas Osx^+ osteoblasts have been found to be sensitive to 5FU

treatment and N-cad$^+$ stromal cells have been found to give rise to Osx$^+$ osteoblasts during recovery post 5FU treatment (Sugimura et al., 2012). A recent study showed dramatic depletion of LepR$^+$ stromal cells in central marrow due to cell death 1 day following irradiation (Zhou et al., 2017). To track the early changes in vascular and endosteal niches, an apoptotic assay was performed at day 1 post 5FU treatment. It was found that the apoptotic CD31$^+$VE-cadherin$^+$ cells greatly increased 1 day post 5FU (Fig. 18F), consistent with previous reports of disrupted blood vessel structure post 5FU (Dominici et al., 2009; Sugimura et al., 2012). To study the endosteal niche, the *N-cad-tdTomato* (*N-cad-TdT*) mouse line was established in which the Tomato$^+$ cells report N-cad expression in both central marrow and bone surface (Fig. 24J). A marked increase of apoptotic N-Cad driven Tomato$^+$ cells in the central marrow was noticed, whereas the Tomato$^+$ cells in endosteal zone remained stable 1 day post 5FU (Fig. 18G). At day 3 post 5FU treatment when hematopoietic regeneration started, N-Cad driven Tomato$^+$ cells in central marrow as well as in bone surface increased by 2.2-fold and 1.7-fold respectively (Fig. 18H, Fig. 24K). The number of CD31$^+$ vessel cells also increased but showed a dilated and damaged architecture (Fig. 18I). Taken together, previous reports and this data showed that vessels and associated stromal cells in the perivascular niche, including LepR$^+$ and N-cad$^+$ cells, suffered immediate damage and were sensitive to 5FU stress, whereas N-cad$^+$ endosteal stromal cells remained stable.

[00295] The data partially explain previous findings that most HSCs are predominantly distributed in perivascular and sinusoidal zones (Acar et al., 2015; Chen et al., 2016; Kunisaki et al., 2013). pHSCs which account for 51.3% of the quiescent HSC population are near perivascular and sinusoid zones in homeostasis. Under stress, however, rHSCs reside closer to the bone surface survive

chemotherapeutic stress. Collectively, the data indicate that the endosteal niche plays a critical role in protecting rHSCs from chemotherapy.

Example B-3

[00296] N-Cad$^+$ niche cells maintain functional HSCs including rHSCs in bone marrow

[00297] Though N-cad$^+$ stromal cells were the first identified HSC niche cells, and though N-cad$^+$ stromal cells at the endosteal niche were resistant while Osx$^+$ osteoblasts were sensitive to chemotherapy, a direct evidence for N-cad$^+$ functionally supporting HSCs was still missing due to lack of proper genetic mouse lines. According to aspects herein, the *N-cad-CreER^T* line was generated (Fig. 25A) and showed that N-cad$^+$ stromal cells gave rise to both Col2.3-GFP$^+$ osteoblastic cells and perivascular cells (Fig. 25B). A previous study showed that depleting the mature Col2.3-GFP$^+$ osteoblasts did not affect overall engraftment of BM cells (Ding et al., 2012; Greenbaum et al., 2013), but only caused impaired regenerative capacity of a subset of LT-HSCs (Bowers et al., 2015). Though N-cad$^+$ stromal cells developmentally proceed Osx$^+$ osteoprogenitor cells, which further give rise to mature Col2.3$^+$ osteoblasts, a functional contribution to HSC maintenance by N-cad$^+$ stromal cells is unknown. To investigate the HSC niche role of N-cad$^+$ cells, *N-cad-CreER^T* induced DTR (encoding diphtheria toxin receptor) line (*N-cad-CreER^T;iDTR*) was generated, in which N-cad$^+$ niche cells were rendered sensitive to diphtheria toxin (DT). Three tamoxifen (TMX) injections were administered and followed with intraperitoneal injections of DT (one injection every other day) to the *N-cad-CreER^T;iDTR* mice and analyzed them on the first day after the last injection (Fig. 19A). The efficient ablation was observed of N-cad$^+$ stromal cells in *N-cad-CreER^T;iDTR*; *R26-tdT* compared to *N-cad-CreER^T*; *R26-tdT* mice treated

concurrently with DT (Fig. 19B). Whether N-cad$^+$ cell ablation would affect HSCs *in vivo* was further examined. After ablating N-cad$^+$ cells, no significant change was observed of cellularity in BM compared to controls (Fig. 19C). However, the numbers of HSCs were dramatically reduced: rHSCs (65.0% reduction), pHSCs (60.0% reduction), ST-HSCs (59.6% reduction), and MPPs (29.3% reduction) (Fig. 19D). This indicated that N-cad$^+$ niche cells contributed to the most primitive, including reserve, HSC maintenance.

[00298] A transplantation assay was also performed to test the functional HSC numbers in N-cad$^+$ stromal cell ablated mice. It was found that bone marrow cells from N-cad$^+$ stromal cell ablated mice gave significantly lower levels of donor cell reconstitution (28.3% reduction at 20 weeks) (Fig. 19E) with reduced myeloid cell production (24.5% to 17.1%) (Fig. 19F). To further investigate whether N-cad$^+$ niche cells contributed to maintaining the long-term self-renewal of HSCs, a secondary transplantation was conducted at 20 weeks post the primary transplantation. It was observed that BM cells from the N-cad$^+$ stromal cell ablated mice had deeper reduction of donor cell reconstitution capacity in the secondary transplantation (40.5% reduction at 16 weeks) (Fig. 19G), although they were capable of multilineage reconstitution (Fig. 19H).

[00299] Furthermore, we found that conditional knockout of *Cxcl12* from N-cad$^+$ stromal cells significantly reduced pHSCs (48% reduction) and ST-HSCs (28.8% reduction), but no significant reduction was observed in rHSCs. There was a slight albeit insignificant increase of MPPs. (Figure 19I). Conditional deletion of *SCF* from N-cad$^+$ stromal cells significantly reduced rHSCs (60% reduction), pHSCs (38.6% reduction), and ST-HSCs (53.7% reduction), but with a slight increase in MPPs (Figure 19J). Overall, we provided the first functional evidence that N-cad$^+$

niche cells contributed to HSC maintenance, including rHSCs, via producing maintenance factors.

Example B-4

[00300] Transcriptome analysis for hematopoietic cells and their BM niche cells

[00301] To understand the molecular mechanisms governing how different niche cells contribute to HSC subpopulation regulation, a transcriptome profiling analysis was performed on 4 types of hematopoietic stem and progenitor cells (HSPCs) during homeostasis and on rHSCs at day 3 post 5FU, as well as on 10 types of BM niche cells. The BM niche cells were harvested from different niche zones of endosteum (B) and central bone marrow (M) (Fig. 26A-B). The pearson distance tree and principal component analysis (PCA) data showed that rHSCs and pHSCs shared a unique transcriptome profiling compared to ST-HSCs and MPPs (Fig. 20A). Interestingly, rHSCs post 5FU treatment appeared to be closer to pHSCs (Fig. 20B), suggesting that surviving rHSCs were primed for activation to support subsequent hematopoietic regeneration post chemotherapy.

[00302] It was found that the rHSCs enriched most of the published HSC specific markers, such as *Slamf1* (*CD150*), *H19, Ctnnal1* (*α-Catulin*), *Fgd5, vWF, Tek*(*Tie2*), *Procr*(*Epcr*), *Hoxb5* and *Meg3* (or *Gtl2*) (Acar et al., 2015; Chen et al., 2016; Qian et al., 2015; Sanjuan-Pla et al., 2013; Venkatraman et al., 2013). Particularly, vWF in rHSCs were 6.1-fold higher than in pHSCs, suggesting that rHSCs enriched most of the vWF^+ HSCs which reside at the apex of the HSC hierarchy (Sanjuan-Pla et al., 2013). Consistently, progenitor signature genes such as *CD34, CD48*, and *Flt3(Flk2)* and *Itga2* (*CD49b*) had low expression in rHSCs (Acar et al., 2015; Chen et al., 2016; Gazit et al., 2014). Interestingly, rHSCs post

5FU had high expression levels of *CXCR4*, *Ctnnal1* (*α-Catulin*)(Park et al., 2002), *Esam* (Endothelial cell-selective adhesion molecule) and *CD150* (encoding *Slamf1*, signaling lymphocytic activated molecule), consistent with their functions associated with the converted primed state (Fig. 20E).

[00303] In niche cell analysis, it was found the N-cad driven tdTomato (N-cad-TdT) (M) had a very similar transcriptome profile compared to other niche cells with mesenchymal stem cell (MSC) potential such as LepR, Cxcl12-RFP, and Nestin-GFP cells in both pearson distance tree (Fig. 20C) and PCA analysis (Fig. 20D), suggesting that N-cad$^+$ cells might have MSC potential and similar function in regulating HSCs. Interestingly, NG2-RFP cells had a very similar transcriptome profile to Col2.3-GFP$^+$ osteoblasts (Fig. 20C-D). It was also found that NG2-RFP cells were predominantly restricted to endosteum in the epiphysis or diaphysis, though they were also detected in the peri-arterial region (Fig. 26C).

[00304] It was found that *Pecam* (CD31), *CDH5* (VE-cadherin) were enriched in Pecam-GFP$^+$ endothelial cells. *PF4* and *Adgre1* were enriched in MKs and macrophages (Macs). *Cspg4* (*NG2*) was enriched in NG2-RFP cells. Nestin-GFP cells did not have endogenous *Nestin* (*Nes*) expression, consistent with previous reports (Ding et al.,2012; Greenbaum et al., 2013). Interestingly, it was found that several marker genes such as *Kitl* (*SCF*), *LepR*, *Cdh2* (N-cadherin, *N-CAD*), *Cxcl12*, *Pdgfrα* were broadly expressed in perivascular niche cells (Fig. 20F). N-cad-TdT(B) cells isolated from the endosteal zone also had high levels of *SCF, Cxcl12, LepR* and *Pdgfrα* expression compared to other cells from the endosteal zone, such as Col2.3-GFP and NG2-RFP cells (Fig. 20F). Our GO term analysis showed that Col2.3-GFP, Pecam-GFP, MK and Mac cells highly enriched RNA metabolism, protein metabolism, other metabolism pathways and translation activities, indicating

that these cells were in a relatively active functional state compared to N-cad-TdT cells and other perivascular zone cells which were in a relatively lower metabolic state. Endothelial cells and perivascular cells had immune system process and stress response activities (Fig. 20G). Because N-cad$^+$ cells had transcriptome profiles similar to other MSCs such as LepR$^+$, Cxcl12-RFP, and Nestin-GFP cells, we next analyzed and compared stromal development related genes from different niche cells (Fig. 20H). It was found that Col2.3-GFP cells enriched osteoblast gene Col1a and progenitor cell gene *Ly6a* (*SCA1*) (Yang et al., 2014). N-Cad-TdT(B) cells from the endosteal region enriched chondrocyte genes *Spock1*, *Col2a1* and *Col1a2* and bone development genes such as *Tnc*. Interestingly both N-Cad-TdT(B) and N-Cad-TdT(M) enriched most of the mesenchymal stem and progenitor cell (MSPC) genes such as *Prrx1*, *Pdgfrβ*, *Pdgfrα*, *Sp7*, *Sox9* and *Grem1*. Marrow harvested NG2-RFP cells also had higher levels of MSPC gene expression, such as *Alcam*, *Sp7*, *Mcam*, *Sox9* and *Gli1*, but with high level osteoblast and chondrocyte related genes such as *Col1a1*, *Col2a1*, and *Col1a2*. It was also found that among all perivascular niche cells, LepR$^+$ cells exclusively enriched *Gla* as well as several osteoblast and chondrocyte markers such as *Atf4* and *Tnc*. Cxcl12-RFP cells significantly enriched MSPC gene *Itgav*. Furthermore, *Grem1* was enriched in N-Cad-TdT(B) and in all perivascular niche cells but not in NG2-RFP cells.

[00305] Consistent with earlier data, Col2.3-GFP cells were enriched for more mature osteo-lineage genes (*Dmp1, Col1a1, Spp1, Bglap*). Nestin-GFP, Cxcl12-RFP and LepR were consistent with their known role in enriching MSC genes (*Prrx1, Pdgfrα, Itgb1, Grem1* (Fig. 20H). Interestingly, apart from expressing MSC genes, N-Cad-TdT(M) and N-Cad-TdT(B) were enriched for chondrogenic (*Sox9, Col2a1* and *Tnc*), adipogenic (*Cebpα, Pparγ, Adipoq*) and osteogenic (*Col1a1,*

Runx2) genes, suggesting a tri-potential nature of N-Cad$^+$ stromal cells. Surprisingly, NG2-RFP was enriched for both bone development genes (*Dmp1, Bglap, Sp7, Runx2, Col1a1*) and chondrogenic genes (*Sox9, Col2a1 and Tnc*), suggesting an osteo-chondrogenic role (Fig. 26D-E). These data strongly indicated the heterogeneity of the MSPCs in BM.

Example B-5

[00306] *N-cad-CreER^T* induced reporter cells largely overlap with LepR$^+$ and Cxcl12$^+$ stem/stromal cells

[00307] To confirm the transcriptional analysis, N-cad *in vivo* lineage tracing was performed using the *TdT* or *ZsG* reporter, and found that, at day 3 post induction, *N-cad-CreER^T* lineage traced cells partially overlapped with Cxcl12-RFP and Nestin-GFP cells (Fig. 20I). Moreover, 98.3% and 97.9% *N-cad-CreER^T* derived cells were positive for LepR and Pdgfrα expression respectively (Fig. 20J). This result further supported that N-cad$^+$ stromal cells have MSC potential as suggested by the transcriptome analysis. To analyze the lineage potential of N-cad$^+$ stromal cells, colony-forming unit-fibroblasts (CFU-F) assay was performed to test their proliferating capacity. It was found that the majority of reported niche cells, whether from endosteal zone or from perivascular zone, had one out of fewer than 10 cells with CFU-F activity, apart from Nestin-GFP$^+$ cells, which had only one out of 17.6 cells with CFU-F activity. N-cad$^+$ cells from bone had one cell with CFU-F activity out of 8.79 cells. *N-cad-CreER^T* derived bone cells had 1 in 10.7 cells with CFU-F activity, and *N-cad-CreER^T* derived marrow cells had 1 in 7.37 cells. (Fig. 20K). Most CFU-F colonies maintained tdTomato signals (Fig. 21A-B), suggesting that N-cad$^+$ cells were the main source of MSPCs with CFU-F activity.

Example B-6

[00308] N-cad$^+$ stromal cells give rise to osteoblasts, chondrocytes, and adipocytes *in vitro* and *in vivo*

[00309] To test the MSC potential of N-cad$^+$ cells, *in vitro* differentiation assay was performed by splitting cells obtained from individual CFU-F colonies formed by N-cad$^+$ cells into three aliquots and sub-cloned them into cultures permissive for bone, fat, or cartilage cell differentiation. It was found that Tomato$^+$ cells underwent multilineage differentiation, giving rising to Alkaline phosphate-positive osteoblastic cells, Oil-red-O-positive adipocytes, and Aggrecan-stained and Toluidine-blue-positive chondrocytes (Fig. 21C-E).

[00310] To characterize *in vivo* function of N-cad$^+$ stromal cells, the dynamic anatomical distribution of N-cad derived cells was analyzed after one dose of TMX treatment (Fig. 21F, G). Interestingly, detected N-cad derived cells were detected in metaphysis of trabecular as early as 6 hours post TMX, but only very few cells were seen in central marrow, suggesting that a large portion of N-cad$^+$ cells originated from the endosteal region (Fig. 21H). It was also observed that the number of N-cad derived cells increased by 2.2 ± 0.2-fold in trabecular bone region from 1 to 2 weeks post TMX treatment and remained stable afterwards; in cortical bone region, the cell number increased by 2.95 ± 0.2-fold at 2 weeks post TMX, but then declined at 6 weeks post TMX, suggesting that N-cad$^+$ cells in trabecular bone region were more quiescent compared to cortical bone region. Moreover, N-cad derived cells continuously increased in central marrow up to 6 weeks, suggesting that N-cad derived cells might be proliferating and differentiating within this area (Fig. 21I).

[00311] Next, an *in vivo* lineage tracing assay was performed and it was observed that N-cad$^+$ cells generated Col2.3-GFP$^+$ osteoblasts (Dacic et al., 2001) in a time dependent manner (Fig. 22A, Fig. 27A-B). N-cad-derived osteoblasts were

detected in the peri-trabecular region as early as 6 hours post TMX induction (Fig. 22B) and in the compact bone region at 14 hours post TMX induction (Fig. 22C). Further analysis showed that at 6 hours post TMX, immature N-cad$^+$ Col2.3$^-$ cells (1.1% ± 0.2%) were 10-times more enriched in trabecular bone region compared to cortical bone region (0.11% ± 0.04%) (Fig. 22D, E). Consistently, more immature N-cad$^+$Col2.3$^-$ cells were enriched in trabecular bone region compared to compact bone region at 24 hours and 2 weeks post TMX induction (Fig. 22F). At 4 weeks post TMX induction, a large portion of Col2.3-GFP cells (72% ± 6%) were derived from N-cad$^+$ cells (Fig. 22G).

[00312] It was further observed that at 4 weeks post TMX injection, N-cad$^+$ stromal cells generated adipocytes in the trabecular bone region, particularly the endosteal cells, (Fig. 22H), and this was further confirmed by BODIPY lipid probe staining (Fig. 22I). Interestingly, the frequency of N-cad$^+$ derived adipocytes increased quickly initially and declined later on, as evidenced by the quantification that 39.3% ± 4.5%, 77.1% ± 6.7% and 17.2% ± 3% of N-cad$^+$ derived cells were observed at 6, 14 and 24 hours respectively after TMX induction, suggesting that adipocytes might have a frequent turnover rate (Fig. 22J-K, Fig. 27C-E). Collectively, the data demonstrated that N-cad$^+$ stromal cells generated both osteoblast and adipocyte lineages *in vivo* during homeostasis in adult mice.

[00313] Furthermore, it was found that Ncad+ MSCs were enriched > 10-fold as compared to other markers. For example, as shown in Fig. 30, just 10K Ncad+ hMSCs produced even higher human thrombopoietin (THPO or TPO) than total hMSCs *in vivo.* Similarly, Ncad- hMSCs exhibited a function similar to the total hMSCs. Accordingly, isolating MSC with N-cadherin antibodies can provide for enrichment of the MSC population.

Example B-7

[00314] N-cad$^+$ stromal cells give rise to chondrocytes during development and post injury

[00315] Chondrogenesis is active in fetal development and rarely active in adulthood (Raghunath et al., 2005; Sophia Fox et al., 2009). In mice with TMX induction at postnatal day 2 (P2), no Tomato expression was detected among Aggrecan$^+$ chondrocytes in the femur of *N-cad-CreER^T; R26-tdT* mice (Fig. 28A) despite Tomato$^+$ osteoblasts and perichondrocytes being adjacent to the growth plate. After *N-cad-CreER^T; R26-tdT* mice were induced with TMX at 1 or 2 weeks when the growth plate develops, Tomato$^+$ chondrocytes in cartilages of femur or tibia remained undetectable (data not shown). TMX induction was started to *N-cad-CreER^T; R26-tdT* mice at embryonic stage E12.5, when MSCs were undergoing condensation and chondrocyte differentiation in the fetal bone (Fig. 23A). It was found that the majority of undifferentiated N-cad derived tdT$^+$ cells were located peripherally, with differentiated N-cad derived Tomato$^+$ chondrocytes located in the central region of the rib at E14.5 embryos (Fig. 23B). Importantly, in the trabecular region of femur at P2, N-cad derived chondrocytes were detected in both the columnar zone where the secondary ossification center forms, and in the superficial zone, which is imperative to resist the sheer force for deeper layer protection (Fig. 23C, D). Consistently, N-cad derived adipocytes were detected at 2 months and up until 10 months after birth (Fig. 23E, Fig. 28B), suggesting that N-cad + cells contributed to early and long-term adipogenesis during development. However, N-cad$^+$ cells derived Osteopontin$^+$ osteoblast and osteocyte were detected at 2 months after birth but not at early P2 (Fig. 23F, Fig. 28C). These data demonstrated that

embryonic N-cad-derived cells gave rise to all three osteo-adipogenic-chondrogenic lineages, and only N-cad$^+$ at embryonic stage could efficiently form chondrocytes.

[00316] Whether N-cad$^+$ cell could generate chondrocytes in adult mice post injury was next investigated. Cartilage perforation was performed in *N-cad-CreER^T; R26-tdT* mice that received TMX induction at E12.5 (Fig. 23G). At 2 to 3 weeks post cartilage damage, we found that N-cad derived chondrocytes were clustered in the callus at the damage site with a 2-fold increase compared to undamaged control mice (Fig. 23H-I). The femorotibial joint was swollen due to articular cartilage damage in mice post-surgery (Fig. 28D). Alcian blue positive cells with a typical chondrocyte feature were dramatically increased in the post injury region (Fig. 23J), indicating that N-cad$^+$ MSCs quickly regenerated chondrocytes in response to injury.

[00317] Taken together, the data proved that N-cad-derived cells induced at the fetal stage (E12.5) could give rise to chondrocyte progenitor in adults and support chondrocyte regeneration in response to injury.

[00318] Discussion

[00319] rHSCs vs. pHSCs

[00320] The heterogeneity of HSCs has been widely studied. HSCs can be maintained in either active, quiescent or deeply quiescent states. It is well known that the quiescence characterization of HSCs is functionally related to their long-term self-renewal potential (Foudi et al., 2008; Wilson et al., 2008). However, how the quiescent HSC population overcomes the consequence of myeloablation *in vivo* is an unanswered question. In spite of their quiescence, the majority of HSCs cannot survive chemotherapeutic stress such as 5FU (Longley et al., 2003). According to aspects herein, it was found that a small portion of the HSC subpopulation could survive 5FU treatment in primary mice and were resistant to 5FU treatment in

transplantation model. Thus, this HSC subpopulation is defined as rHSCs, while other quiescent but chemotherapeutic sensitive HSC subpopulations are defined as pHSCs (Li and Clevers, 2010). Although both HSC subpopulations supported long-term hematopoiesis in transplantation experiments, pHSCs rarely gave rise to rHSCs, whereas the latter were able to give rise to pHSCs. Mechanistically, it was found that rHSCs have an attenuated DNA repair system compared to pHSCs during homeostasis, but rHSCs can quickly activate their DNA repair pathways and the stress-response program to survive chemotherapeutic stress, and support subsequent hematopoiesis to overcome the consequence of myeloablation.

[00321] Niche matters in term of conferring resistance to chemotherapy

[00322] To explore an extrinsic mechanism underlying the chemo-resistance of rHSCs, an idea was tested that they were preserved in a specific microenvironment in BM. Using whole mount HSC staining (Kunisaki et al., 2013), it was first observed that the bulk of HSCs were associated with vessels and MKs as previously reported. However, it was surprisingly found that the rHSCs were predominantly associated with the endosteal niche compared to pHSCs during homeostasis and post 5FU treatment. This indicated that the endosteal niche could form a distinct BM microenvironment to protect rHSCs from chemotherapeutic stress. Consistently, upon chemotherapeutic stress, most rHSCs were protected in the endosteal niche that enriches chemo-resistant N-cad$^+$ stromal cells, whereas the vessel and perivascular cells were sensitive to 5FU treatment, accounting for a large loss of pHSCs induced by chemotherapy. The whole mount HSC staining was done in sternum which has abundant bone branches and extensions inside the marrow. This feature makes it very similar to the trabecular bone region in the femur. The transplantation assay showing that depletion of N-cad$^+$ niche cells affected HSC

maintenance, including rHSCs, supports this notion. HSC quiescence also correlated with their low metabolic state, which may be considered analogous to 'sleeping', and was termed as HSC dormancy or hibernation (Takubo et al., 2013; Wilson et al., 2008; Yamazaki et al., 2011). However, it was further showed according to aspects herein that quiescence was not the only mechanism underlying drug resistance; instead, both the intrinsic stress-response program and the extrinsic niche protection contributed to drug resistance.

[00323] Identity and function of N-cad stromal cell in HSC maintenance in the BM niche

[00324] N-cad$^+$ stromal cells were the first identified HSC niche cells (Zhang et al., 2003) and confirmed by subsequent studies (Arai et al., 2004; Sugiyama et al., 2006). N-cad$^+$ cells were initially proposed as osteoblastic progenitor cells based on their endosteal location. According to apects herein, by using two reporter lines, it was found that N-cad$^+$ stromal cells were distributed in both endosteal region and perivascular sites. More intriguingly, it was found that the majority of N-cad$^+$ cells overlapped with LepR$^+$ cells and Pdgfrα$^+$ cells. Transcriptional analysis showed that N-cad$^+$ cells, LepR$^+$ cells, Cxcl12-RFP (CAR) cells and Nestin-GFP cells had a very similar gene expression pattern. The data strongly indicated that the long-standing controversy of HSC niche concepts might very likely be due to different cell markers being used rather than to their cellular identities.

[00325] To determine the identity of N-Cad$^+$ stromal cells, their regional distribution was visualized relative to other known niche cells in the bone marrow using different niche reporter mice. N-Cad$^+$ stromal cells generated 72% ± 6% Col2.3-GFP$^+$ cells; however, 9.3% ± 4.7% N-cad$^+$Col2.3GFP$^-$ cells were also detected in the endosteal region. These immature cells accounted for the primitive MSCs, which could

explain the insufficient efficiency of Col2.3-Cre genetic model in HSC niche function studies (Ding and Morrison, 2013; Ding et al., 2012; Greenbaum et al., 2013). Though both N-Cad-TdT$^+$ and Nestin-GFP$^+$ were enriched in the trabecular region, N-Cad-TdT$^+$ was concentrated in the trabecular region where engraftment of transplanted HSCs was detected as previously reported (Nilsson et al., 2001; Xie et al., 2009) and survived after stress as observed here. All these data indicated that although N-cad$^+$ cells share a similar transcriptome profile with other MSCs, their anatomic distribution may indicate their unique HSC niche function; indeed, it was shown that the N-cad$^+$ endosteal niche cell plays a critical role in preserving rHSCs.

[00326] By using an inducible DTR system, it was found that ablation of N-cad$^+$ cells eliminated both pHSCs and rHSCs in BM. This could be explained by the anatomical distribution of N-cad$^+$ niche cell in both endosteal and perivascular zones. Furthermore, it was shown that N-cad expression could be detected in a subset of HSCs; however, the *N-cad-TdT* reporter mouse lines did not support this observation (data not shown). This could be partially explained by the inconsistency between their protein and transcription levels, because another mouse line of N-cad-mCherry (fusion at protein level) indeed had a small subset of HSCs (CD49b$^-$CD34$^-$Flt2$^-$LSK) showing a low level of N-cad expression (primary observation). The functional transplantation data showed that ablation of N-cad$^+$ niche cells resulted in the reduced HSCs including rHSCs. By deletion of Cxcl12 and SCF from N-cad$^+$ cells, it was found N-cad$^+$ stromal cells contributed to HSC maintenance and regulation by producing these two factors. Overall, aspects herein demonstrate that N-cad$^+$ stromal cells function as MSCs and support primitive HSC maintenance, especially under stress.

[00327] Transplantation of hematopoietic stem cells (HSCs) from human umbilical cord blood (hUCB) holds great promise for treating a broad spectrum of hematological disorders including cancer, but the limited number of HSCs in a single hUCB unit can restrict its widespread use. Although extensive efforts have developed multiple methods for *ex vivo* expansion of human HSCs by targeting single molecules or pathways, it has been unknown whether simultaneously manipulating a large number of targets essential for stem cell self-renewal could be achievable. Recent studies have emerged that N^6-methyladenosine (m^6A) modulates expression of a group of mRNAs critical for stem cell fate determination by influencing their stability. Among several m^6A readers, Ythdf2 is well recognized to promote the targeted mRNA decay. However, the physiological functions of Ythdf2 on adult stem cells are still elusive. Embodiments herein demonstrate that conditional knockout (KO) mouse *Ythdf2* increased phenotypic and functional HSC numbers, but neither skewed lineage differentiation nor led to hematopoietic malignancies. Furthermore, knockdown (KD) of human *YTHDF2* led to over 10-fold increase in *ex vivo* expansion of hUCB HSCs, 5-fold increase in colony-forming units (CFUs), and more than 8-fold increase in functional hUCB HSCs in the 2 rounds of limiting dilution transplantation assay. Mechanistically, m^6A mapping of RNAs from mouse hematopoietic stem and progenitor cells (HSPCs) as well as from hUCB HSCs revealed m^6A enrichment on mRNAs encoding transcription factors critical for stem cell self-renewal. These m^6A-marked mRNAs were recognized by Ythdf2 and underwent mRNA decay. In *Ythdf2* KO HSPCs and *YTHDF2* KD hUCB HSCs, these mRNAs were stabilized, leading to an increase in protein levels and facilitating HSC expansion which can be rescued by knockdown the mRNA, such as *Tal1* mRNA. Therefore, embodiments show the function of Ythdf2 in adult stem cells maintenance

and identify an important role of Ythdf2 in regulating HSC *ex vivo* expansion via the mechanism of controlling the stability of multiple mRNAs critical for HSC self-renewal, thus having a strong potential for future clinical applications.

[00328] Furthermore, regulation of hematopoietic stem cells (HSCs) by the bone marrow (BM) niches has been substantially studied; however, whether and how HSC subpopulations are distinctively regulated by different BM niches remain largely unclear. Here, reserve HSCs (rHSCs) have been functionally distinguished from primed HSCs (pHSCs) and their respective BM niches have been further examined. It has been found that both pHSCs and rHSCs could support long-term hematopoiesis under homeostasis; however, pHSCs were sensitive to chemotherapy, whereas rHSCs survived chemotherapy and supported subsequent regeneration after myeloablation. The whole-mount HSC distribution study revealed that rHSCs were preferentially maintained in the endosteal region that enriches N-cadherin$^+$ bone-lining cells during homeostasis and post-chemotherapy. pHSCs were predominantly associated with blood vessels which were vulnerable to chemotherapy compared to bone. Transcriptome profiling and *in vivo* lineage tracing results showed N-cadherin$^+$ stromal cells to be functional mesenchymal stem cells, which gave rise to osteoblasts, adipocytes, and chondrocytes during development and regeneration. Finally, it was demonstrated that ablation of N-cadherin$^+$ niche cells or deletion of either *Scf* or *Cxcl12* from N-cadherin$^+$ niche cells affected HSC number and maintenance.

Example C

[00329] **Expansion of CAR-T cells using shRNA**

[00330] The effect of manipulating Ythdf2 on the expansion of CAR-T cells is being assessed using lentivirus driven human Ythdf2 shRNAs. Successful cloning

of YTHDF2 shRNA in a CAR-T lentivector has occurred. The lentivirus has been used to infect human CAR-T cells, and the expansion of the human CAR-T cells is in progress. The expansion is expected to take days to weeks for results. It is believed that significantly enhanced expansion will be demonstrated in the lentivirus-infected CAR-T cell population as compared to a CAR-T control population.

[00331] All sequencing data, including the m^6A-seq, irCLIP-seq and RNA-seq datasets, are available through the Gene Expression Ombibus (GEO) under accession GSE107957.

[00332] Original Data Repository at http://www.stowers.org/research/publications/LIBPB-1248.

[00333]

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TABLE S1

Table S1. Key transcription factors critical for HSC self-renewal and maintenance are labeled by m6A in HSPCs.

Gata2
Gfi1
Pbx1
Lmo2
Etv6
Erg
Runx1
Tal1
Hoxa9
Meis1
Kmt2a
Kmt2b
Kmt2c
Kmt2d
Bmi1
Sox4
Evi1
Stat3
Stat5a
Hoxb4
Zfx
Foxo3
Foxp1

TABLE S2

Table S2. Ythdf2 targeted mRNAs from three irCLIP-seq replicates.

GeneID	Name	Biotype	Description
ENSMUSG00000033793	Atp6v1h	protein_coding	ATPase, H+ transporting, lysosomal V1 subunit H [Source:MGI Symbol;Acc:MGI:1914864]
ENSMUSG00000067851	Arfgef1	protein_coding	ADP-ribosylation factor guanine nucleotide-exchange factor 1 (brefeldin A-inhibited) [Source:MGI Symbol;Acc:MGI:2442988]
ENSMUSG00000005886	Ncoa2	protein_coding	nuclear receptor coactivator 2 [Source:MGI Symbol;Acc:MGI:1276533]
ENSMUSG00000025935	Tram1	protein_coding	translocating chain-associating membrane protein 1 [Source:MGI Symbol;Acc:MGI:1919515]
ENSMUSG00000041859	Mcm3	protein_coding	minichromosome maintenance deficient 3 (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:101845]
ENSMUSG00000033569	Bai3	protein_coding	brain-specific angiogenesis inhibitor 3 [Source:MGI Symbol;Acc:MGI:2441837]
ENSMUSG00000048874	Phf3	protein_coding	PHD finger protein 3 [Source:MGI Symbol;Acc:MGI:2444176]
ENSMUSG00000042215	Bag2	protein_coding	BCL2-associated athanogene 2 [Source:MGI Symbol;Acc:MGI:1891254]
ENSMUSG00000037305	Fam168b	protein_coding	family with sequence similarity 168, member B [Source:MGI Symbol;Acc:MGI:2448487]
ENSMUSG00000037470	Uggt1	protein_coding	UDP-glucose glycoprotein glucosyltransferase 1 [Source:MGI Symbol;Acc:MGI:2443162]
ENSMUSG00000026121	Sema4c	protein_coding	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4C [Source:MGI Symbol;Acc:MGI:1095812]
ENSMUSG00000026113	Inpp4a	protein_coding	inositol polyphosphate-4-phosphatase, type I [Source:MGI Symbol;Acc:MGI:1931123]
ENSMUSG00000037216	Lipt1	protein_coding	lipoyltransferase 1 [Source:MGI Symbol;Acc:MGI:3645211]
ENSMUSG00000026055	Eif3b	protein_coding	eukaryotic translation initiation factor 3B [Source:MGI Symbol;Acc:MGI:2441772]
ENSMUSG00000067138	Aff3	protein_coding	AF4/FMR2 family, member 3 [Source:MGI Symbol;Acc:MGI:106927]
ENSMUSG00000026074	Map4k4	protein_coding	mitogen-activated protein kinase kinase kinase kinase 4 [Source:MGI Symbol;Acc:MGI:1349394]
ENSMUSG00000070939	Tgfbrap1	protein_coding	transforming growth factor, beta receptor associated protein 1 [Source:MGI Symbol;Acc:MGI:2447412]
ENSMUSG00000066877	Nck2	protein_coding	non-catalytic region of tyrosine kinase adaptor protein 2 [Source:MGI Symbol;Acc:MGI:1306821]
ENSMUSG00000048629	1700015D0	protein_coding	RIKEN cDNA 1700015D05 gene [Source:MGI Symbol;Acc:MGI:1914590]
ENSMUSG00000026064	Stk17b	protein_coding	serine/threonine kinase 17b (apoptosis-inducing) [Source:MGI Symbol;Acc:MGI:2138162]
ENSMUSG00000042807	Hecw2	protein_coding	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2 [Source:MGI Symbol;Acc:MGI:2685817]
ENSMUSG00000035321	Ankrd44	protein_coding	ankyrin repeat domain 44 [Source:MGI Symbol;Acc:MGI:2443242]
ENSMUSG00000025982	Sf3b1	protein_coding	splicing factor 3b, subunit 1 [Source:MGI Symbol;Acc:MGI:1932339]
ENSMUSG00000025980	Hspd1	protein_coding	heat shock protein 1 (chaperonin) [Source:MGI Symbol;Acc:MGI:96242]
ENSMUSG00000046924	Mars2	protein_coding	methionine-tRNA synthetase 2 (mitochondrial) [Source:MGI Symbol;Acc:MGI:2444136]
ENSMUSG00000038331	Satb2	protein_coding	special AT-rich sequence binding protein 2 [Source:MGI Symbol;Acc:MGI:2679336]
ENSMUSG00000051223	Bzw1	protein_coding	basic leucine zipper and W2 domains 1 [Source:MGI Symbol;Acc:MGI:1914132]
ENSMUSG00000026031	Cflar	protein_coding	CASP8 and FADD-like apoptosis regulator [Source:MGI Symbol;Acc:MGI:1336166]
ENSMUSG00000026028	Trak2	protein_coding	trafficking protein, kinesin binding 2 [Source:MGI Symbol;Acc:MGI:1918077]
ENSMUSG00000026020	Nop58	protein_coding	NOP58 ribonucleoprotein homolog (yeast) [Source:MGI Symbol;Acc:MGI:1933184]
ENSMUSG00000026782	Abi2	protein_coding	abl-interactor 2 [Source:MGI Symbol;Acc:MGI:106913]
ENSMUSG00000052062	Pard3b	protein_coding	par-3 partitioning defective 3 homolog B (C. elegans) [Source:MGI Symbol;Acc:MGI:1919301]
ENSMUSG00000025967	Eef1b2	protein_coding	eukaryotic translation elongation factor 1 beta 2 [Source:MGI Symbol;Acc:MGI:1929520]
ENSMUSG00000025959	Klf7	protein_coding	Kruppel-like factor 7 (ubiquitous) [Source:MGI Symbol;Acc:MGI:1935151]
ENSMUSG00000062209	Erbb4	protein_coding	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian) [Source:MGI Symbol;Acc:MGI:104771]
ENSMUSG00000050296	Abca12	protein_coding	ATP-binding cassette, sub-family A (ABC1), member 12 [Source:MGI Symbol;Acc:MGI:2676312]
ENSMUSG00000026192	Atic	protein_coding	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase [Source:MGI Symbol;Acc:MGI:1351352]
ENSMUSG00000055322	Tns1	protein_coding	tensin 1 [Source:MGI Symbol;Acc:MGI:104552]
ENSMUSG00000006304	Arpc2	protein_coding	actin related protein 2/3 complex, subunit 2 [Source:MGI Symbol;Acc:MGI:1923959]
ENSMUSG00000006299	Aamp	protein_coding	angio-associated migratory protein [Source:MGI Symbol;Acc:MGI:107809]
ENSMUSG00000026176	Ctdsp1	protein_coding	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 1 [Source:MGI Symbol;Acc:MGI:2654470]
ENSMUSG00000033364	Usp37	protein_coding	ubiquitin specific peptidase 37 [Source:MGI Symbol;Acc:MGI:2442483]
ENSMUSG00000026174	Rqcd1	protein_coding	rcd1 (required for cell differentiation) homolog 1 (S. pombe) [Source:MGI Symbol;Acc:MGI:1928902]
ENSMUSG00000026135	Zfp142	protein_coding	zinc finger protein 142 [Source:MGI Symbol;Acc:MGI:1924514]
ENSMUSG00000033257	Ttll4	protein_coding	tubulin tyrosine ligase-like family, member 4 [Source:MGI Symbol;Acc:MGI:1914784]
ENSMUSG00000045535	Fam134a	protein_coding	family with sequence similarity 134, member A [Source:MGI Symbol;Acc:MGI:2388278]
ENSMUSG00000026211	Obsl1	protein_coding	obscurin-like 1 [Source:MGI Symbol;Acc:MGI:2138628]
ENSMUSG00000026245	Farsb	protein_coding	phenylalanyl-tRNA synthetase, beta subunit [Source:MGI Symbol;Acc:MGI:1346035]
ENSMUSG00000004364	Cul3	protein_coding	cullin 3 [Source:MGI Symbol;Acc:MGI:1347360]
ENSMUSG00000038608	Dock10	protein_coding	dedicator of cytokinesis 10 [Source:MGI Symbol;Acc:MGI:2146320]
ENSMUSG00000026219	Trip12	protein_coding	thyroid hormone receptor interactor 12 [Source:MGI Symbol;Acc:MGI:1309481]
ENSMUSG00000026270	Cab39	protein_coding	calcium binding protein 39 [Source:MGI Symbol;Acc:MGI:107438]
ENSMUSG00000026223	Itm2c	protein_coding	integral membrane protein 2C [Source:MGI Symbol;Acc:MGI:1927594]
ENSMUSG00000026229	Psmd1	protein_coding	proteasome (prosome, macropain) 26S subunit, non-ATPase, 1 [Source:MGI Symbol;Acc:MGI:1917497]
ENSMUSG00000026234	Ncl	protein_coding	nucleolin [Source:MGI Symbol;Acc:MGI:97286]
ENSMUSG00000026238	Ptma	protein_coding	prothymosin alpha [Source:MGI Symbol;Acc:MGI:97803]
ENSMUSG00000048000	Gigyf2	protein_coding	GRB10 interacting GYF protein 2 [Source:MGI Symbol;Acc:MGI:2138584]
ENSMUSG00000026288	Inpp5d	protein_coding	inositol polyphosphate-5-phosphatase D [Source:MGI Symbol;Acc:MGI:107357]
ENSMUSG00000026289	Atg16l1	protein_coding	autophagy-related 16-like 1 (yeast) [Source:MGI Symbol;Acc:MGI:1924290]
ENSMUSG00000055013	Agap1	protein_coding	ArfGAP with GTPase domain, ankyrin repeat and PH domain 1 [Source:MGI Symbol;Acc:MGI:2653690]
ENSMUSG00000034486	Gbx2	protein_coding	gastrulation brain homeobox 2 [Source:MGI Symbol;Acc:MGI:95668]
ENSMUSG00000026837	D130058E(	protein_coding	RIKEN cDNA D130058E05 gene [Source:MGI Symbol;Acc:MGI:2444814]
ENSMUSG00000026301	Iqca	protein_coding	IQ motif containing with AAA domain [Source:MGI Symbol;Acc:MGI:1922158]
ENSMUSG00000034432	Cops8	protein_coding	COP9 (constitutive photomorphogenic) homolog, subunit 8 (Arabidopsis thaliana) [Source:MGI Symbol;Acc:MGI:1915363]
ENSMUSG00000026305	Lrrfip1	protein_coding	leucine rich repeat (in FLII) interacting protein 1 [Source:MGI Symbol;Acc:MGI:1342770]
ENSMUSG00000026269	Rnpepl1	protein_coding	arginyl aminopeptidase (aminopeptidase B)-like 1 [Source:MGI Symbol;Acc:MGI:1914170]
ENSMUSG00000026275	Ppp1r7	protein_coding	protein phosphatase 1, regulatory (inhibitor) subunit 7 [Source:MGI Symbol;Acc:MGI:1913851]
ENSMUSG00000034088	Hdlbp	protein_coding	high density lipoprotein (HDL) binding protein [Source:MGI Symbol;Acc:MGI:99256]
ENSMUSG00000026276	2-Sep	protein_coding	septin 2 [Source:MGI Symbol;Acc:MGI:97298]
ENSMUSG00000026281	Dtymk	protein_coding	deoxythymidylate kinase [Source:MGI Symbol;Acc:MGI:106890]
ENSMUSG00000040648	Ppip5k2	protein_coding	diphosphoinositol pentakisphosphate kinase 2 [Source:MGI Symbol;Acc:MGI:2142810]
ENSMUSG00000038866	Zcchc2	protein_coding	zinc finger, CCHC domain containing 2 [Source:MGI Symbol;Acc:MGI:2444114]
ENSMUSG00000044340	Phlpp1	protein_coding	PH domain and leucine rich repeat protein phosphatase 1 [Source:MGI Symbol;Acc:MGI:2138327]
ENSMUSG00000057329	Bcl2	protein_coding	B cell leukemia/lymphoma 2 [Source:MGI Symbol;Acc:MGI:88138]
ENSMUSG00000070695	Cntnap5a	protein_coding	contactin associated protein-like 5A [Source:MGI Symbol;Acc:MGI:3643623]
ENSMUSG00000064302	Clasp1	protein_coding	CLIP associating protein 1 [Source:MGI Symbol;Acc:MGI:1923957]
ENSMUSG00000026389	Steap3	protein_coding	STEAP family member 3 [Source:MGI Symbol;Acc:MGI:1915678]
ENSMUSG00000036815	Dpp10	protein_coding	dipeptidylpeptidase 10 [Source:MGI Symbol;Acc:MGI:2442409]
ENSMUSG00000026341	Actr3	protein_coding	ARP3 actin-related protein 3 homolog (yeast) [Source:MGI Symbol;Acc:MGI:1921367]
ENSMUSG00000026343	Gpr39	protein_coding	G protein-coupled receptor 39 [Source:MGI Symbol;Acc:MGI:1918361]
ENSMUSG00000049690	Nckap5	protein_coding	NCK-associated protein 5 [Source:MGI Symbol;Acc:MGI:2686394]
ENSMUSG00000036155	Mgat5	protein_coding	mannoside acetylglucosaminyltransferase 5 [Source:MGI Symbol;Acc:MGI:894701]
ENSMUSG00000056211	R3hdm1	protein_coding	R3H domain 1 (binds single-stranded nucleic acids) [Source:MGI Symbol;Acc:MGI:2446214]
ENSMUSG00000026355	Mcm6	protein_coding	minichromosome maintenance deficient 6 (MIS5 homolog, S. pombe) (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1298227]
ENSMUSG00000026356	Dars	protein_coding	aspartyl-tRNA synthetase [Source:MGI Symbol;Acc:MGI:2442544]
ENSMUSG00000042581	Thsd7b	protein_coding	thrombospondin, type I, domain containing 7B [Source:MGI Symbol;Acc:MGI:3443285]
ENSMUSG00000016526	Dyrk3	protein_coding	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 3 [Source:MGI Symbol;Acc:MGI:1330300]
ENSMUSG00000026427	Eif2d	protein_coding	eukaryotic translation initiation factor 2D [Source:MGI Symbol;Acc:MGI:109342]
ENSMUSG00000026430	Rassf5	protein_coding	Ras association (RalGDS/AF-6) domain family member 5 [Source:MGI Symbol;Acc:MGI:1926375]
ENSMUSG00000026434	Nucks1	protein_coding	nuclear casein kinase and cyclin-dependent kinase substrate 1 [Source:MGI Symbol;Acc:MGI:1934811]
ENSMUSG00000026436	Elk4	protein_coding	ELK4, member of ETS oncogene family [Source:MGI Symbol;Acc:MGI:102853]
ENSMUSG00000054387	Mdm4	protein_coding	transformed mouse 3T3 cell double minute 4 [Source:MGI Symbol;Acc:MGI:107934]
ENSMUSG00000046062	Ppp1r15b	protein_coding	protein phosphatase 1, regulatory (inhibitor) subunit 15B [Source:MGI Symbol;Acc:MGI:2444211]
ENSMUSG00000026404	Zc3h11a	protein_coding	zinc finger CCCH type containing 11A [Source:MGI Symbol;Acc:MGI:1917829]
ENSMUSG00000026463	Atp2b4	protein_coding	ATPase, Ca++ transporting, plasma membrane 4 [Source:MGI Symbol;Acc:MGI:88111]
ENSMUSG00000042207	Kdm5b	protein_coding	lysine (K)-specific demethylase 5B [Source:MGI Symbol;Acc:MGI:1922855]
ENSMUSG00000031506	Ptpn7	protein_coding	protein tyrosine phosphatase, non-receptor type 7 [Source:MGI Symbol;Acc:MGI:2156893]
ENSMUSG00000041879	Ipo9	protein_coding	importin 9 [Source:MGI Symbol;Acc:MGI:1918944]
ENSMUSG00000009418	Nav1	protein_coding	neuron navigator 1 [Source:MGI Symbol;Acc:MGI:2183683]
ENSMUSG00000026421	Csrp1	protein_coding	cysteine and glycine-rich protein 1 [Source:MGI Symbol;Acc:MGI:88549]
ENSMUSG00000041801	Phlda3	protein_coding	pleckstrin homology-like domain, family A, member 3 [Source:MGI Symbol;Acc:MGI:1351485]
ENSMUSG00000041642	Kif21b	protein_coding	kinesin family member 21B [Source:MGI Symbol;Acc:MGI:109234]
ENSMUSG00000089980	9810008M	protein_coding	RIKEN cDNA 9810008M14 gene [Source:MGI Symbol;Acc:MGI:1598479]
ENSMUSG00000026395	Ptprc	protein_coding	protein tyrosine phosphatase, receptor type, C [Source:MGI Symbol;Acc:MGI:97810]
ENSMUSG00000033952	Aspm	protein_coding	asp (abnormal spindle)-like, microcephaly associated (Drosophila) [Source:MGI Symbol;Acc:MGI:1334448]

ENSMUSG00000033898	Cfhr2	protein_coding	complement factor H-related 2 [Source:MGI Symbol;Acc:MGI:3611575]
ENSMUSG00000026360	Rgs2	protein_coding	regulator of G-protein signaling 2 [Source:MGI Symbol;Acc:MGI:1098271]
ENSMUSG00000026358	Rgs1	protein_coding	regulator of G-protein signaling 1 [Source:MGI Symbol;Acc:MGI:1354694]
ENSMUSG00000026357	Rgs18	protein_coding	regulator of G-protein signaling 18 [Source:MGI Symbol;Acc:MGI:1927492]
ENSMUSG00000026181	Fam5c	protein_coding	family with sequence similarity 5, member C [Source:MGI Symbol;Acc:MGI:2445025]
ENSMUSG00000026239	Pla2g4a	protein_coding	phospholipase A2, group IVA (cytosolic, calcium-dependent) [Source:MGI Symbol;Acc:MGI:1195256]
ENSMUSG00000006005	Tpr	protein_coding	translocated promoter region [Source:MGI Symbol;Acc:MGI:1922066]
ENSMUSG00000026842	Hmcn1	protein_coding	hemicentin 1 [Source:MGI Symbol;Acc:MGI:2685047]
ENSMUSG00000026159	Ivns1abp	protein_coding	influenza virus NS1A binding protein [Source:MGI Symbol;Acc:MGI:2152389]
ENSMUSG00000026484	Rnf2	protein_coding	ring finger protein 2 [Source:MGI Symbol;Acc:MGI:1101759]
ENSMUSG00000026483	Fam129a	protein_coding	family with sequence similarity 129, member A [Source:MGI Symbol;Acc:MGI:2137237]
ENSMUSG00000048019	Edem3	protein_coding	ER degradation enhancer, mannosidase alpha-like 3 [Source:MGI Symbol;Acc:MGI:1914217]
ENSMUSG00000026487	Rgl1	protein_coding	ral guanine nucleotide dissociation stimulator,-like 1 [Source:MGI Symbol;Acc:MGI:107484]
ENSMUSG00000042772	Smg7	protein_coding	Smg-7 homolog, nonsense mediated mRNA decay factor (C. elegans) [Source:MGI Symbol;Acc:MGI:2682334]
ENSMUSG00000042699	Dhx9	protein_coding	DEAH (Asp-Glu-Ala-His) box polypeptide 9 [Source:MGI Symbol;Acc:MGI:108177]
ENSMUSG00000033021	Rgs8	protein_coding	regulator of G-protein signaling 8 [Source:MGI Symbol;Acc:MGI:105402]
ENSMUSG00000026475	Rgs16	protein_coding	regulator of G-protein signaling 16 [Source:MGI Symbol;Acc:MGI:108407]
ENSMUSG00000026473	Glul	protein_coding	glutamate-ammonia ligase (glutamine synthetase) [Source:MGI Symbol;Acc:MGI:95739]
ENSMUSG00000075422	A330023A1	protein_coding	RIKEN cDNA A330023A10 gene [Source:MGI Symbol;Acc:MGI:2441728]
ENSMUSG00000079223	Gm11074	protein_coding	predicted gene 11074 [Source:MGI Symbol;Acc:MGI:3779501]
ENSMUSG00000033671	Cep350	protein_coding	centrosomal protein 350 [Source:MGI Symbol;Acc:MGI:1921331]
ENSMUSG00000050565	Tor1aip2	protein_coding	torsin A interacting protein 2 [Source:MGI Symbol;Acc:MGI:3582695]
ENSMUSG00000072512	Tor1aip2	protein_coding	torsin A interacting protein 2 [Source:MGI Symbol;Acc:MGI:3582695]
ENSMUSG00000026602	Nphs2	protein_coding	nephrosis 2 homolog, podocin (human) [Source:MGI Symbol;Acc:MGI:2157018]
ENSMUSG00000026600	Soat1	protein_coding	sterol O-acyltransferase 1 [Source:MGI Symbol;Acc:MGI:104665]
ENSMUSG00000026596	Abl2	protein_coding	v-abl Abelson murine leukemia viral oncogene homolog 2 (arg, Abelson-related gene) [Source:MGI Symbol;Acc:MGI:87860]
ENSMUSG00000033557	Fam20b	protein_coding	family with sequence similarity 20, member B [Source:MGI Symbol;Acc:MGI:2443990]
ENSMUSG00000026594	Ralgps2	protein_coding	Ral GEF with PH domain and SH3 binding motif 2 [Source:MGI Symbol;Acc:MGI:1925505]
ENSMUSG00000040752	Rnf2	protein_coding	ring finger and WD repeat domain 2 [Source:MGI Symbol;Acc:MGI:1347046]
ENSMUSG00000040435	Rc3h1	protein_coding	RING CCCH (C3H) domains 1 [Source:MGI Symbol;Acc:MGI:2685397]
ENSMUSG00000026701	Prdx6	protein_coding	peroxiredoxin 6 [Source:MGI Symbol;Acc:MGI:894320]
ENSMUSG00000026277	4930558K0	protein_coding	RIKEN cDNA 4930558K02 gene [Source:MGI Symbol;Acc:MGI:1922418]
ENSMUSG00000026698	Pigc	protein_coding	phosphatidylinositol glycan anchor biosynthesis, class C [Source:MGI Symbol;Acc:MGI:1914542]
ENSMUSG00000040235	Prrc2c	protein_coding	proline-rich coiled-coil 2C [Source:MGI Symbol;Acc:MGI:1913754]
ENSMUSG00000026585	Kifap3	protein_coding	kinesin-associated protein 3 [Source:MGI Symbol;Acc:MGI:107566]
ENSMUSG00000040408	BC055324	protein_coding	cDNA sequence BC055324 [Source:MGI Symbol;Acc:MGI:3590554]
ENSMUSG00000026576	Atp1b1	protein_coding	ATPase, Na+/K+ transporting, beta 1 polypeptide [Source:MGI Symbol;Acc:MGI:88108]
ENSMUSG00000040723	Rcsd1	protein_coding	RCSD domain containing 1 [Source:MGI Symbol;Acc:MGI:2676394]
ENSMUSG00000026703	Cd247	protein_coding	CD247 antigen [Source:MGI Symbol;Acc:MGI:88334]
ENSMUSG00000026565	Pou2f1	protein_coding	POU domain, class 2, transcription factor 1 [Source:MGI Symbol;Acc:MGI:101898]
ENSMUSG00000026558	Uck2	protein_coding	uridine-cytidine kinase 2 [Source:MGI Symbol;Acc:MGI:1931744]
ENSMUSG00000026627	Aldh9a1	protein_coding	aldehyde dehydrogenase 9, subfamily A1 [Source:MGI Symbol;Acc:MGI:1861622]
ENSMUSG00000052534	Pbx1	protein_coding	pre B cell leukemia homeobox 1 [Source:MGI Symbol;Acc:MGI:97495]
ENSMUSG00000026667	Uhmk1	protein_coding	U2AF homology motif (UHM) kinase 1 [Source:MGI Symbol;Acc:MGI:1341908]
ENSMUSG00000059498	Fcgr3	protein_coding	Fc receptor, IgG, low affinity III [Source:MGI Symbol;Acc:MGI:95500]
ENSMUSG00000013593	Ndufs2	protein_coding	NADH dehydrogenase (ubiquinone) Fe-S protein 2 [Source:MGI Symbol;Acc:MGI:2385112]
ENSMUSG00000066411	Pvrl4	protein_coding	poliovirus receptor-related 4 [Source:MGI Symbol;Acc:MGI:1918990]
ENSMUSG00000040865	Arhgap30	protein_coding	Rho GTPase activating protein 30 [Source:MGI Symbol;Acc:MGI:2684948]
ENSMUSG00000026553	Copa	protein_coding	coatomer protein complex subunit alpha [Source:MGI Symbol;Acc:MGI:1334462]
ENSMUSG00000026554	Dcaf8	protein_coding	DDB1 and CUL4 associated factor 8 [Source:MGI Symbol;Acc:MGI:1916031]
ENSMUSG00000026547	Tagln2	protein_coding	transgelin 2 [Source:MGI Symbol;Acc:MGI:1312985]
ENSMUSG00000057335	Cep170	protein_coding	centrosomal protein 170 [Source:MGI Symbol;Acc:MGI:1918348]
ENSMUSG00000026504	Sdccag8	protein_coding	serologically defined colon cancer antigen 8 [Source:MGI Symbol;Acc:MGI:1924096]
ENSMUSG00000026502	Pppde1	protein_coding	PPPDE peptidase domain containing 1 [Source:MGI Symbol;Acc:MGI:1926923]
ENSMUSG00000039630	Hnrnpu	protein_coding	heterogeneous nuclear ribonucleoprotein U [Source:MGI Symbol;Acc:MGI:1858195]
ENSMUSG00000055067	Smyd3	protein_coding	SET and MYND domain containing 3 [Source:MGI Symbol;Acc:MGI:1916976]
ENSMUSG00000032649	Cnst	protein_coding	consortin, connexin sorting protein [Source:MGI Symbol;Acc:MGI:2445141]
ENSMUSG00000026491	Ahctf1	protein_coding	AT hook containing transcription factor 1 [Source:MGI Symbol;Acc:MGI:1915033]
ENSMUSG00000032855	Itpkb	protein_coding	inositol 1,4,5-trisphosphate 3-kinase B [Source:MGI Symbol;Acc:MGI:109235]
ENSMUSG00000026496	Parp1	protein_coding	poly (ADP-ribose) polymerase family, member 1 [Source:MGI Symbol;Acc:MGI:1340806]
ENSMUSG00000007743	H3f3a	protein_coding	H3 histone, family 3A [Source:MGI Symbol;Acc:MGI:1097686]
ENSMUSG00000068008	BC031781	protein_coding	cDNA sequence BC031781 [Source:MGI Symbol;Acc:MGI:2384788]
ENSMUSG00000026519	Tmem63a	protein_coding	transmembrane protein 63a [Source:MGI Symbol;Acc:MGI:2384789]
ENSMUSG00000026703	Wdr26	protein_coding	WD repeat domain 26 [Source:MGI Symbol;Acc:MGI:1923825]
ENSMUSG00000004030	Lbr	protein_coding	lamin B receptor [Source:MGI Symbol;Acc:MGI:2138281]
ENSMUSG00000026510	Trp53bp2	protein_coding	transformation related protein 53 binding protein 2 [Source:MGI Symbol;Acc:MGI:2138319]
ENSMUSG00000026518	Rab3gap2	protein_coding	RAB3 GTPase activating protein subunit 2 [Source:MGI Symbol;Acc:MGI:1916043]
ENSMUSG00000026615	Eprs	protein_coding	glutamyl-prolyl-tRNA synthetase [Source:MGI Symbol;Acc:MGI:97838]
ENSMUSG00000026609	Ush2a	protein_coding	Usher syndrome 2A (autosomal recessive, mild) homolog (human) [Source:MGI Symbol;Acc:MGI:1341292]
ENSMUSG00000026608	Kctd3	protein_coding	potassium channel tetramerisation domain containing 3 [Source:MGI Symbol;Acc:MGI:2444629]
ENSMUSG00000037568	Vash2	protein_coding	vasohibin 2 [Source:MGI Symbol;Acc:MGI:2444826]
ENSMUSG00000026626	Ppp2r5a	protein_coding	protein phosphatase 2, regulatory subunit B (B56), alpha isoform [Source:MGI Symbol;Acc:MGI:2388479]
ENSMUSG00000038740	Kcnh1	protein_coding	potassium voltage-gated channel, subfamily H (eag-related), member 1 [Source:MGI Symbol;Acc:MGI:1341721]
ENSMUSG00000037375	Hhat	protein_coding	hedgehog acyltransferase [Source:MGI Symbol;Acc:MGI:2444681]
ENSMUSG00000016494	Cd34	protein_coding	CD34 antigen [Source:MGI Symbol;Acc:MGI:88329]
ENSMUSG00000050530	Fam171a1	protein_coding	family with sequence similarity 171, member A1 [Source:MGI Symbol;Acc:MGI:2442917]
ENSMUSG00000026645	Olah	protein_coding	oleoyl-ACP hydrolase [Source:MGI Symbol;Acc:MGI:2139018]
ENSMUSG00000051396	Hspa14	protein_coding	heat shock protein 14 [Source:MGI Symbol;Acc:MGI:1354164]
ENSMUSG00000026655	Fam107b	protein_coding	family with sequence similarity 107, member B [Source:MGI Symbol;Acc:MGI:1912790]
ENSMUSG00000026657	Frmd4a	protein_coding	FERM domain containing 4A [Source:MGI Symbol;Acc:MGI:1919850]
ENSMUSG00000026662	Sephs1	protein_coding	selenophosphate synthetase 1 [Source:MGI Symbol;Acc:MGI:1923580]
ENSMUSG00000032046	Usp9nl	protein_coding	USP6 N-terminal like [Source:MGI Symbol;Acc:MGI:2152855]
ENSMUSG00000002107	Celf2	protein_coding	CUGBP, Elav-like family member 2 [Source:MGI Symbol;Acc:MGI:1338822]
ENSMUSG00000026778	Prkcq	protein_coding	protein kinase C, theta [Source:MGI Symbol;Acc:MGI:97601]
ENSMUSG00000026727	Rsu1	protein_coding	Ras suppressor protein 1 [Source:MGI Symbol;Acc:MGI:103040]
ENSMUSG00000026728	Vim	protein_coding	vimentin [Source:MGI Symbol;Acc:MGI:98932]
ENSMUSG00000057914	Cacnb2	protein_coding	calcium channel, voltage-dependent, beta 2 subunit [Source:MGI Symbol;Acc:MGI:894644]
ENSMUSG00000026748	Plxdc2	protein_coding	plexin domain containing 2 [Source:MGI Symbol;Acc:MGI:1914698]
ENSMUSG00000026617	Etl4	protein_coding	enhancer trap locus 4 [Source:MGI Symbol;Acc:MGI:95454]
ENSMUSG00000026730	Arhgap21	protein_coding	Rho GTPase activating protein 21 [Source:MGI Symbol;Acc:MGI:1918685]
ENSMUSG00000026730	Apbb1ip	protein_coding	amyloid beta (A4) precursor protein-binding, family B, member 1 interacting protein [Source:MGI Symbol;Acc:MGI:1861354]
ENSMUSG00000026973	Psd4	protein_coding	pleckstrin and Sec7 domain containing 4 [Source:MGI Symbol;Acc:MGI:2674093]
ENSMUSG00000026974	Zmynd19	protein_coding	zinc finger, MYND domain containing 19 [Source:MGI Symbol;Acc:MGI:1914487]
ENSMUSG00000036752	Tubb4b	protein_coding	tubulin, beta 4B class IVB [Source:MGI Symbol;Acc:MGI:1915472]
ENSMUSG00000045707	Tprn	protein_coding	taperin [Source:MGI Symbol;Acc:MGI:2139535]
ENSMUSG00000026965	Anapc2	protein_coding	anaphase promoting complex subunit 2 [Source:MGI Symbol;Acc:MGI:2139135]
ENSMUSG00000026933	1010001B2	protein_coding	RIKEN cDNA 1010001B22 gene [Source:MGI Symbol;Acc:MGI:1915880]
ENSMUSG00000026941	Mamdc4	protein_coding	MAM domain containing 4 [Source:MGI Symbol;Acc:MGI:2685041]
ENSMUSG00000036504	Phpt1	protein_coding	phosphohistidine phosphatase 1 [Source:MGI Symbol;Acc:MGI:1922704]
ENSMUSG00000015087	B830028B13	protein_coding	RIKEN cDNA B830028B13 gene [Source:MGI Symbol;Acc:MGI:2442866]
ENSMUSG00000015774	Med22	protein_coding	mediator complex subunit 22 [Source:MGI Symbol;Acc:MGI:98446]
ENSMUSG00000062647	Rpl7a	protein_coding	ribosomal protein L7A [Source:MGI Symbol;Acc:MGI:1353472]
ENSMUSG00000014852	Adamts13	protein_coding	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 13 [Source:MGI Symbol;Acc:MGI:2685556]
ENSMUSG00000026918	Brd3	protein_coding	bromodomain containing 3 [Source:MGI Symbol;Acc:MGI:1914632]
ENSMUSG00000015846	Rxra	protein_coding	retinoid X receptor alpha [Source:MGI Symbol;Acc:MGI:98214]
ENSMUSG00000035773	Mrps2	protein_coding	mitochondrial ribosomal protein S2 [Source:MGI Symbol;Acc:MGI:2153080]
ENSMUSG00000026807	Ak8	protein_coding	adenylate kinase 8 [Source:MGI Symbol;Acc:MGI:1916130]

ENSMUSG00000035666	Gtf3c4	protein_coding	general transcription factor IIIC, polypeptide 4 [Source:MGI Symbol;Acc:MGI:2138937]
ENSMUSG00000043535	Setx	protein_coding	senataxin [Source:MGI Symbol;Acc:MGI:2443480]
ENSMUSG00000035513	Ntng2	protein_coding	netrin G2 [Source:MGI Symbol;Acc:MGI:2159341]
ENSMUSG00000032844	Rapgef1	protein_coding	Rap guanine nucleotide exchange factor (GEF) 1 [Source:MGI Symbol;Acc:MGI:104580]
ENSMUSG00000057738	Spna2	protein_coding	spectrin alpha 2 [Source:MGI Symbol;Acc:MGI:98386]
ENSMUSG00000022715	Wdr34	protein_coding	WD repeat domain 34 [Source:MGI Symbol;Acc:MGI:1915970]
ENSMUSG00000054766	Set	protein_coding	SET nuclear oncogene [Source:MGI Symbol;Acc:MGI:1860267]
ENSMUSG00000028315	Ppp2r4	protein_coding	protein phosphatase 2A, regulatory subunit B (PR 53) [Source:MGI Symbol;Acc:MGI:1346004]
ENSMUSG00000026849	Tor1a	protein_coding	torsin family 1, member A (torsin A) [Source:MGI Symbol;Acc:MGI:1353568]
ENSMUSG00000075415	Fnbp1	protein_coding	formin binding protein 1 [Source:MGI Symbol;Acc:MGI:109606]
ENSMUSG00000026842	Abl1	protein_coding	c-abl oncogene 1, non-receptor tyrosine kinase [Source:MGI Symbol;Acc:MGI:87859]
ENSMUSG00000001855	Nup214	protein_coding	nucleoporin 214 [Source:MGI Symbol;Acc:MGI:1095411]
ENSMUSG00000039262	Prrc2b	protein_coding	proline-rich coiled-coil 2B [Source:MGI Symbol;Acc:MGI:1923304]
ENSMUSG00000026814	Eng	protein_coding	endoglin [Source:MGI Symbol;Acc:MGI:95392]
ENSMUSG00000009555	Cdk9	protein_coding	cyclin-dependent kinase 9 (CDC2-related kinase) [Source:MGI Symbol;Acc:MGI:1328368]
ENSMUSG00000038900	Rpl12	protein_coding	ribosomal protein L12 [Source:MGI Symbol;Acc:MGI:98002]
ENSMUSG00000038831	Ralgps1	protein_coding	Ral GEF with PH domain and SH3 binding motif 1 [Source:MGI Symbol;Acc:MGI:1922008]
ENSMUSG00000038765	Lmx1b	protein_coding	LIM homeobox transcription factor 1 beta [Source:MGI Symbol;Acc:MGI:1100513]
ENSMUSG00000038740	Fam125b	protein_coding	family with sequence similarity 125, member B [Source:MGI Symbol;Acc:MGI:1919728]
ENSMUSG00000038718	Pbx3	protein_coding	pre B-cell leukemia homeobox 3 [Source:MGI Symbol;Acc:MGI:97496]
ENSMUSG00000026864	Hspa5	protein_coding	heat shock protein 5 [Source:MGI Symbol;Acc:MGI:95835]
ENSMUSG00000026869	Psmd5	protein_coding	proteasome (prosome, macropain) 26S subunit, non-ATPase, 5 [Source:MGI Symbol;Acc:MGI:1914248]
ENSMUSG00000035778	Ggta1	protein_coding	glycoprotein galactosyltransferase alpha 1, 3 [Source:MGI Symbol;Acc:MGI:95704]
ENSMUSG00000026883	Dab2ip	protein_coding	disabled homolog 2 (Drosophila) interacting protein [Source:MGI Symbol;Acc:MGI:1916851]
ENSMUSG00000035392	Dennd1a	protein_coding	DENN/MADD domain containing 1A [Source:MGI Symbol;Acc:MGI:2442794]
ENSMUSG00000000247	Lhx2	protein_coding	LIM homeobox protein 2 [Source:MGI Symbol;Acc:MGI:96785]
ENSMUSG00000049313	Lrp1b	protein_coding	low density lipoprotein-related protein 1B (deleted in tumors) [Source:MGI Symbol;Acc:MGI:2151136]
ENSMUSG00000049744	Arhgap15	protein_coding	Rho GTPase activating protein 15 [Source:MGI Symbol;Acc:MGI:1923367]
ENSMUSG00000026872	Zeb2	protein_coding	zinc finger E-box binding homeobox 2 [Source:MGI Symbol;Acc:MGI:1344407]
ENSMUSG00000026753	Mbd5	protein_coding	methyl-CpG binding domain protein 5 [Source:MGI Symbol;Acc:MGI:2138934]
ENSMUSG00000026764	Kif5c	protein_coding	kinesin family member 5C [Source:MGI Symbol;Acc:MGI:1098269]
ENSMUSG00000026202	Rif1	protein_coding	Rap1 interacting factor 1 homolog (yeast) [Source:MGI Symbol;Acc:MGI:1098622]
ENSMUSG00000026827	Gpd2	protein_coding	glycerol phosphate dehydrogenase 2, mitochondrial [Source:MGI Symbol;Acc:MGI:99778]
ENSMUSG00000026977	7-Mar	protein_coding	membrane-associated ring finger (C3HC4) 7 [Source:MGI Symbol;Acc:MGI:1931053]
ENSMUSG00000026914	Psmd14	protein_coding	proteasome (prosome, macropain) 26S subunit, non-ATPase, 14 [Source:MGI Symbol;Acc:MGI:1913284]
ENSMUSG00000035033	Tbr1	protein_coding	T-box brain gene 1 [Source:MGI Symbol;Acc:MGI:107404]
ENSMUSG00000027068	Dhrs9	protein_coding	dehydrogenase/reductase (SDR family) member 9 [Source:MGI Symbol;Acc:MGI:2442798]
ENSMUSG00000068882	Ssb	protein_coding	Sjogren syndrome antigen B [Source:MGI Symbol;Acc:MGI:98423]
ENSMUSG00000041997	Tlk1	protein_coding	tousled-like kinase 1 [Source:MGI Symbol;Acc:MGI:2441683]
ENSMUSG00000027111	Itga6	protein_coding	integrin alpha 6 [Source:MGI Symbol;Acc:MGI:96605]
ENSMUSG00000049044	Rapgef4	protein_coding	Rap guanine nucleotide exchange factor (GEF) 4 [Source:MGI Symbol;Acc:MGI:1917723]
ENSMUSG00000027109	Sp3	protein_coding	trans-acting transcription factor 3 [Source:MGI Symbol;Acc:MGI:1277166]
ENSMUSG00000068859	Sp9	protein_coding	trans-acting transcription factor 9 [Source:MGI Symbol;Acc:MGI:3574660]
ENSMUSG00000075284	Wipf1	protein_coding	WAS/WASL interacting protein family, member 1 [Source:MGI Symbol;Acc:MGI:2178801]
ENSMUSG00000027104	Atf2	protein_coding	activating transcription factor 2 [Source:MGI Symbol;Acc:MGI:109349]
ENSMUSG00000018770	Atp5g3	protein_coding	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C3 (subunit 9) [Source:MGI Symbol;Acc:MGI:2442035]
ENSMUSG00000043342	Hoxd9	protein_coding	homeobox D9 [Source:MGI Symbol;Acc:MGI:96210]
ENSMUSG00000015839	Nfe2l2	protein_coding	nuclear factor, erythroid derived 2, like 2 [Source:MGI Symbol;Acc:MGI:108420]
ENSMUSG00000051747	Ttn	protein_coding	titin [Source:MGI Symbol;Acc:MGI:98864]
ENSMUSG00000027014	Cwc22	protein_coding	CWC22 spliceosome-associated protein homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2136773]
ENSMUSG00000027007	Ssfa2	protein_coding	sperm specific antigen 2 [Source:MGI Symbol;Acc:MGI:1917849]
ENSMUSG00000027002	Nckap1	protein_coding	NCK-associated protein 1 [Source:MGI Symbol;Acc:MGI:1355333]
ENSMUSG00000027091	Zc3h15	protein_coding	zinc finger CCCH-type containing 15 [Source:MGI Symbol;Acc:MGI:1915747]
ENSMUSG00000059588	Calcrl	protein_coding	calcitonin receptor-like [Source:MGI Symbol;Acc:MGI:1926944]
ENSMUSG00000034101	Ctnnd1	protein_coding	catenin (cadherin associated protein), delta 1 [Source:MGI Symbol;Acc:MGI:105100]
ENSMUSG00000025314	Ptprj	protein_coding	protein tyrosine phosphatase, receptor type, J [Source:MGI Symbol;Acc:MGI:104574]
ENSMUSG00000002102	Psmc3	protein_coding	proteasome (prosome, macropain) 26S subunit, ATPase 3 [Source:MGI Symbol;Acc:MGI:1098754]
ENSMUSG00000002111	Spi1	protein_coding	SFFV proviral integration 1 [Source:MGI Symbol;Acc:MGI:98282]
ENSMUSG00000040549	Ckap5	protein_coding	cytoskeleton associated protein 5 [Source:MGI Symbol;Acc:MGI:1923036]
ENSMUSG00000040506	Ambra1	protein_coding	autophagy/beclin 1 regulator 1 [Source:MGI Symbol;Acc:MGI:2443564]
ENSMUSG00000040479	Dgkz	protein_coding	diacylglycerol kinase zeta [Source:MGI Symbol;Acc:MGI:1278339]
ENSMUSG00000058318	Phf21a	protein_coding	PHD finger protein 21A [Source:MGI Symbol;Acc:MGI:2384756]
ENSMUSG00000049922	Slc35c1	protein_coding	solute carrier family 35, member C1 [Source:MGI Symbol;Acc:MGI:2443301]
ENSMUSG00000075028	Prdm11	protein_coding	PR domain containing 11 [Source:MGI Symbol;Acc:MGI:2685553]
ENSMUSG00000027195	Hsd17b12	protein_coding	hydroxysteroid (17-beta) dehydrogenase 12 [Source:MGI Symbol;Acc:MGI:1926967]
ENSMUSG00000048058	Ldlrad3	protein_coding	low density lipoprotein receptor class A domain containing 3 [Source:MGI Symbol;Acc:MGI:2138856]
ENSMUSG00000005087	Cd44	protein_coding	CD44 antigen [Source:MGI Symbol;Acc:MGI:88338]
ENSMUSG00000027184	Caprin1	protein_coding	cell cycle associated protein 1 [Source:MGI Symbol;Acc:MGI:1858234]
ENSMUSG00000068572	D430041D05Rik	protein_coding	RIKEN cDNA D430041D05 gene [Source:MGI Symbol;Acc:MGI:2181742]
ENSMUSG00000027177	Hipk3	protein_coding	homeodomain interacting protein kinase 3 [Source:MGI Symbol;Acc:MGI:1314882]
ENSMUSG00000057378	Ryr3	protein_coding	ryanodine receptor 3 [Source:MGI Symbol;Acc:MGI:99684]
ENSMUSG00000041219	Arhgap11a	protein_coding	Rho GTPase activating protein 11A [Source:MGI Symbol;Acc:MGI:2444300]
ENSMUSG00000040383	Aqr	protein_coding	aquarius [Source:MGI Symbol;Acc:MGI:1276102]
ENSMUSG00000027351	Spred1	protein_coding	sprouty protein with EVH-1 domain 1, related sequence [Source:MGI Symbol;Acc:MGI:2150016]
ENSMUSG00000034216	Vps18	protein_coding	vacuolar protein sorting 18 (yeast) [Source:MGI Symbol;Acc:MGI:2443626]
ENSMUSG00000027304	Rtf1	protein_coding	Rtf1, Paf1/RNA polymerase II complex component, homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1309480]
ENSMUSG00000033943	Mga	protein_coding	MAX gene associated [Source:MGI Symbol;Acc:MGI:1352483]
ENSMUSG00000027230	Zfp106	protein_coding	zinc finger protein 106 [Source:MGI Symbol;Acc:MGI:1270153]
ENSMUSG00000027263	Tubgcp4	protein_coding	tubulin, gamma complex associated protein 4 [Source:MGI Symbol;Acc:MGI:1196288]
ENSMUSG00000033486	Catsper2	protein_coding	cation channel, sperm associated 2 [Source:MGI Symbol;Acc:MGI:2387404]
ENSMUSG00000027248	Pdia3	protein_coding	protein disulfide isomerase associated 3 [Source:MGI Symbol;Acc:MGI:95834]
ENSMUSG00000027203	Dut	protein_coding	deoxyuridine triphosphatase [Source:MGI Symbol;Acc:MGI:1346051]
ENSMUSG00000027365	Trpm7	protein_coding	transient receptor potential cation channel, subfamily M, member 7 [Source:MGI Symbol;Acc:MGI:1929996]
ENSMUSG00000027369	Snrnp200	protein_coding	small nuclear ribonucleoprotein 200 (U5) [Source:MGI Symbol;Acc:MGI:2444401]
ENSMUSG00000034850	Tmem127	protein_coding	transmembrane protein 127 [Source:MGI Symbol;Acc:MGI:1916770]
ENSMUSG00000027367	Stard7	protein_coding	START domain containing 7 [Source:MGI Symbol;Acc:MGI:2139095]
ENSMUSG00000014355	Anapc1	protein_coding	anaphase promoting complex subunit 1 [Source:MGI Symbol;Acc:MGI:103097]
ENSMUSG00000027394	Ttl	protein_coding	tubulin tyrosine ligase [Source:MGI Symbol;Acc:MGI:1916987]
ENSMUSG00000027397	Slc20a1	protein_coding	solute carrier family 20, member 1 [Source:MGI Symbol;Acc:MGI:108392]
ENSMUSG00000037902	Sirpa	protein_coding	signal-regulatory protein alpha [Source:MGI Symbol;Acc:MGI:108563]
ENSMUSG00000037885	Stk35	protein_coding	serine/threonine kinase 35 [Source:MGI Symbol;Acc:MGI:1914550]
ENSMUSG00000027404	Snrpb	protein_coding	small nuclear ribonucleoprotein B [Source:MGI Symbol;Acc:MGI:98342]
ENSMUSG00000027405	Nop56	protein_coding	NOP56 ribonucleoprotein homolog (yeast) [Source:MGI Symbol;Acc:MGI:1914384]
ENSMUSG00000027302	Ptpra	protein_coding	protein tyrosine phosphatase, receptor type, A [Source:MGI Symbol;Acc:MGI:97808]
ENSMUSG00000027329	Spef1	protein_coding	sperm flagellar 1 [Source:MGI Symbol;Acc:MGI:2315546]
ENSMUSG00000068267	Cenpb	protein_coding	centromere protein B [Source:MGI Symbol;Acc:MGI:88376]
ENSMUSG00000039942	Plcb4	protein_coding	phospholipase C, beta 4 [Source:MGI Symbol;Acc:MGI:107464]
ENSMUSG00000068205	Macrod2	protein_coding	MACRO domain containing 2 [Source:MGI Symbol;Acc:MGI:1920149]
ENSMUSG00000027423	Snx5	protein_coding	sorting nexin 5 [Source:MGI Symbol;Acc:MGI:1916428]
ENSMUSG00000027425	Csrp2bp	protein_coding	cysteine and glycine-rich protein 2 binding protein [Source:MGI Symbol;Acc:MGI:1917264]
ENSMUSG00000027429	Sec23b	protein_coding	SEC23B (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1350925]
ENSMUSG00000063873	Slc24a3	protein_coding	solute carrier family 24 (sodium/potassium/calcium exchanger), member 3 [Source:MGI Symbol;Acc:MGI:2137513]
ENSMUSG00000037110	Ralgapa2	protein_coding	Ral GTPase activating protein, alpha subunit 2 (catalytic) [Source:MGI Symbol;Acc:MGI:3058249]
ENSMUSG00000027435	Cd93	protein_coding	CD93 antigen [Source:MGI Symbol;Acc:MGI:106664]
ENSMUSG00000074754	Tmem90b	protein_coding	transmembrane protein 90B [Source:MGI Symbol;Acc:MGI:2670133]
ENSMUSG00000033059	Pygb	protein_coding	brain glycogen phosphorylase [Source:MGI Symbol;Acc:MGI:97828]
ENSMUSG00000027459	Fam110a	protein_coding	family with sequence similarity 110, member A [Source:MGI Symbol;Acc:MGI:1921097]

ENSMUSG00000060257	Scrt2	protein_coding	scratch homolog 2, zinc finger protein (Drosophila) [Source:MGI Symbol;Acc:MGI:2139287]
ENSMUSG00000074698	Csnk2a1	protein_coding	casein kinase 2, alpha 1 polypeptide [Source:MGI Symbol;Acc:MGI:88543]
ENSMUSG00000007659	Bcl2l1	protein_coding	BCL2-like 1 [Source:MGI Symbol;Acc:MGI:88139]
ENSMUSG00000027469	Tpx2	protein_coding	TPX2, microtubule-associated protein homolog (Xenopus laevis) [Source:MGI Symbol;Acc:MGI:1919369]
ENSMUSG00000042662	Dusp15	protein_coding	dual specificity phosphatase-like 15 [Source:MGI Symbol;Acc:MGI:1934928]
ENSMUSG00000051413	Plagl2	protein_coding	pleiomorphic adenoma gene-like 2 [Source:MGI Symbol;Acc:MGI:1933165]
ENSMUSG00000042548	Asxl1	protein_coding	additional sex combs like 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:2684063]
ENSMUSG00000027478	Dnmt3b	protein_coding	DNA methyltransferase 3B [Source:MGI Symbol;Acc:MGI:1261819]
ENSMUSG00000027487	Cdk5rap1	protein_coding	CDK5 regulatory subunit associated protein 1 [Source:MGI Symbol;Acc:MGI:1914221]
ENSMUSG00000038467	Chmp4b	protein_coding	charged multivesicular body protein 4B [Source:MGI Symbol;Acc:MGI:1922858]
ENSMUSG00000027593	Raly	protein_coding	hnRNP-associated with lethal yellow [Source:MGI Symbol;Acc:MGI:97850]
ENSMUSG00000027596	a	protein_coding	nonagouti [Source:MGI Symbol;Acc:MGI:87853]
ENSMUSG00000038369	Ncoa6	protein_coding	nuclear receptor coactivator 6 [Source:MGI Symbol;Acc:MGI:1929915]
ENSMUSG00000038324	Trpc4ap	protein_coding	transient receptor potential cation channel, subfamily C, member 4 associated protein [Source:MGI Symbol;Acc:MGI:1930751]
ENSMUSG00000074643	Cpne1	protein_coding	copine I [Source:MGI Symbol;Acc:MGI:1921271]
ENSMUSG00000027618	Nfs1	protein_coding	nitrogen fixation gene 1 (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1316706]
ENSMUSG00000089824	Rbm12	protein_coding	RNA binding motif protein 12 [Source:MGI Symbol;Acc:MGI:1922960]
ENSMUSG00000062175	Tgif2	protein_coding	TGFB-induced factor homeobox 2 [Source:MGI Symbol;Acc:MGI:1915299]
ENSMUSG00000074627	4923501G1	protein_coding	RIKEN cDNA 4923501G14 gene [Source:MGI Symbol;Acc:MGI:3608328]
ENSMUSG00000027642	Rpn2	protein_coding	ribophorin II [Source:MGI Symbol;Acc:MGI:98085]
ENSMUSG00000027651	Rprd1b	protein_coding	regulation of nuclear pre-mRNA domain containing 1B [Source:MGI Symbol;Acc:MGI:1917720]
ENSMUSG00000037761	Actr5	protein_coding	ARP5 actin-related protein 5 homolog (yeast) [Source:MGI Symbol;Acc:MGI:1924748]
ENSMUSG00000027655	Dhx35	protein_coding	DEAH (Asp-Glu-Ala-His) box polypeptide 35 [Source:MGI Symbol;Acc:MGI:1918965]
ENSMUSG00000070544	Top1	protein_coding	topoisomerase (DNA) I [Source:MGI Symbol;Acc:MGI:98788]
ENSMUSG00000016933	Plcg1	protein_coding	phospholipase C, gamma 1 [Source:MGI Symbol;Acc:MGI:97615]
ENSMUSG00000057133	Chd6	protein_coding	chromodomain helicase DNA binding protein 6 [Source:MGI Symbol;Acc:MGI:1918639]
ENSMUSG00000016921	Srsf6	protein_coding	serine/arginine-rich splicing factor 6 [Source:MGI Symbol;Acc:MGI:1915245]
ENSMUSG00000017817	Jph2	protein_coding	junctophilin 2 [Source:MGI Symbol;Acc:MGI:1891496]
ENSMUSG00000035268	Pkig	protein_coding	protein kinase inhibitor, gamma [Source:MGI Symbol;Acc:MGI:1343086]
ENSMUSG00000017697	Ada	protein_coding	adenosine deaminase [Source:MGI Symbol;Acc:MGI:87916]
ENSMUSG00000018326	Ywhab	protein_coding	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide [Source:MGI Symbol;Acc:MGI:1891917]
ENSMUSG00000039849	Pcif1	protein_coding	PDX1 C-terminal inhibiting factor 1 [Source:MGI Symbol;Acc:MGI:2443858]
ENSMUSG00000035604	Ncoa5	protein_coding	nuclear receptor coactivator 5 [Source:MGI Symbol;Acc:MGI:2385324]
ENSMUSG00000017897	Eya2	protein_coding	eyes absent 2 homolog (Drosophila) [Source:MGI Symbol;Acc:MGI:109341]
ENSMUSG00000039671	Zmynd8	protein_coding	zinc finger, MYND-type containing 8 [Source:MGI Symbol;Acc:MGI:1918025]
ENSMUSG00000027678	Ncoa3	protein_coding	nuclear receptor coactivator 3 [Source:MGI Symbol;Acc:MGI:1276535]
ENSMUSG00000027559	Ddx27	protein_coding	DEAD (Asp-Glu-Ala-Asp) box polypeptide 27 [Source:MGI Symbol;Acc:MGI:2385884]
ENSMUSG00000074578	1500012F01	protein_coding	RIKEN cDNA 1500012F01 gene [Source:MGI Symbol;Acc:MGI:1916199]
ENSMUSG00000047030	Spata2	protein_coding	spermatogenesis associated 2 [Source:MGI Symbol;Acc:MGI:2148805]
ENSMUSG00000027540	Ptpn1	protein_coding	protein tyrosine phosphatase, non-receptor type 1 [Source:MGI Symbol;Acc:MGI:97805]
ENSMUSG00000051149	Adnp	protein_coding	activity-dependent neuroprotective protein [Source:MGI Symbol;Acc:MGI:1338758]
ENSMUSG00000047907	Tshz2	protein_coding	teashirt zinc finger family member 2 [Source:MGI Symbol;Acc:MGI:2153084]
ENSMUSG00000052056	Zfp217	protein_coding	zinc finger protein 217 [Source:MGI Symbol;Acc:MGI:2685492]
ENSMUSG00000027560	Dok5	protein_coding	docking protein 5 [Source:MGI Symbol;Acc:MGI:1924079]
ENSMUSG00000027509	Rae1	protein_coding	RAE1 RNA export 1 homolog (S. pombe) [Source:MGI Symbol;Acc:MGI:1913939]
ENSMUSG00000027518	1700021F0	protein_coding	RIKEN cDNA 1700021F07 gene [Source:MGI Symbol;Acc:MGI:1916471]
ENSMUSG00000027523	Gnas	protein_coding	GNAS (guanine nucleotide binding protein, alpha stimulating) complex locus [Source:MGI Symbol;Acc:MGI:95777]
ENSMUSG00000050821	AU019823	protein_coding	
ENSMUSG00000074520	C330013F1	protein_coding	RIKEN cDNA C330013F16 gene [Source:MGI Symbol;Acc:MGI:1925919]
ENSMUSG00000038963	Slco4a1	protein_coding	solute carrier organic anion transporter family, member 4a1 [Source:MGI Symbol;Acc:MGI:1351866]
ENSMUSG00000038914	Dido1	protein_coding	death inducer-obliterator 1 [Source:MGI Symbol;Acc:MGI:1344352]
ENSMUSG00000038848	Ythdf1	protein_coding	YTH domain family 1 [Source:MGI Symbol;Acc:MGI:1917431]
ENSMUSG00000040209	Zfp704	protein_coding	zinc finger protein 704 [Source:MGI Symbol;Acc:MGI:2180715]
ENSMUSG00000019528	Gyg	protein_coding	glycogenin [Source:MGI Symbol;Acc:MGI:1351614]
ENSMUSG00000039260	Fndc3b	protein_coding	fibronectin type III domain containing 3B [Source:MGI Symbol;Acc:MGI:1919257]
ENSMUSG00000027692	Tnik	protein_coding	TRAF2 and NCK interacting kinase [Source:MGI Symbol;Acc:MGI:1916264]
ENSMUSG00000027684	Mecom	protein_coding	MDS1 and EVI1 complex locus [Source:MGI Symbol;Acc:MGI:95457]
ENSMUSG00000027667	Zfp639	protein_coding	zinc finger protein 639 [Source:MGI Symbol;Acc:MGI:1915025]
ENSMUSG00000027669	Gnb4	protein_coding	guanine nucleotide binding protein (G protein), beta 4 [Source:MGI Symbol;Acc:MGI:104581]
ENSMUSG00000037400	Atp11b	protein_coding	ATPase, class VI, type 11B [Source:MGI Symbol;Acc:MGI:1923945]
ENSMUSG00000027712	Anxa5	protein_coding	annexin A5 [Source:MGI Symbol;Acc:MGI:106008]
ENSMUSG00000027715	Ccna2	protein_coding	cyclin A2 [Source:MGI Symbol;Acc:MGI:108069]
ENSMUSG00000049940	Pgrmc2	protein_coding	progesterone receptor membrane component 2 [Source:MGI Symbol;Acc:MGI:1918054]
ENSMUSG00000037174	Elf2	protein_coding	E74-like factor 2 [Source:MGI Symbol;Acc:MGI:1916507]
ENSMUSG00000063273	Naa15	protein_coding	N(alpha)-acetyltransferase 15, NatA auxiliary subunit [Source:MGI Symbol;Acc:MGI:1922088]
ENSMUSG00000074604	Mgst2	protein_coding	microsomal glutathione S-transferase 2 [Source:MGI Symbol;Acc:MGI:2448481]
ENSMUSG00000061142	Maml3	protein_coding	mastermind like 3 (Drosophila) [Source:MGI Symbol;Acc:MGI:2389461]
ENSMUSG00000027799	Nbea	protein_coding	neurobeachin [Source:MGI Symbol;Acc:MGI:1347075]
ENSMUSG00000027763	Mbnl1	protein_coding	muscleblind-like 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:1928482]
ENSMUSG00000036894	Rap2b	protein_coding	RAP2B, member of RAS oncogene family [Source:MGI Symbol;Acc:MGI:1921262]
ENSMUSG00000034349	Smc4	protein_coding	structural maintenance of chromosomes 4 [Source:MGI Symbol;Acc:MGI:1917349]
ENSMUSG00000027782	Kpna4	protein_coding	karyopherin (importin) alpha 4 [Source:MGI Symbol;Acc:MGI:1100848]
ENSMUSG00000028020	Accn5	protein_coding	amiloride-sensitive cation channel 5, intestinal [Source:MGI Symbol;Acc:MGI:1929259]
ENSMUSG00000033910	Gucy1a3	protein_coding	guanylate cyclase 1, soluble, alpha 3 [Source:MGI Symbol;Acc:MGI:1926562]
ENSMUSG00000037787	D930015E0	protein_coding	RIKEN cDNA D930015E06 gene [Source:MGI Symbol;Acc:MGI:2440599]
ENSMUSG00000074513	Arfip1	protein_coding	ADP-ribosylation factor interacting protein 1 [Source:MGI Symbol;Acc:MGI:1927130]
ENSMUSG00000028081	Rps3a	protein_coding	ribosomal protein S3A [Source:MGI Symbol;Acc:MGI:1202063]
ENSMUSG00000028080	Lrba	protein_coding	LPS-responsive beige-like anchor [Source:MGI Symbol;Acc:MGI:1933162]
ENSMUSG00000004895	Prcc	protein_coding	papillary renal cell carcinoma (translocation-associated) [Source:MGI Symbol;Acc:MGI:2137738]
ENSMUSG00000004897	Hdgf	protein_coding	hepatoma-derived growth factor [Source:MGI Symbol;Acc:MGI:1194494]
ENSMUSG00000028068	Iqgap3	protein_coding	IQ motif containing GTPase activating protein 3 [Source:MGI Symbol;Acc:MGI:2183842]
ENSMUSG00000001415	Smg5	protein_coding	Smg-5 homolog, nonsense mediated mRNA decay factor (C. elegans) [Source:MGI Symbol;Acc:MGI:2447364]
ENSMUSG00000028064	Ubqln4	protein_coding	ubiquilin 4 [Source:MGI Symbol;Acc:MGI:2150152]
ENSMUSG00000054199	Gon4l	protein_coding	gon-4-like (C.elegans) [Source:MGI Symbol;Acc:MGI:1917375]
ENSMUSG00000059743	Fdps	protein_coding	farnesyl diphosphate synthetase [Source:MGI Symbol;Acc:MGI:104888]
ENSMUSG00000027947	Il6ra	protein_coding	interleukin 6 receptor, alpha [Source:MGI Symbol;Acc:MGI:105304]
ENSMUSG00000042520	Ubap2l	protein_coding	ubiquitin associated protein 2-like [Source:MGI Symbol;Acc:MGI:1921430]
ENSMUSG00000038902	Pogz	protein_coding	pogo transposable element with ZNF domain [Source:MGI Symbol;Acc:MGI:2442117]
ENSMUSG00000038861	Pi4kb	protein_coding	phosphatidylinositol 4-kinase, catalytic, beta polypeptide [Source:MGI Symbol;Acc:MGI:1334433]
ENSMUSG00000019338	Zfp687	protein_coding	zinc finger protein 687 [Source:MGI Symbol;Acc:MGI:1925518]
ENSMUSG00000028126	Pip5k1a	protein_coding	phosphatidylinositol-4-phosphate 5-kinase, type 1 alpha [Source:MGI Symbol;Acc:MGI:107929]
ENSMUSG00000015714	Lass2	protein_coding	LAG1 homolog, ceramide synthase 2 [Source:MGI Symbol;Acc:MGI:1924143]
ENSMUSG00000046515	Golph3l	protein_coding	golgi phosphoprotein 3-like [Source:MGI Symbol;Acc:MGI:1917139]
ENSMUSG00000015748	Prpf3	protein_coding	PRP3 pre-mRNA processing factor 3 homolog (yeast) [Source:MGI Symbol;Acc:MGI:1918017]
ENSMUSG00000015749	Anp32e	protein_coding	acidic (leucine-rich) nuclear phosphoprotein 32 family, member E [Source:MGI Symbol;Acc:MGI:1913721]
ENSMUSG00000038495	Otud7b	protein_coding	OTU domain containing 7B [Source:MGI Symbol;Acc:MGI:2654703]
ENSMUSG00000068855	Hist2h2ac	protein_coding	histone cluster 2, H2ac [Source:MGI Symbol;Acc:MGI:2448516]
ENSMUSG00000038256	Bcl9	protein_coding	B-cell CLL/lymphoma 9 [Source:MGI Symbol;Acc:MGI:1924828]
ENSMUSG00000038170	Pde4dip	protein_coding	phosphodiesterase 4D interacting protein (myomegalin) [Source:MGI Symbol;Acc:MGI:1891434]
ENSMUSG00000027878	Notch2	protein_coding	Notch gene homolog 2 (Drosophila) [Source:MGI Symbol;Acc:MGI:97364]
ENSMUSG00000068823	Csde1	protein_coding	cold shock domain containing E1, RNA binding [Source:MGI Symbol;Acc:MGI:1919786]
ENSMUSG00000033014	Trim33	protein_coding	tripartite motif-containing 33 [Source:MGI Symbol;Acc:MGI:2137357]
ENSMUSG00000073680	Gm10564	protein_coding	predicted gene 10564 [Source:MGI Symbol;Acc:MGI:3779779]
ENSMUSG00000008730	Hipk1	protein_coding	homeodomain interacting protein kinase 1 [Source:MGI Symbol;Acc:MGI:1314873]
ENSMUSG00000052539	Magi3	protein_coding	membrane associated guanylate kinase, WW and PDZ domain containing 3 [Source:MGI Symbol;Acc:MGI:1923484]
ENSMUSG00000032902	Slc16a1	protein_coding	solute carrier family 16 (monocarboxylic acid transporters), member 1 [Source:MGI Symbol;Acc:MGI:106013]
ENSMUSG00000000563	Atp5f1	protein_coding	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit B1 [Source:MGI Symbol;Acc:MGI:1100495]

ENSMUSG00000055891	Ubl4b	protein_coding	ubiquitin-like 4B [Source:MGI Symbol;Acc:MGI:1914941]
ENSMUSG00000000001	Gnai3	protein_coding	guanine nucleotide binding protein (G protein), alpha inhibiting 3 [Source:MGI Symbol;Acc:MGI:95773]
ENSMUSG00000040370	Fndc7	protein_coding	fibronectin type III domain containing 7 [Source:MGI Symbol;Acc:MGI:2445331]
ENSMUSG00000044442	4921515J0	protein_coding	RIKEN cDNA 4921515J06 gene [Source:MGI Symbol;Acc:MGI:1912541]
ENSMUSG00000022131	Bcar3	protein_coding	breast cancer anti-estrogen resistance 3 [Source:MGI Symbol;Acc:MGI:1352501]
ENSMUSG00000022785	Fnbp1l	protein_coding	formin binding protein 1-like [Source:MGI Symbol;Acc:MGI:1925642]
ENSMUSG00000044068	Tifa	protein_coding	TRAF-interacting protein with forkhead-associated domain [Source:MGI Symbol;Acc:MGI:2183940]
ENSMUSG00000022034	Enpep	protein_coding	glutamyl aminopeptidase [Source:MGI Symbol;Acc:MGI:102643]
ENSMUSG00000021032	Sec24b	protein_coding	Sec24 related gene family, member B (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2139764]
ENSMUSG00000027984	Hadh	protein_coding	hydroxyacyl-Coenzyme A dehydrogenase [Source:MGI Symbol;Acc:MGI:96009]
ENSMUSG00000028158	Mttp	protein_coding	microsomal triglyceride transfer protein [Source:MGI Symbol;Acc:MGI:106926]
ENSMUSG00000028149	Rapgds1	protein_coding	RAP1, GTP-GDP dissociation stimulator 1 [Source:MGI Symbol;Acc:MGI:2385189]
ENSMUSG00000047040	0610007N1	protein_coding	RIKEN cDNA 0610007N19 gene [Source:MGI Symbol;Acc:MGI:2685846]
ENSMUSG00000074102	Zmynd	protein_coding	zinc finger, HIT type 6 [Source:MGI Symbol;Acc:MGI:1914990]
ENSMUSG00000036003	Syde2	protein_coding	synapse defective 1, Rho GTPase, homolog 2 (C. elegans) [Source:MGI Symbol;Acc:MGI:3036264]
ENSMUSG00000036125	Dnase2b	protein_coding	deoxyribonuclease II beta [Source:MGI Symbol;Acc:MGI:1913283]
ENSMUSG00000005034	Prkacb	protein_coding	protein kinase, cAMP dependent, catalytic, beta [Source:MGI Symbol;Acc:MGI:97594]
ENSMUSG00000036975	Rabggtb	protein_coding	RAB geranylgeranyl transferase, b subunit [Source:MGI Symbol;Acc:MGI:99537]
ENSMUSG00000003228	Lyn	protein_coding	Yamaguchi sarcoma viral (v-yes-1) oncogene homolog [Source:MGI Symbol;Acc:MGI:96892]
ENSMUSG00000036224	Rps20	protein_coding	ribosomal protein S20 [Source:MGI Symbol;Acc:MGI:1914677]
ENSMUSG00000066324	Impad1	protein_coding	inositol monophosphatase domain containing 1 [Source:MGI Symbol;Acc:MGI:1915720]
ENSMUSG00000028249	Sdcbp	protein_coding	syndecan binding protein [Source:MGI Symbol;Acc:MGI:1337026]
ENSMUSG00000040231	Pdp1	protein_coding	pyruvate dehyrogenase phosphatase catalytic subunit 1 [Source:MGI Symbol;Acc:MGI:2685870]
ENSMUSG00000006586	Runx1t1	protein_coding	runt-related transcription factor 1; translocated to, 1 (cyclin D-related) [Source:MGI Symbol;Acc:MGI:104793]
ENSMUSG00000040751	Tmem64	protein_coding	transmembrane protein 64 [Source:MGI Symbol;Acc:MGI:2140359]
ENSMUSG00000028220	Cpne3	protein_coding	copine III [Source:MGI Symbol;Acc:MGI:1917838]
ENSMUSG00000040470	Prdm15	protein_coding	PR domain containing 15 [Source:MGI Symbol;Acc:MGI:2445176]
ENSMUSG00000050008	Mdn1	protein_coding	midasin homolog (yeast) [Source:MGI Symbol;Acc:MGI:1926159]
ENSMUSG00000040138	Pnrc1	protein_coding	proline-rich nuclear receptor coactivator 1 [Source:MGI Symbol;Acc:MGI:1917838]
ENSMUSG00000022867	Zfp292	protein_coding	zinc finger protein 292 [Source:MGI Symbol;Acc:MGI:1353423]
ENSMUSG00000040055	Lingo2	protein_coding	leucine rich repeat and Ig domain containing 2 [Source:MGI Symbol;Acc:MGI:2442128]
ENSMUSG00000028832	Topors	protein_coding	topoisomerase I binding, arginine/serine-rich [Source:MGI Symbol;Acc:MGI:2146182]
ENSMUSG00000028413	B4galt1	protein_coding	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1 [Source:MGI Symbol;Acc:MGI:95705]
ENSMUSG00000028416	Bag1	protein_coding	BCL2-associated athanogene 1 [Source:MGI Symbol;Acc:MGI:108047]
ENSMUSG00000028433	Ubap2	protein_coding	ubiquitin-associated protein 2 [Source:MGI Symbol;Acc:MGI:1914878]
ENSMUSG00000028400	Dcaf12	protein_coding	DDB1 and CUL4 associated factor 12 [Source:MGI Symbol;Acc:MGI:1916220]
ENSMUSG00000078009	Il11ra2	protein_coding	interleukin 11 receptor, alpha chain 2 [Source:MGI Symbol;Acc:MGI:107426]
ENSMUSG00000028078	Sigmar1	protein_coding	sigma non-opioid intracellular receptor 1 [Source:MGI Symbol;Acc:MGI:1195268]
ENSMUSG00000028451	1700022I1	protein_coding	RIKEN cDNA 1700022I11 gene [Source:MGI Symbol;Acc:MGI:1914187]
ENSMUSG00000028452	Vcp	protein_coding	valosin containing protein [Source:MGI Symbol;Acc:MGI:99919]
ENSMUSG00000036401	Ccdc107	protein_coding	coiled-coil domain containing 107 [Source:MGI Symbol;Acc:MGI:1913435]
ENSMUSG00000028465	Tln1	protein_coding	talin 1 [Source:MGI Symbol;Acc:MGI:1099832]
ENSMUSG00000035426	Rnf38	protein_coding	ring finger protein 38 [Source:MGI Symbol;Acc:MGI:1920719]
ENSMUSG00000035615	Frmpd1	protein_coding	FERM and PDZ domain containing 1 [Source:MGI Symbol;Acc:MGI:2446274]
ENSMUSG00000045972	Mcart1	protein_coding	mitochondrial carrier triple repeat 1 [Source:MGI Symbol;Acc:MGI:2384924]
ENSMUSG00000035522	Anp32b	protein_coding	acidic (leucine-rich) nuclear phosphoprotein 32 family, member B [Source:MGI Symbol;Acc:MGI:1914878]
ENSMUSG00000035527	Coro2a	protein_coding	coronin, actin binding protein 2A [Source:MGI Symbol;Acc:MGI:1345968]
ENSMUSG00000039809	Gabbr2	protein_coding	gamma-aminobutyric acid (GABA) B receptor, 2 [Source:MGI Symbol;Acc:MGI:2386030]
ENSMUSG00000053317	Sec61b	protein_coding	Sec61 beta subunit [Source:MGI Symbol;Acc:MGI:1913462]
ENSMUSG00000028311	2810432L1	protein_coding	RIKEN cDNA 2810432L12 gene [Source:MGI Symbol;Acc:MGI:1914615]
ENSMUSG00000028430	Rad23b	protein_coding	RAD23b homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:105128]
ENSMUSG00000028434	Epb4.1l4b	protein_coding	erythrocyte protein band 4.1-like 4b [Source:MGI Symbol;Acc:MGI:1859149]
ENSMUSG00000028941	Gm20459	protein_coding	predicted gene 20459 [Source:MGI Symbol;Acc:MGI:5141924]
ENSMUSG00000028467	Txn1	protein_coding	thioredoxin 1 [Source:MGI Symbol;Acc:MGI:98874]
ENSMUSG00000028709	Txndc8	protein_coding	thioredoxin domain containing 8 [Source:MGI Symbol;Acc:MGI:1914412]
ENSMUSG00000028812	AI314180	protein_coding	expressed sequence AI314180 [Source:MGI Symbol;Acc:MGI:2140339]
ENSMUSG00000028358	AI481877	protein_coding	expressed sequence AI481877 [Source:MGI Symbol;Acc:MGI:2140815]
ENSMUSG00000028378	Susd1	protein_coding	sushi domain containing 1 [Source:MGI Symbol;Acc:MGI:2682545]
ENSMUSG00000028382	Rod1	protein_coding	ROD1 regulator of differentiation 1 (S. pombe) [Source:MGI Symbol;Acc:MGI:1923284]
ENSMUSG00000049071	C130080A1	protein_coding	RIKEN cDNA C130080A19 gene [Source:MGI Symbol;Acc:MGI:2442144]
ENSMUSG00000028393	Alad	protein_coding	aminolevulinate, delta-, dehydratase [Source:MGI Symbol;Acc:MGI:96853]
ENSMUSG00000028373	Astn2	protein_coding	astrotactin 2 [Source:MGI Symbol;Acc:MGI:1889277]
ENSMUSG00000028399	Ptprd	protein_coding	protein tyrosine phosphatase, receptor type, D [Source:MGI Symbol;Acc:MGI:97812]
ENSMUSG00000070923	Klhl9	protein_coding	kelch-like 9 (Drosophila) [Source:MGI Symbol;Acc:MGI:2180122]
ENSMUSG00000052684	Jun	protein_coding	Jun oncogene [Source:MGI Symbol;Acc:MGI:96646]
ENSMUSG00000028133	Cyp2j12	protein_coding	cytochrome P450, family 2, subfamily j, polypeptide 12 [Source:MGI Symbol;Acc:MGI:2717027]
ENSMUSG00000028565	Nfia	protein_coding	nuclear factor I/A [Source:MGI Symbol;Acc:MGI:108056]
ENSMUSG00000035407	Kank4	protein_coding	KN motif and ankyrin repeat domains 4 [Source:MGI Symbol;Acc:MGI:3043381]
ENSMUSG00000028560	Usp1	protein_coding	ubiquitin specific peptidase 1 [Source:MGI Symbol;Acc:MGI:2385198]
ENSMUSG00000028530	Jak1	protein_coding	Janus kinase 1 [Source:MGI Symbol;Acc:MGI:96628]
ENSMUSG00000028525	Pde4b	protein_coding	phosphodiesterase 4B, cAMP specific [Source:MGI Symbol;Acc:MGI:99557]
ENSMUSG00000075017	Gm10902	protein_coding	predicted gene 10902 [Source:MGI Symbol;Acc:MGI:3779174]
ENSMUSG00000028519	Dab1	protein_coding	disabled homolog 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:108554]
ENSMUSG00000028514	Usp24	protein_coding	ubiquitin specific peptidase 24 [Source:MGI Symbol;Acc:MGI:1919936]
ENSMUSG00000034926	Dhcr24	protein_coding	24-dehydrocholesterol reductase [Source:MGI Symbol;Acc:MGI:1922004]
ENSMUSG00000034871	Fam151a	protein_coding	family with sequence similarity 151, member A [Source:MGI Symbol;Acc:MGI:2657115]
ENSMUSG00000034853	Acot11	protein_coding	acyl-CoA thioesterase 11 [Source:MGI Symbol;Acc:MGI:1913736]
ENSMUSG00000061887	Ssbp3	protein_coding	single-stranded DNA binding protein 3 [Source:MGI Symbol;Acc:MGI:1919725]
ENSMUSG00000047145	Dmrta2	protein_coding	doublesex and mab-3 related transcription factor like family A2 [Source:MGI Symbol;Acc:MGI:2652635]
ENSMUSG00000041258	Agbl4	protein_coding	ATP/GTP binding protein-like 4 [Source:MGI Symbol;Acc:MGI:1918244]
ENSMUSG00000072358	Skint3	protein_coding	selection and upkeep of intraepithelial T cells 3 [Source:MGI Symbol;Acc:MGI:2680151]
ENSMUSG00000022718	Stil	protein_coding	Scl/Tal1 interrupting locus [Source:MGI Symbol;Acc:MGI:107477]
ENSMUSG00000022717	Tal1	protein_coding	T-cell acute lymphocytic leukemia 1 [Source:MGI Symbol;Acc:MGI:98480]
ENSMUSG00000022707	Dmbx1	protein_coding	diencephalon/mesencephalon homeobox 1 [Source:MGI Symbol;Acc:MGI:2135318]
ENSMUSG00000028692	Akr1a1	protein_coding	aldo-keto reductase family 1, member A1 (aldehyde reductase) [Source:MGI Symbol;Acc:MGI:1929955]
ENSMUSG00000047675	Rps8	protein_coding	ribosomal protein S8 [Source:MGI Symbol;Acc:MGI:98166]
ENSMUSG00000028677	Rnf220	protein_coding	ring finger protein 220 [Source:MGI Symbol;Acc:MGI:1915990]
ENSMUSG00000028679	Atp6v0b	protein_coding	ATPase, H+ transporting, lysosomal V0 subunit B [Source:MGI Symbol;Acc:MGI:1890510]
ENSMUSG00000028628	Kdm4a	protein_coding	lysine (K)-specific demethylase 4A [Source:MGI Symbol;Acc:MGI:2446210]
ENSMUSG00000028630	Elovl1	protein_coding	elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 1 [Source:MGI Symbol;Acc:MGI:1858959]
ENSMUSG00000006389	Mpl	protein_coding	myeloproliferative leukemia virus oncogene [Source:MGI Symbol;Acc:MGI:97076]
ENSMUSG00000028645	Slc2a1	protein_coding	solute carrier family 2 (facilitated glucose transporter), member 1 [Source:MGI Symbol;Acc:MGI:95755]
ENSMUSG00000028644	Ermap	protein_coding	erythroblast membrane-associated protein [Source:MGI Symbol;Acc:MGI:1349816]
ENSMUSG00000075524	AU022252	protein_coding	expressed sequence AU022252 [Source:MGI Symbol;Acc:MGI:2140480]
ENSMUSG00000028639	Ybx1	protein_coding	Y box protein 1 [Source:MGI Symbol;Acc:MGI:99146]
ENSMUSG00000032897	Nfyc	protein_coding	nuclear transcription factor-Y gamma [Source:MGI Symbol;Acc:MGI:107901]
ENSMUSG00000064141	Zfp69	protein_coding	zinc finger protein 69 [Source:MGI Symbol;Acc:MGI:107794]
ENSMUSG00000032870	Smap2	protein_coding	stromal membrane-associated GTPase-activating protein 2 [Source:MGI Symbol;Acc:MGI:1917030]
ENSMUSG00000028657	Ppt1	protein_coding	palmitoyl-protein thioesterase 1 [Source:MGI Symbol;Acc:MGI:1298204]
ENSMUSG00000028656	Cap1	protein_coding	CAP, adenylate cyclase-associated protein 1 (yeast) [Source:MGI Symbol;Acc:MGI:88262]
ENSMUSG00000028649	Macf1	protein_coding	microtubule-actin crosslinking factor 1 [Source:MGI Symbol;Acc:MGI:108559]
ENSMUSG00000028646	Rragc	protein_coding	Ras-related GTP binding C [Source:MGI Symbol;Acc:MGI:1858751]
ENSMUSG00000028894	Inpp5b	protein_coding	inositol polyphosphate-5-phosphatase B [Source:MGI Symbol;Acc:MGI:103257]
ENSMUSG00000072579	1110065P2	protein_coding	RIKEN cDNA 1110065P20 gene [Source:MGI Symbol;Acc:MGI:1916170]
ENSMUSG00000001985	Grik3	protein_coding	glutamate receptor, ionotropic, kainate 3 [Source:MGI Symbol;Acc:MGI:95816]
ENSMUSG00000042563	Thrap3	protein_coding	thyroid hormone receptor associated protein 3 [Source:MGI Symbol;Acc:MGI:2442637]
ENSMUSG00000028649	Map7d1	protein_coding	microtubule-associated protein 7 domain containing 1 [Source:MGI Symbol;Acc:MGI:1891397]

ENSMUSG00000042558	Adprhl2	protein_coding	ADP-ribosylhydrolase like 2 [Source:MGI Symbol;Acc:MGI:2140364]
ENSMUSG00000028837	Psmb2	protein_coding	proteasome (prosome, macropain) subunit, beta type 2 [Source:MGI Symbol;Acc:MGI:1347045]
ENSMUSG00000028820	Sfpq	protein_coding	splicing factor proline/glutamine rich (polypyrimidine tract binding protein associated) [Source:MGI Symbol;Acc:MGI:1918764]
ENSMUSG00000028804	Csmd2	protein_coding	CUB and Sushi multiple domains 2 [Source:MGI Symbol;Acc:MGI:2386401]
ENSMUSG00000028758	Phc2	protein_coding	polyhomeotic-like 2 (Drosophila) [Source:MGI Symbol;Acc:MGI:1860454]
ENSMUSG00000028792	Ak2	protein_coding	adenylate kinase 2 [Source:MGI Symbol;Acc:MGI:87978]
ENSMUSG00000028811	Yars	protein_coding	tyrosyl-tRNA synthetase [Source:MGI Symbol;Acc:MGI:2147627]
ENSMUSG00000057236	Rbbp4	protein_coding	retinoblastoma binding protein 4 [Source:MGI Symbol;Acc:MGI:1194912]
ENSMUSG00000047945	Marcksl1	protein_coding	MARCKS-like 1 [Source:MGI Symbol;Acc:MGI:97143]
ENSMUSG00000028840	Tnln	protein_coding	taulin alpha [Source:MGI Symbol;Acc:MGI:105916]
ENSMUSG00000028730	Khdrbs1	protein_coding	KH domain containing, RNA binding, signal transduction associated 1 [Source:MGI Symbol;Acc:MGI:893579]
ENSMUSG00000028708	Ptp4a2	protein_coding	protein tyrosine phosphatase 4a2 [Source:MGI Symbol;Acc:MGI:1277117]
ENSMUSG00000074088	Snrnp40	protein_coding	small nuclear ribonucleoprotein 40 (U5) [Source:MGI Symbol;Acc:MGI:1913835]
ENSMUSG00000028580	Pum1	protein_coding	pumilio 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:1931749]
ENSMUSG00000028930	Laptm5	protein_coding	lysosomal-associated protein transmembrane 5 [Source:MGI Symbol;Acc:MGI:108046]
ENSMUSG00000028911	Srsf4	protein_coding	serine/arginine-rich splicing factor 4 [Source:MGI Symbol;Acc:MGI:1890577]
ENSMUSG00000028906	Epb4.1	protein_coding	erythrocyte protein band 4.1 [Source:MGI Symbol;Acc:MGI:95401]
ENSMUSG00000040025	Ythdf2	protein_coding	YTH domain family 2 [Source:MGI Symbol;Acc:MGI:2444233]
ENSMUSG00000028826	Rcc1	protein_coding	regulator of chromosome condensation 1 [Source:MGI Symbol;Acc:MGI:1913989]
ENSMUSG00000028830	Eya3	protein_coding	eyes absent 3 homolog (Drosophila) [Source:MGI Symbol;Acc:MGI:109339]
ENSMUSG00000028822	Ppp1r8	protein_coding	protein phosphatase 1, regulatory (inhibitor) subunit 8 [Source:MGI Symbol;Acc:MGI:2140494]
ENSMUSG00000037692	Ahdc1	protein_coding	AT hook, DNA binding motif, containing 1 [Source:MGI Symbol;Acc:MGI:2444218]
ENSMUSG00000028868	Wasf2	protein_coding	WAS protein family, member 2 [Source:MGI Symbol;Acc:MGI:1098641]
ENSMUSG00000028851	Nudc	protein_coding	nuclear distribution gene C homolog (Aspergillus) [Source:MGI Symbol;Acc:MGI:106014]
ENSMUSG00000007880	Arid1a	protein_coding	AT rich interactive domain 1A (SWI-like) [Source:MGI Symbol;Acc:MGI:1935147]
ENSMUSG00000003644	Rps6ka1	protein_coding	ribosomal protein S6 kinase polypeptide 1 [Source:MGI Symbol;Acc:MGI:104558]
ENSMUSG00000078521	2610002J02Rik	protein_coding	RIKEN cDNA 2610002J02 gene [Source:MGI Symbol;Acc:MGI:1917135]
ENSMUSG00000057716	D4Wsu53e	protein_coding	DNA segment, Chr 4, Wayne State University 53, expressed [Source:MGI Symbol;Acc:MGI:104498]
ENSMUSG00000028809	Srrm1	protein_coding	serine/arginine repetitive matrix 1 [Source:MGI Symbol;Acc:MGI:1858303]
ENSMUSG00000066037	Hnrnpr	protein_coding	heterogeneous nuclear ribonucleoprotein R [Source:MGI Symbol;Acc:MGI:1891692]
ENSMUSG00000070687	Htr1d	protein_coding	5-hydroxytryptamine (serotonin) receptor 1D [Source:MGI Symbol;Acc:MGI:96276]
ENSMUSG00000036940	Kdm1a	protein_coding	lysine (K)-specific demethylase 1A [Source:MGI Symbol;Acc:MGI:1196256]
ENSMUSG00000057530	Ece1	protein_coding	endothelin converting enzyme 1 [Source:MGI Symbol;Acc:MGI:1101357]
ENSMUSG00000066036	Ubr4	protein_coding	ubiquitin protein ligase E3 component n-recognin 4 [Source:MGI Symbol;Acc:MGI:1916366]
ENSMUSG00000041025	Iffo2	protein_coding	intermediate filament family orphan 2 [Source:MGI Symbol;Acc:MGI:2140675]
ENSMUSG00000040972	Igsf21	protein_coding	immunoglobulin superfamily, member 21 [Source:MGI Symbol;Acc:MGI:2681842]
ENSMUSG00000040945	Rcc2	protein_coding	regulator of chromosome condensation 2 [Source:MGI Symbol;Acc:MGI:1919784]
ENSMUSG00000036622	Atp13a2	protein_coding	ATPase type 13A2 [Source:MGI Symbol;Acc:MGI:1922022]
ENSMUSG00000040761	Spen	protein_coding	SPEN homolog, transcriptional regulator (Drosophila) [Source:MGI Symbol;Acc:MGI:1891706]
ENSMUSG00000078515	Ddi2	protein_coding	DNA-damage inducible protein 2 [Source:MGI Symbol;Acc:MGI:1917244]
ENSMUSG00000044426	2210065G01Rik	protein_coding	RIKEN cDNA 2210065G01 gene [Source:MGI Symbol;Acc:MGI:1934124]
ENSMUSG00000028991	Mtor	protein_coding	mechanistic target of rapamycin (serine/threonine kinase) [Source:MGI Symbol;Acc:MGI:1928394]
ENSMUSG00000041459	Tardbp	protein_coding	TAR DNA binding protein [Source:MGI Symbol;Acc:MGI:2387629]
ENSMUSG00000028977	Casz1	protein_coding	castor homolog 1, zinc finger (Drosophila) [Source:MGI Symbol;Acc:MGI:1196251]
ENSMUSG00000028961	Pgd	protein_coding	phosphogluconate dehydrogenase [Source:MGI Symbol;Acc:MGI:97553]
ENSMUSG00000063524	Eno1	protein_coding	enolase 1, alpha non-neuron [Source:MGI Symbol;Acc:MGI:95393]
ENSMUSG00000039852	Rere	protein_coding	arginine glutamic acid dipeptide (RE) repeats [Source:MGI Symbol;Acc:MGI:2683486]
ENSMUSG00000028964	Park7	protein_coding	Parkinson disease (autosomal recessive, early onset) 7 [Source:MGI Symbol;Acc:MGI:2135637]
ENSMUSG00000014592	Camta1	protein_coding	calmodulin binding transcription activator 1 [Source:MGI Symbol;Acc:MGI:2140230]
ENSMUSG00000028940	Nol9	protein_coding	nucleolar protein 9 [Source:MGI Symbol;Acc:MGI:1921285]
ENSMUSG00000028937	Acot7	protein_coding	acyl-CoA thioesterase 7 [Source:MGI Symbol;Acc:MGI:1917275]
ENSMUSG00000028936	Rpl22	protein_coding	ribosomal protein L22 [Source:MGI Symbol;Acc:MGI:99262]
ENSMUSG00000028931	Kcnab2	protein_coding	potassium voltage-gated channel, shaker-related subfamily, beta member 2 [Source:MGI Symbol;Acc:MGI:109239]
ENSMUSG00000028877	Nphp4	protein_coding	nephronophthisis 4 (juvenile) homolog (human) [Source:MGI Symbol;Acc:MGI:2384210]
ENSMUSG00000057751	Megf6	protein_coding	multiple EGF-like-domains 6 [Source:MGI Symbol;Acc:MGI:1919351]
ENSMUSG00000039410	Prdm16	protein_coding	PR domain containing 16 [Source:MGI Symbol;Acc:MGI:1917835]
ENSMUSG00000029050	Ski	protein_coding	ski sarcoma viral oncogene homolog (avian) [Source:MGI Symbol;Acc:MGI:98310]
ENSMUSG00000042202	Slc35e2	protein_coding	solute carrier family 35, member E2 [Source:MGI Symbol;Acc:MGI:2444240]
ENSMUSG00000040274	Cdk8	protein_coding	cyclin-dependent kinase 8 [Source:MGI Symbol;Acc:MGI:1277162]
ENSMUSG00000040351	Ankib1	protein_coding	ankyrin repeat and IBR domain containing 1 [Source:MGI Symbol;Acc:MGI:1918047]
ENSMUSG00000001467	Cyp51	protein_coding	cytochrome P450, family 51 [Source:MGI Symbol;Acc:MGI:106040]
ENSMUSG00000028926	Cdk14	protein_coding	cyclin-dependent kinase 14 [Source:MGI Symbol;Acc:MGI:894318]
ENSMUSG00000002297	Dbf4	protein_coding	DBF4 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1351328]
ENSMUSG00000040118	Cacna2d1	protein_coding	calcium channel, voltage-dependent, alpha2/delta subunit 1 [Source:MGI Symbol;Acc:MGI:88295]
ENSMUSG00000028780	Sema3c	protein_coding	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C [Source:MGI Symbol;Acc:MGI:107557]
ENSMUSG00000040003	Magi2	protein_coding	membrane associated guanylate kinase, WW and PDZ domain containing 2 [Source:MGI Symbol;Acc:MGI:1354953]
ENSMUSG00000039968	Rsbn1l	protein_coding	round spermatid basic protein 1-like [Source:MGI Symbol;Acc:MGI:2684137]
ENSMUSG00000028771	Ptpn12	protein_coding	protein tyrosine phosphatase, non-receptor type 12 [Source:MGI Symbol;Acc:MGI:104673]
ENSMUSG00000028932	Psmc2	protein_coding	proteasome (prosome, macropain) 26S subunit, ATPase 2 [Source:MGI Symbol;Acc:MGI:109555]
ENSMUSG00000029004	Mll5	protein_coding	myeloid/lymphoid or mixed-lineage leukemia 5 [Source:MGI Symbol;Acc:MGI:1924825]
ENSMUSG00000028973	Abcb8	protein_coding	ATP-binding cassette, sub-family B (MDR/TAP), member 8 [Source:MGI Symbol;Acc:MGI:1351667]
ENSMUSG00000028969	Cdk5	protein_coding	cyclin-dependent kinase 5 [Source:MGI Symbol;Acc:MGI:101765]
ENSMUSG00000038181	Chpf2	protein_coding	chondroitin polymerizing factor 2 [Source:MGI Symbol;Acc:MGI:1917522]
ENSMUSG00000028949	Smarcd3	protein_coding	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3 [Source:MGI Symbol;Acc:MGI:1914243]
ENSMUSG00000025747	Tyms	protein_coding	thymidylate synthase [Source:MGI Symbol;Acc:MGI:98878]
ENSMUSG00000029163	Emilin1	protein_coding	elastin microfibril interfacer 1 [Source:MGI Symbol;Acc:MGI:1926189]
ENSMUSG00000045302	Preb	protein_coding	prolactin regulatory element binding [Source:MGI Symbol;Acc:MGI:1355326]
ENSMUSG00000013629	Cad	protein_coding	carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotase [Source:MGI Symbol;Acc:MGI:1916969]
ENSMUSG00000029147	Ppm1g	protein_coding	protein phosphatase 1G (formerly 2C), magnesium-dependent, gamma isoform [Source:MGI Symbol;Acc:MGI:106065]
ENSMUSG00000029484	Gckr	protein_coding	glucokinase regulatory protein [Source:MGI Symbol;Acc:MGI:1096345]
ENSMUSG00000029374	RP23-118...	protein_coding	MGC2221, isoform CRA_h, Uncharacterized protein [Source:UniProtKB/TrEMBL;Acc:Q3TI24]
ENSMUSG00000094269	C330019G07Rik	protein_coding	RIKEN cDNA C330019G07 gene [Source:MGI Symbol;Acc:MGI:3443658]
ENSMUSG00000037373	Ctbp1	protein_coding	C-terminal binding protein 1 [Source:MGI Symbol;Acc:MGI:1201685]
ENSMUSG00000079562	Maea	protein_coding	macrophage erythroblast attacher [Source:MGI Symbol;Acc:MGI:1891748]
ENSMUSG00000029110	Rnf4	protein_coding	ring finger protein 4 [Source:MGI Symbol;Acc:MGI:1201691]
ENSMUSG00000037210	Fam193a	protein_coding	family with sequence similarity 193, member A [Source:MGI Symbol;Acc:MGI:2447785]
ENSMUSG00000029104	Htt	protein_coding	huntingtin [Source:MGI Symbol;Acc:MGI:96067]
ENSMUSG00000045318	Adra2c	protein_coding	adrenergic receptor, alpha 2c [Source:MGI Symbol;Acc:MGI:87936]
ENSMUSG00000029094	Afap1	protein_coding	actin filament associated protein 1 [Source:MGI Symbol;Acc:MGI:1917542]
ENSMUSG00000029093	Sorcs2	protein_coding	sortilin-related VPS10 domain containing receptor 2 [Source:MGI Symbol;Acc:MGI:1932289]
ENSMUSG00000048450	Psapl1	protein_coding	prosaposin-like 1 [Source:MGI Symbol;Acc:MGI:1920495]
ENSMUSG00000035120	D5Ertd579e	protein_coding	DNA segment, Chr 5, ERATO Doi 579, expressed [Source:MGI Symbol;Acc:MGI:1261845]
ENSMUSG00000029122	Evc	protein_coding	Ellis van Creveld gene homolog (human) [Source:MGI Symbol;Acc:MGI:1890596]
ENSMUSG00000005103	Wdr1	protein_coding	WD repeat domain 1 [Source:MGI Symbol;Acc:MGI:1337100]
ENSMUSG00000029088	Kcnip4	protein_coding	Kv channel interacting protein 4 [Source:MGI Symbol;Acc:MGI:1933131]
ENSMUSG00000029108	Pcdh7	protein_coding	protocadherin 7 [Source:MGI Symbol;Acc:MGI:1860487]
ENSMUSG00000037795	N4bp2	protein_coding	NEDD4 binding protein 2 [Source:MGI Symbol;Acc:MGI:2684410]
ENSMUSG00000029206	Nsun7	protein_coding	NOL1/NOP2/Sun domain family, member 7 [Source:MGI Symbol;Acc:MGI:1914108]
ENSMUSG00000092060	Bend4	protein_coding	BEN domain containing 4 [Source:MGI Symbol;Acc:MGI:3648414]
ENSMUSG00000029212	Gabrb1	protein_coding	gamma-aminobutyric acid (GABA) A receptor, subunit beta 1 [Source:MGI Symbol;Acc:MGI:95619]
ENSMUSG00000070733	Fryl	protein_coding	furry homolog-like (Drosophila) [Source:MGI Symbol;Acc:MGI:1919563]
ENSMUSG00000029227	Fip1l1	protein_coding	FIP1 like 1 (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1914149]
ENSMUSG00000005672	Kit	protein_coding	kit oncogene [Source:MGI Symbol;Acc:MGI:96677]
ENSMUSG00000029277	C530008M17Rik	protein_coding	RIKEN cDNA C530008M17 gene [Source:MGI Symbol;Acc:MGI:2444817]
ENSMUSG00000029249	Rest	protein_coding	RE1-silencing transcription factor [Source:MGI Symbol;Acc:MGI:104897]
ENSMUSG00000029250	Polr2b	protein_coding	polymerase (RNA) II (DNA directed) polypeptide B [Source:MGI Symbol;Acc:MGI:2388280]
ENSMUSG00000055204	Ankrd17	protein_coding	ankyrin repeat domain 17 [Source:MGI Symbol;Acc:MGI:1932101]

ENSMUSG00000029373	Pf4	protein_coding	platelet factor 4 [Source:MGI Symbol;Acc:MGI:1888711]
ENSMUSG00000022403	G3bp2	protein_coding	GTPase activating protein (SH3 domain) binding protein 2 [Source:MGI Symbol;Acc:MGI:2442040]
ENSMUSG00000034613	Bmp2k	protein_coding	BMP2 inducible kinase [Source:MGI Symbol;Acc:MGI:2155456]
ENSMUSG00000022735	Paqr5	protein_coding	progestin and adipoQ receptor family member III [Source:MGI Symbol;Acc:MGI:2678383]
ENSMUSG00000027810	1700007G11	protein_coding	RIKEN cDNA 1700007G11 gene [Source:MGI Symbol;Acc:MGI:1916371]
ENSMUSG00000022285	Rasgef1b	protein_coding	RasGEF domain family, member 1B [Source:MGI Symbol;Acc:MGI:2442755]
ENSMUSG00000000568	Hnrnpd	protein_coding	heterogeneous nuclear ribonucleoprotein D [Source:MGI Symbol;Acc:MGI:101947]
ENSMUSG00000022238	Hnrpdl	protein_coding	heterogeneous nuclear ribonucleoprotein D-like [Source:MGI Symbol;Acc:MGI:1355299]
ENSMUSG00000022235	Sec31a	protein_coding	Sec31 homolog A (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1916412]
ENSMUSG00000035273	Hpse	protein_coding	heparanase [Source:MGI Symbol;Acc:MGI:1343124]
ENSMUSG00000043940	Wdfy3	protein_coding	WD repeat and FYVE domain containing 3 [Source:MGI Symbol;Acc:MGI:1096875]
ENSMUSG00000029313	Aff1	protein_coding	AF4/FMR2 family, member 1 [Source:MGI Symbol;Acc:MGI:1100819]
ENSMUSG00000070033	Lrrc8b	protein_coding	leucine rich repeat containing 8 family, member B [Source:MGI Symbol;Acc:MGI:2140839]
ENSMUSG00000044079	Lrrc8d	protein_coding	leucine rich repeat containing 8D [Source:MGI Symbol;Acc:MGI:1922368]
ENSMUSG00000049606	Zfp644	protein_coding	zinc finger protein 644 [Source:MGI Symbol;Acc:MGI:1277212]
ENSMUSG00000011831	Evi5	protein_coding	ecotropic viral integration site 5 [Source:MGI Symbol;Acc:MGI:104736]
ENSMUSG00000058558	Rpl5	protein_coding	ribosomal protein L5 [Source:MGI Symbol;Acc:MGI:102854]
ENSMUSG00000039107	Mtf2	protein_coding	metal response element binding transcription factor 2 [Source:MGI Symbol;Acc:MGI:105050]
ENSMUSG00000033324	Gak	protein_coding	cyclin G associated kinase [Source:MGI Symbol;Acc:MGI:2442153]
ENSMUSG00000048522	Fbrsl1	protein_coding	fibrosin-like 1 [Source:MGI Symbol;Acc:MGI:1919207]
ENSMUSG00000039107	Pus1	protein_coding	pseudouridine synthase 1 [Source:MGI Symbol;Acc:MGI:1929237]
ENSMUSG00000022345	Tfip11	protein_coding	tuftelin interacting protein 11 [Source:MGI Symbol;Acc:MGI:1930075]
ENSMUSG00000030113	Sesn1	protein_coding	seizure related 6 homolog like [Source:MGI Symbol;Acc:MGI:1930321]
ENSMUSG00000040013	Selplg	protein_coding	selectin, platelet (p-selectin) ligand [Source:MGI Symbol;Acc:MGI:106689]
ENSMUSG00000004530	Coro1c	protein_coding	coronin, actin binding protein 1C [Source:MGI Symbol;Acc:MGI:1345964]
ENSMUSG00000042010	Acacb	protein_coding	acetyl-Coenzyme A carboxylase beta [Source:MGI Symbol;Acc:MGI:2140940]
ENSMUSG00000008511	Myo1h	protein_coding	myosin 1H [Source:MGI Symbol;Acc:MGI:1914674]
ENSMUSG00000001090	Kctd10	protein_coding	potassium channel tetramerisation domain containing 10 [Source:MGI Symbol;Acc:MGI:2141207]
ENSMUSG00000022377	Ube2b	protein_coding	ubiquitin protein ligase E3B [Source:MGI Symbol;Acc:MGI:1331128]
ENSMUSG00000041890	Git2	protein_coding	G protein-coupled receptor kinase-interactor 2 [Source:MGI Symbol;Acc:MGI:1347053]
ENSMUSG00000041870	Ankrd13a	protein_coding	ankyrin repeat domain 13a [Source:MGI Symbol;Acc:MGI:1915670]
ENSMUSG00000022559	Sppl3	protein_coding	signal peptide peptidase 3 [Source:MGI Symbol;Acc:MGI:1891433]
ENSMUSG00000072655	Gm10401	protein_coding	predicted gene 10401 [Source:MGI Symbol;Acc:MGI:3704254]
ENSMUSG00000042378	Mlec	protein_coding	malectin [Source:MGI Symbol;Acc:MGI:1924015]
ENSMUSG00000041740	Rnf10	protein_coding	ring finger protein 10 [Source:MGI Symbol;Acc:MGI:1859162]
ENSMUSG00000029153	Tnap1	protein_coding	TP53 regulated inhibitor of apoptosis 1 [Source:MGI Symbol;Acc:MGI:1915828]
ENSMUSG00000041697	Cox6a1	protein_coding	cytochrome c oxidase, subunit VI a, polypeptide 1 [Source:MGI Symbol;Acc:MGI:103099]
ENSMUSG00000029528	Pxn	protein_coding	paxillin [Source:MGI Symbol;Acc:MGI:108295]
ENSMUSG00000029518	Rab35	protein_coding	RAB35, member RAS oncogene family [Source:MGI Symbol;Acc:MGI:1924657]
ENSMUSG00000029516	Cit	protein_coding	citron [Source:MGI Symbol;Acc:MGI:105313]
ENSMUSG00000029582	Rfc5	protein_coding	replication factor C (activator 1) 5 [Source:MGI Symbol;Acc:MGI:1919401]
ENSMUSG00000029361	Nos1	protein_coding	nitric oxide synthase 1, neuronal [Source:MGI Symbol;Acc:MGI:97360]
ENSMUSG00000016076	Med13l	protein_coding	mediator complex subunit 13-like [Source:MGI Symbol;Acc:MGI:2670175]
ENSMUSG00000043733	Ptpn11	protein_coding	protein tyrosine phosphatase, non-receptor type 11 [Source:MGI Symbol;Acc:MGI:99511]
ENSMUSG00000029614	Rpl6	protein_coding	ribosomal protein L6 [Source:MGI Symbol;Acc:MGI:108057]
ENSMUSG00000043744	Gm15800	protein_coding	predicted gene 15800 [Source:MGI Symbol;Acc:MGI:3647820]
ENSMUSG00000029616	Erp29	protein_coding	endoplasmic reticulum protein 29 [Source:MGI Symbol;Acc:MGI:1914647]
ENSMUSG00000029455	Aldh2	protein_coding	aldehyde dehydrogenase 2, mitochondrial [Source:MGI Symbol;Acc:MGI:99600]
ENSMUSG00000042594	Sh2b3	protein_coding	SH2B adaptor protein 3 [Source:MGI Symbol;Acc:MGI:893598]
ENSMUSG00000042589	Cux2	protein_coding	cut-like homeobox 2 [Source:MGI Symbol;Acc:MGI:107321]
ENSMUSG00000064267	Hvcn1	protein_coding	hydrogen voltage-gated channel 1 [Source:MGI Symbol;Acc:MGI:1921346]
ENSMUSG00000032582	Pptc7	protein_coding	PTC7 protein phosphatase homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2444593]
ENSMUSG00000029465	Arpc3	protein_coding	actin related protein 2/3 complex, subunit 3 [Source:MGI Symbol;Acc:MGI:1928375]
ENSMUSG00000029467	Atp2a2	protein_coding	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2 [Source:MGI Symbol;Acc:MGI:88110]
ENSMUSG00000029475	Kdm2b	protein_coding	lysine (K)-specific demethylase 2B [Source:MGI Symbol;Acc:MGI:1354737]
ENSMUSG00000042680	Orai1	protein_coding	ORAI calcium release-activated calcium modulator 1 [Source:MGI Symbol;Acc:MGI:1925542]
ENSMUSG00000029454	Setd1b	protein_coding	SET domain containing 1B [Source:MGI Symbol;Acc:MGI:2652820]
ENSMUSG00000029438	Bcl7a	protein_coding	B cell CLL/lymphoma 7A [Source:MGI Symbol;Acc:MGI:1924290]
ENSMUSG00000029343	Mlxip	protein_coding	MLX interacting protein [Source:MGI Symbol;Acc:MGI:2141183]
ENSMUSG00000029108	Denr	protein_coding	density-regulated protein [Source:MGI Symbol;Acc:MGI:1915434]
ENSMUSG00000029394	Cdk2ap1	protein_coding	CDK2 (cyclin dependent kinase 2)-associated protein 1 [Source:MGI Symbol;Acc:MGI:1202069]
ENSMUSG00000038025	Sbno1	protein_coding	sno, strawberry notch homolog 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:2158790]
ENSMUSG00000038023	Atp6v0a2	protein_coding	ATPase, H+ transporting, lysosomal V0 subunit A2 [Source:MGI Symbol;Acc:MGI:104855]
ENSMUSG00000079215	Zfp664	protein_coding	zinc finger protein 664 [Source:MGI Symbol;Acc:MGI:2442105]
ENSMUSG00000051913	Zfp664	protein_coding	zinc finger protein 664 [Source:MGI Symbol;Acc:MGI:2442105]
ENSMUSG00000029478	Ncor2	protein_coding	nuclear receptor co-repressor 2 [Source:MGI Symbol;Acc:MGI:1337080]
ENSMUSG00000037965	Bri3bp	protein_coding	Bri3 binding protein [Source:MGI Symbol;Acc:MGI:1934035]
ENSMUSG00000029422	Aacs	protein_coding	acetoacetyl-CoA synthetase [Source:MGI Symbol;Acc:MGI:1926144]
ENSMUSG00000045524	Tmem132c	protein_coding	transmembrane protein 132C [Source:MGI Symbol;Acc:MGI:3442061]
ENSMUSG00000045510	Tmem132d	protein_coding	transmembrane protein 132D [Source:MGI Symbol;Acc:MGI:3044963]
ENSMUSG00000029420	Rimbp2	protein_coding	RIMS binding protein 2 [Source:MGI Symbol;Acc:MGI:2443235]
ENSMUSG00000029433	Sfswap	protein_coding	splicing factor, suppressor of white-apricot homolog (Drosophila) [Source:MGI Symbol;Acc:MGI:1017469]
ENSMUSG00000029447	Cct6a	protein_coding	chaperonin containing Tcp1, subunit 6a (zeta) [Source:MGI Symbol;Acc:MGI:107943]
ENSMUSG00000025537	Phkg1	protein_coding	phosphorylase kinase gamma 1 [Source:MGI Symbol;Acc:MGI:97579]
ENSMUSG00000025340	Rabgef1	protein_coding	RAB guanine nucleotide exchange factor (GEF) 1 [Source:MGI Symbol;Acc:MGI:1929459]
ENSMUSG00000034040	Wbscr17	protein_coding	Williams-Beuren syndrome chromosome region 17 homolog (human) [Source:MGI Symbol;Acc:MGI:2137594]
ENSMUSG00000029673	Auts2	protein_coding	autism susceptibility candidate 2 [Source:MGI Symbol;Acc:MGI:1919847]
ENSMUSG00000060261	Gtf2i	protein_coding	general transcription factor II I [Source:MGI Symbol;Acc:MGI:1202722]
ENSMUSG00000063146	Clip2	protein_coding	CAP-GLY domain containing linker protein 2 [Source:MGI Symbol;Acc:MGI:1313136]
ENSMUSG00000040731	Eif4h	protein_coding	eukaryotic translation initiation factor 4H [Source:MGI Symbol;Acc:MGI:1341822]
ENSMUSG00000002748	Baz1b	protein_coding	bromodomain adjacent to zinc finger domain, 1B [Source:MGI Symbol;Acc:MGI:1353499]
ENSMUSG00000032255	Pom121	protein_coding	nuclear pore membrane protein 121 [Source:MGI Symbol;Acc:MGI:2137624]
ENSMUSG00000019179	Mdh2	protein_coding	malate dehydrogenase 2, NAD (mitochondrial) [Source:MGI Symbol;Acc:MGI:97050]
ENSMUSG00000021251	Ywhag	protein_coding	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, gamma polypeptide [Source:MGI Symbol;Acc:MGI:108109]
ENSMUSG00000029705	Cux1	protein_coding	cut-like homeobox 1 [Source:MGI Symbol;Acc:MGI:88568]
ENSMUSG00000037411	Serpine1	protein_coding	serine (or cysteine) peptidase inhibitor, clade E, member 1 [Source:MGI Symbol;Acc:MGI:97608]
ENSMUSG00000048379	Trim56	protein_coding	tripartite motif-containing 56 [Source:MGI Symbol;Acc:MGI:2685298]
ENSMUSG00000037364	Srrt	protein_coding	serrate RNA effector molecule homolog (Arabidopsis) [Source:MGI Symbol;Acc:MGI:1933527]
ENSMUSG00000029711	Epo	protein_coding	erythropoietin [Source:MGI Symbol;Acc:MGI:95407]
ENSMUSG00000029723	Tsc22d4	protein_coding	TSC22 domain family, member 4 [Source:MGI Symbol;Acc:MGI:1926079]
ENSMUSG00000029726	Mepce	protein_coding	methylphosphate capping enzyme [Source:MGI Symbol;Acc:MGI:1098477]
ENSMUSG00000029730	Mcm7	protein_coding	minichromosome maintenance deficient 7 (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1298398]
ENSMUSG00000035808	Get4	protein_coding	golgi to ER traffic protein 4 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1914654]
ENSMUSG00000029547	Ints1	protein_coding	integrator complex subunit 1 [Source:MGI Symbol;Acc:MGI:1915780]
ENSMUSG00000029554	Mad1l1	protein_coding	MAD1 mitotic arrest deficient 1-like 1 [Source:MGI Symbol;Acc:MGI:1341857]
ENSMUSG00000036076	Eif3b	protein_coding	eukaryotic translation initiation factor 3, subunit B [Source:MGI Symbol;Acc:MGI:106478]
ENSMUSG00000035105	Ttyh3	protein_coding	tweety homolog 3 (Drosophila) [Source:MGI Symbol;Acc:MGI:1925583]
ENSMUSG00000050022	Amz1	protein_coding	archaelysin family metallopeptidase 1 [Source:MGI Symbol;Acc:MGI:2442253]
ENSMUSG00000000149	Gna12	protein_coding	guanine nucleotide binding protein, alpha 12 [Source:MGI Symbol;Acc:MGI:95767]
ENSMUSG00000038582	Sdk1	protein_coding	sidekick homolog 1 (chicken) [Source:MGI Symbol;Acc:MGI:2444413]
ENSMUSG00000038495	Foxk1	protein_coding	forkhead box K1 [Source:MGI Symbol;Acc:MGI:1347488]
ENSMUSG00000029580	Actb	protein_coding	actin, beta [Source:MGI Symbol;Acc:MGI:87904]
ENSMUSG00000032744	E130309D02	protein_coding	RIKEN cDNA E130309D02 gene [Source:MGI Symbol;Acc:MGI:2442871]
ENSMUSG00000001847	Rac1	protein_coding	RAS-related C3 botulinum substrate 1 [Source:MGI Symbol;Acc:MGI:97845]
ENSMUSG00000051306	Usp42	protein_coding	ubiquitin specific peptidase 42 [Source:MGI Symbol;Acc:MGI:1924050]
ENSMUSG00000044453	Trrap	protein_coding	transformation/transcription domain-associated protein [Source:MGI Symbol;Acc:MGI:2153272]
ENSMUSG00000029633	Arpc1b	protein_coding	actin related protein 2/3 complex, subunit 1B [Source:MGI Symbol;Acc:MGI:1346142]

ENSMUSG00000025823	Pdap1	protein_coding	PDGFA associated protein 1 [Source:MGI Symbol;Acc:MGI:2448034]
ENSMUSG00000018510	Mtif3	protein_coding	mitochondrial translational initiation factor 3 [Source:MGI Symbol;Acc:MGI:1923616]
ENSMUSG00000025847	Pan3	protein_coding	PAN3 polyA specific ribonuclease subunit homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1919037]
ENSMUSG00000022051	Mtus2	protein_coding	microtubule associated tumor suppressor candidate 2 [Source:MGI Symbol;Acc:MGI:1915286]
ENSMUSG00000041313	Slc7a1	protein_coding	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1 [Source:MGI Symbol;Acc:MGI:88117]
ENSMUSG00000022058	Wdr95	protein_coding	WD40 repeat domain 95 [Source:MGI Symbol;Acc:MGI:1918043]
ENSMUSG00000022057	Hsph1	protein_coding	heat shock 105kDa/110kDa protein 1 [Source:MGI Symbol;Acc:MGI:105053]
ENSMUSG00000024031	Pds5b	protein_coding	PDS5, regulator of cohesion maintenance, homolog B (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2140945]
ENSMUSG00000001274	Ccdc122	protein_coding	coiled-coil domain containing 122 [Source:MGI Symbol;Acc:MGI:1920528]
ENSMUSG00000032027	Ppp1r9a6	protein_coding	protein phosphatase 1, regulatory (inhibitor) subunit 9A [Source:MGI Symbol;Acc:MGI:2442401]
ENSMUSG00000040032	Kcnd2	protein_coding	potassium voltage-gated channel, Shal-related family, member 2 [Source:MGI Symbol;Acc:MGI:102663]
ENSMUSG00000042500	A430107O13	protein_coding	RIKEN cDNA A430107O13 gene [Source:MGI Symbol;Acc:MGI:2444304]
ENSMUSG00000027978	Cadps2	protein_coding	Ca2+-dependent activator protein for secretion 2 [Source:MGI Symbol;Acc:MGI:2443963]
ENSMUSG00000029708	Gcc1	protein_coding	golgi coiled coil 1 [Source:MGI Symbol;Acc:MGI:1921625]
ENSMUSG00000001424	Snd1	protein_coding	staphylococcal nuclease and tudor domain containing 1 [Source:MGI Symbol;Acc:MGI:1929266]
ENSMUSG00000045923	Lrrc4	protein_coding	leucine rich repeat containing 4 [Source:MGI Symbol;Acc:MGI:2182081]
ENSMUSG00000058831	Opn1sw	protein_coding	opsin 1 (cone pigments), short-wave-sensitive (color blindness, tritan) [Source:MGI Symbol;Acc:MGI:99438]
ENSMUSG00000078103	Klf14	protein_coding	Kruppel-like factor 14 [Source:MGI Symbol;Acc:MGI:3577024]
ENSMUSG00000039703	Plxna4	protein_coding	plexin A4 [Source:MGI Symbol;Acc:MGI:2179061]
ENSMUSG00000015925	Slc35b4	protein_coding	solute carrier family 35, member B4 [Source:MGI Symbol;Acc:MGI:1931242]
ENSMUSG00000085723	Nup205	protein_coding	nucleoporin 205 [Source:MGI Symbol;Acc:MGI:2141622]
ENSMUSG00000029840	Mtpn	protein_coding	myotrophin [Source:MGI Symbol;Acc:MGI:99445]
ENSMUSG00000029833	Trim24	protein_coding	tripartite motif-containing 24 [Source:MGI Symbol;Acc:MGI:109275]
ENSMUSG00000047749	Zc3hav1l	protein_coding	zinc finger CCCH-type, antiviral 1-like [Source:MGI Symbol;Acc:MGI:2443387]
ENSMUSG00000029826	Zc3hav1	protein_coding	zinc finger CCCH type, antiviral 1 [Source:MGI Symbol;Acc:MGI:1926031]
ENSMUSG00000001436	Hipk2	protein_coding	homeodomain interacting protein kinase 2 [Source:MGI Symbol;Acc:MGI:1314872]
ENSMUSG00000042599	Jhdm1d	protein_coding	jumonji C domain-containing histone demethylase 1 homolog D (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2443388]
ENSMUSG00000029863	Casp2	protein_coding	caspase 2 [Source:MGI Symbol;Acc:MGI:97295]
ENSMUSG00000029859	Zyx	protein_coding	zyxin [Source:MGI Symbol;Acc:MGI:103072]
ENSMUSG00000039419	Cntnap2	protein_coding	contactin associated protein-like 2 [Source:MGI Symbol;Acc:MGI:1914047]
ENSMUSG00000029831	Zfp282	protein_coding	zinc finger protein 282 [Source:MGI Symbol;Acc:MGI:2141418]
ENSMUSG00000071477	Zfp777	protein_coding	zinc finger protein 777 [Source:MGI Symbol;Acc:MGI:1919338]
ENSMUSG00000029891	Zfp746	protein_coding	zinc finger protein 746 [Source:MGI Symbol;Acc:MGI:1914475]
ENSMUSG00000029819	Tmem176b	protein_coding	transmembrane protein 176B [Source:MGI Symbol;Acc:MGI:1916348]
ENSMUSG00000004980	Hnrnpa2b1	protein_coding	heterogeneous nuclear ribonucleoprotein A2/B1 [Source:MGI Symbol;Acc:MGI:104819]
ENSMUSG00000059182	Skap2	protein_coding	src family associated phosphoprotein 2 [Source:MGI Symbol;Acc:MGI:1889206]
ENSMUSG00000029844	Hoxa1	protein_coding	homeobox A1 [Source:MGI Symbol;Acc:MGI:96170]
ENSMUSG00000098417	RP23-301L	protein_coding	
ENSMUSG00000079560	Hoxa2	protein_coding	homeobox A2 [Source:MGI Symbol;Acc:MGI:96174]
ENSMUSG00000059723	Hoxa2	protein_coding	homeobox A2 [Source:MGI Symbol;Acc:MGI:96174]
ENSMUSG00000004535	Tax1bp1	protein_coding	Tax1 (human T-cell leukemia virus type I) binding protein 1 [Source:MGI Symbol;Acc:MGI:1289308]
ENSMUSG00000025408	Jazf1	protein_coding	JAZF zinc finger 1 [Source:MGI Symbol;Acc:MGI:2141450]
ENSMUSG00000003920	Ppp1r17	protein_coding	protein phosphatase 1, regulatory subunit 17 [Source:MGI Symbol;Acc:MGI:1353876]
ENSMUSG00000038978	Fam120a	protein_coding	family with sequence similarity 120, member A [Source:MGI Symbol;Acc:MGI:2446234]
ENSMUSG00000071424	Grid2	protein_coding	glutamate receptor, ionotropic, delta 2 [Source:MGI Symbol;Acc:MGI:95813]
ENSMUSG00000049001	A330093E20	protein_coding	RIKEN cDNA A330093E20 gene [Source:MGI Symbol;Acc:MGI:1915412]
ENSMUSG00000008571	Serbp1	protein_coding	serpine1 mRNA binding protein 1 [Source:MGI Symbol;Acc:MGI:1914120]
ENSMUSG00000002732	Rmnd5a	protein_coding	required for meiotic nuclear division 5 homolog A (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1913727]
ENSMUSG00000003824	Ptcd3	protein_coding	pentatricopeptide repeat domain 3 [Source:MGI Symbol;Acc:MGI:1917206]
ENSMUSG00000037831	Atoh8	protein_coding	atonal homolog 8 (Drosophila) [Source:MGI Symbol;Acc:MGI:1918343]
ENSMUSG00000056305	Usp39	protein_coding	ubiquitin specific peptidase 39 [Source:MGI Symbol;Acc:MGI:107622]
ENSMUSG00000053907	Mat2a	protein_coding	methionine adenosyltransferase II, alpha [Source:MGI Symbol;Acc:MGI:2443731]
ENSMUSG00000055799	Tcf7l1	protein_coding	transcription factor 7 like 1 (T cell specific, HMG box) [Source:MGI Symbol;Acc:MGI:1202876]
ENSMUSG00000052581	Lrtm4	protein_coding	leucine rich repeat transmembrane neuronal 4 [Source:MGI Symbol;Acc:MGI:2389180]
ENSMUSG00000030036	Mogs	protein_coding	mannosyl-oligosaccharide glucosidase [Source:MGI Symbol;Acc:MGI:1929872]
ENSMUSG00000040943	Tet3	protein_coding	tet methylcytosine dioxygenase 3 [Source:MGI Symbol;Acc:MGI:2446229]
ENSMUSG00000048415	Cyp26b1	protein_coding	cytochrome P450, family 26, subfamily b, polypeptide 1 [Source:MGI Symbol;Acc:MGI:2176159]
ENSMUSG00000033769	Exoc6b	protein_coding	exocyst complex component 6B [Source:MGI Symbol;Acc:MGI:1923164]
ENSMUSG00000030007	Cct7	protein_coding	chaperonin containing Tcp1, subunit 7 (eta) [Source:MGI Symbol;Acc:MGI:107184]
ENSMUSG00000051695	Pcbp1	protein_coding	poly(rC) binding protein 1 [Source:MGI Symbol;Acc:MGI:1345635]
ENSMUSG00000029992	Gfpt1	protein_coding	glutamine fructose-6-phosphate transaminase 1 [Source:MGI Symbol;Acc:MGI:95698]
ENSMUSG00000030047	Arhgap25	protein_coding	Rho GTPase activating protein 25 [Source:MGI Symbol;Acc:MGI:2443687]
ENSMUSG00000030055	Rab43	protein_coding	RAB43, member RAS oncogene family [Source:MGI Symbol;Acc:MGI:1917084]
ENSMUSG00000030057	Cnbp	protein_coding	cellular nucleic acid binding protein [Source:MGI Symbol;Acc:MGI:88431]
ENSMUSG00000094510	Gm5577	protein_coding	predicted gene 5577 [Source:MGI Symbol;Acc:MGI:3648215]
ENSMUSG00000079477	Rab7	protein_coding	RAB7, member RAS oncogene family [Source:MGI Symbol;Acc:MGI:105068]
ENSMUSG00000015932	Gata2	protein_coding	GATA binding protein 2 [Source:MGI Symbol;Acc:MGI:95662]
ENSMUSG00000038116	Eefsec	protein_coding	eukaryotic elongation factor, selenocysteine-tRNA-specific [Source:MGI Symbol;Acc:MGI:2137092]
ENSMUSG00000030082	Sec61a1	protein_coding	Sec61 alpha 1 subunit (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1858417]
ENSMUSG00000003870	Mcm2	protein_coding	minichromosome maintenance deficient 2 mitotin (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:105380]
ENSMUSG00000030926	Chchd6	protein_coding	coiled-coil-helix-coiled-coil-helix domain containing 6 [Source:MGI Symbol;Acc:MGI:1913348]
ENSMUSG00000034430	Zxdc	protein_coding	ZXD family zinc finger C [Source:MGI Symbol;Acc:MGI:1922108]
ENSMUSG00000030091	Nup210	protein_coding	nucleoporin 210 [Source:MGI Symbol;Acc:MGI:1859555]
ENSMUSG00000030096	Slc6a6	protein_coding	solute carrier family 6 (neurotransmitter transporter, taurine), member 6 [Source:MGI Symbol;Acc:MGI:98488]
ENSMUSG00000040095	Magi1	protein_coding	membrane associated guanylate kinase, WW and PDZ domain containing 1 [Source:MGI Symbol;Acc:MGI:1203522]
ENSMUSG00000020667	Gm765	protein_coding	predicted gene 765 [Source:MGI Symbol;Acc:MGI:2685611]
ENSMUSG00000030067	Foxp1	protein_coding	forkhead box P1 [Source:MGI Symbol;Acc:MGI:1914004]
ENSMUSG00000030257	Srgap3	protein_coding	SLIT-ROBO Rho GTPase activating protein 3 [Source:MGI Symbol;Acc:MGI:2152938]
ENSMUSG00000034269	Setd5	protein_coding	SET domain containing 5 [Source:MGI Symbol;Acc:MGI:1920145]
ENSMUSG00000072430	Arpc4	protein_coding	actin related protein 2/3 complex, subunit 4 [Source:MGI Symbol;Acc:MGI:1915339]
ENSMUSG00000030274	Ttll3	protein_coding	tubulin tyrosine ligase-like family, member 3 [Source:MGI Symbol;Acc:MGI:2141418]
ENSMUSG00000091258	Jagn1	protein_coding	jagunal homolog 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:1915017]
ENSMUSG00000030314	Atg7	protein_coding	autophagy-related 7 (yeast) [Source:MGI Symbol;Acc:MGI:1921494]
ENSMUSG00000000441	Raf1	protein_coding	v-raf-leukemia viral oncogene 1 [Source:MGI Symbol;Acc:MGI:97847]
ENSMUSG00000057041	Rpl32	protein_coding	ribosomal protein L32 [Source:MGI Symbol;Acc:MGI:98038]
ENSMUSG00000030123	Plxnd1	protein_coding	plexin D1 [Source:MGI Symbol;Acc:MGI:2154244]
ENSMUSG00000030126	Tmcc1	protein_coding	transmembrane and coiled coil domains 1 [Source:MGI Symbol;Acc:MGI:2442368]
ENSMUSG00000042079	Hnrnpf	protein_coding	heterogeneous nuclear ribonucleoprotein F [Source:MGI Symbol;Acc:MGI:2138741]
ENSMUSG00000030110	Ret	protein_coding	ret proto-oncogene [Source:MGI Symbol;Acc:MGI:97902]
ENSMUSG00000030168	Adipor2	protein_coding	adiponectin receptor 2 [Source:MGI Symbol;Acc:MGI:93830]
ENSMUSG00000030170	Wnt5b	protein_coding	wingless-related MMTV integration site 5B [Source:MGI Symbol;Acc:MGI:98959]
ENSMUSG00000030018	Fbxl14	protein_coding	F-box and leucine-rich repeat protein 14 [Source:MGI Symbol;Acc:MGI:2141676]
ENSMUSG00000045962	Wnk1	protein_coding	WNK lysine deficient protein kinase 1 [Source:MGI Symbol;Acc:MGI:2442092]
ENSMUSG00000030120	Kdm5a	protein_coding	lysine (K)-specific demethylase 5A [Source:MGI Symbol;Acc:MGI:2136980]
ENSMUSG00000002897	Il17ra	protein_coding	interleukin 17 receptor A [Source:MGI Symbol;Acc:MGI:107399]
ENSMUSG00000051526	Mical3	protein_coding	microtubule associated monooxygenase, calponin and LIM domain containing 3 [Source:MGI Symbol;Acc:MGI:2442733]
ENSMUSG00000040669	Phc1	protein_coding	polyhomeotic-like 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:103248]
ENSMUSG00000004264	Phb2	protein_coding	prohibitin 2 [Source:MGI Symbol;Acc:MGI:102520]
ENSMUSG00000004266	Ptpn6	protein_coding	protein tyrosine phosphatase, non-receptor type 6 [Source:MGI Symbol;Acc:MGI:96055]
ENSMUSG00000004263	Atn1	protein_coding	atrophin 1 [Source:MGI Symbol;Acc:MGI:104725]
ENSMUSG00000063870	Chd4	protein_coding	chromodomain helicase DNA binding protein 4 [Source:MGI Symbol;Acc:MGI:1344380]
ENSMUSG00000030272	Ncapd2	protein_coding	non-SMC condensin I complex, subunit D2 [Source:MGI Symbol;Acc:MGI:1915548]
ENSMUSG00000030339	Ltbr	protein_coding	lymphotoxin B receptor [Source:MGI Symbol;Acc:MGI:104875]
ENSMUSG00000030342	Cd9	protein_coding	CD9 antigen [Source:MGI Symbol;Acc:MGI:88348]
ENSMUSG00000030119	Ano2	protein_coding	anoctamin 2 [Source:MGI Symbol;Acc:MGI:2387214]
ENSMUSG00000000184	Ccnd2	protein_coding	cyclin D2 [Source:MGI Symbol;Acc:MGI:88314]
ENSMUSG00000001517	Foxm1	protein_coding	forkhead box M1 [Source:MGI Symbol;Acc:MGI:1347487]

ENSMUSG00000030357	Fkbp4	protein_coding	FK506 binding protein 4 [Source:MGI Symbol;Acc:MGI:95543]
ENSMUSG00000030161	Gabarapl1	protein_coding	gamma-aminobutyric acid (GABA) A receptor-associated protein-like 1 [Source:MGI Symbol;Acc:MGI:1914980]
ENSMUSG00000030189	Csda	protein_coding	cold shock domain protein A [Source:MGI Symbol;Acc:MGI:2137670]
ENSMUSG00000030199	Etv6	protein_coding	ets variant gene 6 (TEL oncogene) [Source:MGI Symbol;Acc:MGI:109328]
ENSMUSG00000030201	Lrp6	protein_coding	low density lipoprotein receptor-related protein 6 [Source:MGI Symbol;Acc:MGI:1298218]
ENSMUSG00000030205	Dusp16	protein_coding	dual specificity phosphatase 16 [Source:MGI Symbol;Acc:MGI:1917936]
ENSMUSG00000030204	Ddx47	protein_coding	DEAD (Asp-Glu-Ala-Asp) box polypeptide 47 [Source:MGI Symbol;Acc:MGI:1915005]
ENSMUSG00000030209	Grin2b	protein_coding	glutamate receptor, ionotropic, NMDA2B (epsilon 2) [Source:MGI Symbol;Acc:MGI:95821]
ENSMUSG00000030220	Arhgdib	protein_coding	Rho, GDP dissociation inhibitor (GDI) beta [Source:MGI Symbol;Acc:MGI:101940]
ENSMUSG00000030224	Strap	protein_coding	serine/threonine kinase receptor associated protein [Source:MGI Symbol;Acc:MGI:1329037]
ENSMUSG00000041741	Pde3a	protein_coding	phosphodiesterase 3A, cGMP inhibited [Source:MGI Symbol;Acc:MGI:1860764]
ENSMUSG00000030279	1720041[illegible]	protein_coding	RIKEN cDNA 1720041[illegible] gene [Source:MGI Symbol;Acc:MGI:19[illegible]]
ENSMUSG00000030275	Etnk1	protein_coding	ethanolamine kinase 1 [Source:MGI Symbol;Acc:MGI:1922570]
ENSMUSG00000041540	Sox5	protein_coding	SRY box containing gene 5 [Source:MGI Symbol;Acc:MGI:98367]
ENSMUSG00000030306	Tmtc1	protein_coding	transmembrane and tetratricopeptide repeat containing 1 [Source:MGI Symbol;Acc:MGI:3039590]
ENSMUSG00000040029	Ipo8	protein_coding	importin 8 [Source:MGI Symbol;Acc:MGI:2444611]
ENSMUSG00000008683	Rps15a	protein_coding	ribosomal protein S15A [Source:MGI Symbol;Acc:MGI:1354086]
ENSMUSG00000019254	Ppp1r12c	protein_coding	protein phosphatase 1, regulatory (inhibitor) subunit 12C [Source:MGI Symbol;Acc:MGI:1924258]
ENSMUSG00000008502	Hspbp1	protein_coding	HSPA (heat shock 70kDa) binding protein, cytoplasmic cochaperone 1 [Source:MGI Symbol;Acc:MGI:1918490]
ENSMUSG00000030435	U2af2	protein_coding	U2 small nuclear ribonucleoprotein auxiliary factor (U2AF) 2 [Source:MGI Symbol;Acc:MGI:98886]
ENSMUSG00000035102	Epn1	protein_coding	epsin 1 [Source:MGI Symbol;Acc:MGI:1333782]
ENSMUSG00000012848	Rps5	protein_coding	ribosomal protein S5 [Source:MGI Symbol;Acc:MGI:1097682]
ENSMUSG00000040600	Zbtb45	protein_coding	zinc finger and BTB domain containing 45 [Source:MGI Symbol;Acc:MGI:2685070]
ENSMUSG00000030344	Trim 28	protein_coding	tripartite motif-containing 28 [Source:MGI Symbol;Acc:MGI:109274]
ENSMUSG00000041540	Glscr2	protein_coding	glioma tumor suppressor candidate region gene 2 [Source:MGI Symbol;Acc:MGI:2154441]
ENSMUSG00000006024	Napa	protein_coding	N-ethylmaleimide sensitive fusion protein attachment protein alpha [Source:MGI Symbol;Acc:MGI:104563]
ENSMUSG00000052833	Sae1	protein_coding	SUMO1 activating enzyme subunit 1 [Source:MGI Symbol;Acc:MGI:1929264]
ENSMUSG00000059972	Zc3h4	protein_coding	zinc finger CCCH-type containing 4 [Source:MGI Symbol;Acc:MGI:2682314]
ENSMUSG00000012158	Tmem160	protein_coding	transmembrane protein 160 [Source:MGI Symbol;Acc:MGI:1916544]
ENSMUSG00000052889	Grlf1	protein_coding	glucocorticoid receptor DNA binding factor 1 [Source:MGI Symbol;Acc:MGI:1929494]
ENSMUSG00000048920	Fkrp	protein_coding	fukutin related protein [Source:MGI Symbol;Acc:MGI:2447586]
ENSMUSG00000019370	Calm3	protein_coding	calmodulin 3 [Source:MGI Symbol;Acc:MGI:103249]
ENSMUSG00000044030	Irf2bp1	protein_coding	interferon regulatory factor 2 binding protein 1 [Source:MGI Symbol;Acc:MGI:2443125]
ENSMUSG00000022118	Synpo	protein_coding	synaptopodin [Source:MGI Symbol;Acc:MGI:1919428]
ENSMUSG00000040011	Eml2	protein_coding	echinoderm microtubule associated protein like 2 [Source:MGI Symbol;Acc:MGI:1919455]
ENSMUSG00000030403	Vasp	protein_coding	vasodilator-stimulated phosphoprotein [Source:MGI Symbol;Acc:MGI:109268]
ENSMUSG00000047254	Ppp1r15l	protein_coding	protein phosphatase 1, regulatory (inhibitor) subunit 15 like [Source:MGI Symbol;Acc:MGI:2125378]
ENSMUSG00000044709	Gemin7	protein_coding	gem (nuclear organelle) associated protein 7 [Source:MGI Symbol;Acc:MGI:1914921]
ENSMUSG00000002984	Tomm40	protein_coding	translocase of outer mitochondrial membrane 40 homolog (yeast) [Source:MGI Symbol;Acc:MGI:1858215]
ENSMUSG00000040940	Arhgef1	protein_coding	Rho guanine nucleotide exchange factor (GEF) 1 [Source:MGI Symbol;Acc:MGI:1353510]
ENSMUSG00000065758	Grik5	protein_coding	glutamate receptor, ionotropic, kainate 5 (gamma 2) [Source:MGI Symbol;Acc:MGI:95818]
ENSMUSG00000045112	Zfp574	protein_coding	zinc finger protein 574 [Source:MGI Symbol;Acc:MGI:2442931]
ENSMUSG00000057177	Gsk3a	protein_coding	glycogen synthase kinase 3 alpha [Source:MGI Symbol;Acc:MGI:2152453]
ENSMUSG00000040827	Erf	protein_coding	Ets2 repressor factor [Source:MGI Symbol;Acc:MGI:109637]
ENSMUSG00000005442	Cic	protein_coding	capicua homolog (Drosophila) [Source:MGI Symbol;Acc:MGI:1918972]
ENSMUSG00000061226	Exosc5	protein_coding	exosome component 5 [Source:MGI Symbol;Acc:MGI:107889]
ENSMUSG00000002603	Tgfb1	protein_coding	transforming growth factor, beta 1 [Source:MGI Symbol;Acc:MGI:98725]
ENSMUSG00000002633	Ccdc97	protein_coding	coiled-coil domain containing 97 [Source:MGI Symbol;Acc:MGI:1196455]
ENSMUSG00000040725	Hnrnpul1	protein_coding	heterogeneous nuclear ribonucleoprotein U-like 1 [Source:MGI Symbol;Acc:MGI:2443517]
ENSMUSG00000052409	Egln2	protein_coding	EGL nine homolog 2 (C. elegans) [Source:MGI Symbol;Acc:MGI:1932287]
ENSMUSG00000011751	Sptbn4	protein_coding	spectrin beta 4 [Source:MGI Symbol;Acc:MGI:1890574]
ENSMUSG00000070709	1700049G17Rik	protein_coding	RIKEN cDNA 1700049G17 gene [Source:MGI Symbol;Acc:MGI:1920880]
ENSMUSG00000003435	Supt5h	protein_coding	suppressor of Ty 5 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1202400]
ENSMUSG00000037563	Rps16	protein_coding	ribosomal protein S16 [Source:MGI Symbol;Acc:MGI:98118]
ENSMUSG00000026009	Lrfn1	protein_coding	leucine rich repeat and fibronectin type III domain containing 1 [Source:MGI Symbol;Acc:MGI:2136810]
ENSMUSG00000015165	Hnrnpl	protein_coding	heterogeneous nuclear ribonucleoprotein L [Source:MGI Symbol;Acc:MGI:104816]
ENSMUSG00000054083	Capn12	protein_coding	calpain 12 [Source:MGI Symbol;Acc:MGI:1891369]
ENSMUSG00000030591	Psmd8	protein_coding	proteasome (prosome, macropain) 26S subunit, non-ATPase, 8 [Source:MGI Symbol;Acc:MGI:1888668]
ENSMUSG00000037166	Ppp1r14a	protein_coding	protein phosphatase 1, regulatory (inhibitor) subunit 14A [Source:MGI Symbol;Acc:MGI:1931139]
ENSMUSG00000060135	Sipa1l3	protein_coding	signal-induced proliferation-associated 1 like 3 [Source:MGI Symbol;Acc:MGI:1921456]
ENSMUSG00000001794	Capns1	protein_coding	calpain, small subunit 1 [Source:MGI Symbol;Acc:MGI:88266]
ENSMUSG00000074211	Sdhaf1	protein_coding	succinate dehydrogenase complex assembly factor 1 [Source:MGI Symbol;Acc:MGI:1915582]
ENSMUSG00000074210	C130030F[illegible]Rik	protein_coding	RIKEN cDNA C130030F[illegible] gene [Source:MGI Symbol;Acc:MGI:3042278]
ENSMUSG00000089755	Rbm42	protein_coding	RNA binding motif protein 42 [Source:MGI Symbol;Acc:MGI:1915285]
ENSMUSG00000078787	Haus5	protein_coding	HAUS augmin-like complex, subunit 5 [Source:MGI Symbol;Acc:MGI:1919159]
ENSMUSG00000058239	Usf2	protein_coding	upstream transcription factor 2 [Source:MGI Symbol;Acc:MGI:99961]
ENSMUSG00000052997	Uba2	protein_coding	ubiquitin-like modifier activating enzyme 2 [Source:MGI Symbol;Acc:MGI:1858313]
ENSMUSG00000036427	Gpi1	protein_coding	glucose phosphate isomerase 1 [Source:MGI Symbol;Acc:MGI:95797]
ENSMUSG00000066568	Lsm14a	protein_coding	LSM14 homolog A (SCD6, S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1914320]
ENSMUSG00000006402	Chst8	protein_coding	carbohydrate (N-acetylgalactosamine 4-0) sulfotransferase 8 [Source:MGI Symbol;Acc:MGI:1916197]
ENSMUSG00000034957	Cebpa	protein_coding	CCAAT/enhancer binding protein (C/EBP), alpha [Source:MGI Symbol;Acc:MGI:99480]
ENSMUSG00000034867	Ankrd27	protein_coding	ankyrin repeat domain 27 (VPS9 domain) [Source:MGI Symbol;Acc:MGI:2444103]
ENSMUSG00000044412	Zfp507	protein_coding	zinc finger protein 507 [Source:MGI Symbol;Acc:MGI:1916378]
ENSMUSG00000046431	2410002F23Rik	protein_coding	RIKEN cDNA 2410002F23 gene [Source:MGI Symbol;Acc:MGI:1904228]
ENSMUSG00000047085	Lrrc4b	protein_coding	leucine rich repeat containing 4B [Source:MGI Symbol;Acc:MGI:3027390]
ENSMUSG00000006340	2310044H10Rik	protein_coding	RIKEN cDNA 2310044H10 gene [Source:MGI Symbol;Acc:MGI:1919368]
ENSMUSG00000002781	Kcnc3	protein_coding	potassium voltage gated channel, Shaw-related subfamily, member 3 [Source:MGI Symbol;Acc:MGI:96669]
ENSMUSG00000030739	Myh14	protein_coding	myosin, heavy polypeptide 14 [Source:MGI Symbol;Acc:MGI:1919210]
ENSMUSG00000048012	Zfp473	protein_coding	zinc finger protein 473 [Source:MGI Symbol;Acc:MGI:2442697]
ENSMUSG00000002205	Vrk3	protein_coding	vaccinia related kinase 3 [Source:MGI Symbol;Acc:MGI:2182465]
ENSMUSG00000048858	Nup62	protein_coding	nucleoporin 62 [Source:MGI Symbol;Acc:MGI:1351500]
ENSMUSG00000074141	Il4i1	protein_coding	interleukin 4 induced 1 [Source:MGI Symbol;Acc:MGI:109552]
ENSMUSG00000038503	Ptov1	protein_coding	prostate tumor over expressed gene 1 [Source:MGI Symbol;Acc:MGI:1933946]
ENSMUSG00000038400	Scaf1	protein_coding	SR-related CTD-associated factor 1 [Source:MGI Symbol;Acc:MGI:2141980]
ENSMUSG00000041524	Prr12	protein_coding	proline rich 12 [Source:MGI Symbol;Acc:MGI:2679002]
ENSMUSG00000003429	Rps11	protein_coding	ribosomal protein S11 [Source:MGI Symbol;Acc:MGI:1351329]
ENSMUSG00000038260	Trpm4	protein_coding	transient receptor potential cation channel, subfamily M, member 4 [Source:MGI Symbol;Acc:MGI:1915917]
ENSMUSG00000063511	Snrnp70	protein_coding	small nuclear ribonucleoprotein 70 (U1) [Source:MGI Symbol;Acc:MGI:98341]
ENSMUSG00000003873	Bax	protein_coding	BCL2-associated X protein [Source:MGI Symbol;Acc:MGI:99702]
ENSMUSG00000030826	Bcat2	protein_coding	branched chain aminotransferase 2, mitochondrial [Source:MGI Symbol;Acc:MGI:1276534]
ENSMUSG00000057342	Sphk2	protein_coding	sphingosine kinase 2 [Source:MGI Symbol;Acc:MGI:1861380]
ENSMUSG00000038801	Grwd1	protein_coding	glutamate-rich WD repeat containing 1 [Source:MGI Symbol;Acc:MGI:2141989]
ENSMUSG00000002771	Grin2d	protein_coding	glutamate receptor, ionotropic, NMDA2D (epsilon 4) [Source:MGI Symbol;Acc:MGI:95823]
ENSMUSG00000002778	Kdelr1	protein_coding	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 1 [Source:MGI Symbol;Acc:MGI:1915387]
ENSMUSG00000030835	Nomo1	protein_coding	nodal modulator 1 [Source:MGI Symbol;Acc:MGI:2385850]
ENSMUSG00000040136	Abcc8	protein_coding	ATP-binding cassette, sub-family C (CFTR/MRP), member 8 [Source:MGI Symbol;Acc:MGI:1352629]
ENSMUSG00000030835	Sergef	protein_coding	secretion regulating guanine nucleotide exchange factor [Source:MGI Symbol;Acc:MGI:1351630]
ENSMUSG00000063229	Ldha	protein_coding	lactate dehydrogenase A [Source:MGI Symbol;Acc:MGI:96759]
ENSMUSG00000052512	Nav2	protein_coding	neuron navigator 2 [Source:MGI Symbol;Acc:MGI:2183691]
ENSMUSG00000055409	Nell1	protein_coding	NEL-like 1 (chicken) [Source:MGI Symbol;Acc:MGI:2443902]
ENSMUSG00000030451	Herc2	protein_coding	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 2 [Source:MGI Symbol;Acc:MGI:103234]
ENSMUSG00000063040	Snrpn	protein_coding	small nuclear ribonucleoprotein N [Source:MGI Symbol;Acc:MGI:98347]
ENSMUSG00000032840	Klf13	protein_coding	Kruppel-like factor 13 [Source:MGI Symbol;Acc:MGI:1354948]
ENSMUSG00000030518	Fam189a1	protein_coding	family with sequence similarity 189, member A1 [Source:MGI Symbol;Acc:MGI:1917888]
ENSMUSG00000015133	Lrrk1	protein_coding	leucine-rich repeat kinase 1 [Source:MGI Symbol;Acc:MGI:2142227]
ENSMUSG00000005533	Igf1r	protein_coding	insulin-like growth factor I receptor [Source:MGI Symbol;Acc:MGI:96433]
ENSMUSG00000078671	Chd2	protein_coding	chromodomain helicase DNA binding protein 2 [Source:MGI Symbol;Acc:MGI:2448567]

ENSMUSG00000025938	Slco5a1	protein_coding	solute carrier organic anion transporter family, member 5a1 [Source:MGI Symbol;Acc:MGI:1351867]
ENSMUSG00000066406	Akap13	protein_coding	A kinase (PRKA) anchor protein 13 [Source:MGI Symbol;Acc:MGI:2676556]
ENSMUSG00000030605	Mfge8	protein_coding	milk fat globule-EGF factor 8 protein [Source:MGI Symbol;Acc:MGI:102768]
ENSMUSG00000030534	Vps33b	protein_coding	vacuolar protein sorting 33B (yeast) [Source:MGI Symbol;Acc:MGI:2446237]
ENSMUSG00000038886	Man2a2	protein_coding	mannosidase 2, alpha 2 [Source:MGI Symbol;Acc:MGI:2150656]
ENSMUSG00000030530	Furin	protein_coding	furin (paired basic amino acid cleaving enzyme) [Source:MGI Symbol;Acc:MGI:97513]
ENSMUSG00000030536	Iqgap1	protein_coding	IQ motif containing GTPase activating protein 1 [Source:MGI Symbol;Acc:MGI:1352757]
ENSMUSG00000005621	Zfp592	protein_coding	zinc finger protein 592 [Source:MGI Symbol;Acc:MGI:2443241]
ENSMUSG00000092770	Mex3b	protein_coding	mex3 homolog B (C. elegans) [Source:MGI Symbol;Acc:MGI:1918231]
ENSMUSG00000068902	Gm7964	protein_coding	predicted gene 7964 [Source:MGI Symbol;Acc:MGI:3646110]
ENSMUSG00000070407	Mesdc1	protein_coding	mesoderm development candidate 1 [Source:MGI Symbol;Acc:MGI:1891420]
ENSMUSG00000068459	Fam108c	protein_coding	family with sequence similarity 108, member C [Source:MGI Symbol;Acc:MGI:1917478]
ENSMUSG00000039361	Picalm	protein_coding	phosphatidylinositol binding clathrin assembly protein [Source:MGI Symbol;Acc:MGI:2385902]
ENSMUSG00000052572	Dlg2	protein_coding	discs, large homolog 2 (Drosophila) [Source:MGI Symbol;Acc:MGI:1344351]
ENSMUSG00000041328	Pcf11	protein_coding	cleavage and polyadenylation factor subunit homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1919579]
ENSMUSG00000054981	Gm5854	protein_coding	predicted gene 5854 [Source:MGI Symbol;Acc:MGI:3641742]
ENSMUSG00000048078	Odz4	protein_coding	odd Oz/ten-m homolog 4 (Drosophila) [Source:MGI Symbol;Acc:MGI:1447063]
ENSMUSG00000035623	Rsf1	protein_coding	remodeling and spacing factor 1 [Source:MGI Symbol;Acc:MGI:2682305]
ENSMUSG00000030732	Prkrir	protein_coding	protein-kinase, interferon-inducible double stranded RNA dependent inhibitor, repressor of (P58 repressor) [Source:MGI Symbol;Acc:MGI:1330281]
ENSMUSG00000030744	Rps3	protein_coding	ribosomal protein S3 [Source:MGI Symbol;Acc:MGI:1350917]
ENSMUSG00000018909	Arrb1	protein_coding	arrestin, beta 1 [Source:MGI Symbol;Acc:MGI:99473]
ENSMUSG00000075376	Rnf169	protein_coding	ring finger protein 169 [Source:MGI Symbol;Acc:MGI:1920257]
ENSMUSG00000047248	C2cd3	protein_coding	C2 calcium-dependent domain containing 3 [Source:MGI Symbol;Acc:MGI:2142166]
ENSMUSG00000029461	Fam168a	protein_coding	family with sequence similarity 168, member A [Source:MGI Symbol;Acc:MGI:2442372]
ENSMUSG00000032875	Arhgef17	protein_coding	Rho guanine nucleotide exchange factor (GEF) 17 [Source:MGI Symbol;Acc:MGI:1929002]
ENSMUSG00000066306	Numa1	protein_coding	nuclear mitotic apparatus protein 1 [Source:MGI Symbol;Acc:MGI:2443665]
ENSMUSG00000073982	Rhog	protein_coding	ras homolog gene family, member G [Source:MGI Symbol;Acc:MGI:1928370]
ENSMUSG00000030978	Rrm1	protein_coding	ribonucleotide reductase M1 [Source:MGI Symbol;Acc:MGI:98180]
ENSMUSG00000036862	Dchs1	protein_coding	dachsous 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:2685011]
ENSMUSG00000031029	Eif3f	protein_coding	eukaryotic translation initiation factor 3, subunit F [Source:MGI Symbol;Acc:MGI:1913335]
ENSMUSG00000046364	Rpl27a	protein_coding	ribosomal protein L27A [Source:MGI Symbol;Acc:MGI:1347076]
ENSMUSG00000035901	Dennd5a	protein_coding	DENN/MADD domain containing 5A [Source:MGI Symbol;Acc:MGI:1261821]
ENSMUSG00000066232	Ipo7	protein_coding	importin 7 [Source:MGI Symbol;Acc:MGI:2152414]
ENSMUSG00000031015	Swap70	protein_coding	SWA-70 protein [Source:MGI Symbol;Acc:MGI:1298390]
ENSMUSG00000005610	Eif4g2	protein_coding	eukaryotic translation initiation factor 4, gamma 2 [Source:MGI Symbol;Acc:MGI:109207]
ENSMUSG00000059263	Usp47	protein_coding	ubiquitin specific peptidase 47 [Source:MGI Symbol;Acc:MGI:1922248]
ENSMUSG00000038187	Btbd10	protein_coding	BTB (POZ) domain containing 10 [Source:MGI Symbol;Acc:MGI:1914005]
ENSMUSG00000051910	Sox6	protein_coding	SRY-box containing gene 6 [Source:MGI Symbol;Acc:MGI:98368]
ENSMUSG00000045659	Plekha7	protein_coding	pleckstrin homology domain containing, family A member 7 [Source:MGI Symbol;Acc:MGI:2445094]
ENSMUSG00000030872	Gga2	protein_coding	golgi associated, gamma adaptin ear containing, ARF binding protein 2 [Source:MGI Symbol;Acc:MGI:1921355]
ENSMUSG00000030870	Ubfd1	protein_coding	ubiquitin family domain containing 1 [Source:MGI Symbol;Acc:MGI:107201]
ENSMUSG00000052889	Prkcb	protein_coding	protein kinase C, beta [Source:MGI Symbol;Acc:MGI:97596]
ENSMUSG00000030779	Rbbp6	protein_coding	retinoblastoma binding protein 6 [Source:MGI Symbol;Acc:MGI:894835]
ENSMUSG00000030748	Il4ra	protein_coding	interleukin 4 receptor, alpha [Source:MGI Symbol;Acc:MGI:105367]
ENSMUSG00000046182	Gsg1l	protein_coding	GSG1-like [Source:MGI Symbol;Acc:MGI:2683455]
ENSMUSG00000030131	Xpo6	protein_coding	exportin 6 [Source:MGI Symbol;Acc:MGI:2429950]
ENSMUSG00000032637	Atxn2l	protein_coding	ataxin 2-like [Source:MGI Symbol;Acc:MGI:2446242]
ENSMUSG00000030738	Eif3c	protein_coding	eukaryotic translation initiation factor 3, subunit C [Source:MGI Symbol;Acc:MGI:1926966]
ENSMUSG00000030707	Coro1a	protein_coding	coronin, actin binding protein 1A [Source:MGI Symbol;Acc:MGI:1345961]
ENSMUSG00000030695	Aldoa	protein_coding	aldolase A, fructose-bisphosphate [Source:MGI Symbol;Acc:MGI:87994]
ENSMUSG00000030689	Ino80e	protein_coding	INO80 complex subunit E [Source:MGI Symbol;Acc:MGI:2141881]
ENSMUSG00000030680	2900092E1	protein_coding	RIKEN cDNA 2900092E17 gene [Source:MGI Symbol;Acc:MGI:1914523]
ENSMUSG00000030678	Maz	protein_coding	MYC-associated zinc finger protein (purine-binding transcription factor) [Source:MGI Symbol;Acc:MGI:1338823]
ENSMUSG00000042165	AI467606	protein_coding	expressed sequence AI467606 [Source:MGI Symbol;Acc:MGI:2141979]
ENSMUSG00000051457	Spn	protein_coding	sialophorin [Source:MGI Symbol;Acc:MGI:98384]
ENSMUSG00000042502	Cd2bp2	protein_coding	CD2 antigen (cytoplasmic tail) binding protein 2 [Source:MGI Symbol;Acc:MGI:1917488]
ENSMUSG00000049091	Sephs2	protein_coding	selenophosphate synthetase 2 [Source:MGI Symbol;Acc:MGI:108388]
ENSMUSG00000053877	Srcap	protein_coding	Snf2-related CREBBP activator protein [Source:MGI Symbol;Acc:MGI:2444036]
ENSMUSG00000090665	Srcap	protein_coding	Snf2-related CREBBP activator protein [Source:MGI Symbol;Acc:MGI:2444036]
ENSMUSG00000030811	Fbxl19	protein_coding	F-box and leucine-rich repeat protein 19 [Source:MGI Symbol;Acc:MGI:3039600]
ENSMUSG00000042308	Setd1a	protein_coding	SET domain containing 1A [Source:MGI Symbol;Acc:MGI:2446244]
ENSMUSG00000042289	Hsd3b7	protein_coding	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 7 [Source:MGI Symbol;Acc:MGI:2141879]
ENSMUSG00000049728	Zfp668	protein_coding	zinc finger protein 668 [Source:MGI Symbol;Acc:MGI:3039412]
ENSMUSG00000030795	Fus	protein_coding	fusion, derived from t(12;16) malignant liposarcoma (human) [Source:MGI Symbol;Acc:MGI:1353633]
ENSMUSG00000030786	Itgam	protein_coding	integrin alpha M [Source:MGI Symbol;Acc:MGI:96607]
ENSMUSG00000030846	Tial1	protein_coding	Tia1 cytotoxic granule-associated RNA binding protein-like 1 [Source:MGI Symbol;Acc:MGI:107913]
ENSMUSG00000030849	Fgfr2	protein_coding	fibroblast growth factor receptor 2 [Source:MGI Symbol;Acc:MGI:95523]
ENSMUSG00000066979	Bub3	protein_coding	budding uninhibited by benzimidazoles 3 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1343463]
ENSMUSG00000040125	Gpr26	protein_coding	G protein-coupled receptor 26 [Source:MGI Symbol;Acc:MGI:2441758]
ENSMUSG00000030930	Chst15	protein_coding	carbohydrate (N-acetylgalactosamine 4-sulfate 6-O) sulfotransferase 15 [Source:MGI Symbol;Acc:MGI:1924840]
ENSMUSG00000030946	Lhpp	protein_coding	phospholysine phosphohistidine inorganic pyrophosphate phosphatase [Source:MGI Symbol;Acc:MGI:1915079]
ENSMUSG00000030956	Fam53b	protein_coding	family with sequence similarity 53, member B [Source:MGI Symbol;Acc:MGI:1925188]
ENSMUSG00000030970	Ctbp2	protein_coding	C-terminal binding protein 2 [Source:MGI Symbol;Acc:MGI:1201686]
ENSMUSG00000030979	Uros	protein_coding	uroporphyrinogen III synthase [Source:MGI Symbol;Acc:MGI:98917]
ENSMUSG00000041836	Ptpre	protein_coding	protein tyrosine phosphatase, receptor type, E [Source:MGI Symbol;Acc:MGI:97813]
ENSMUSG00000031004	Mki67	protein_coding	antigen identified by monoclonal antibody Ki 67 [Source:MGI Symbol;Acc:MGI:106035]
ENSMUSG00000025491	Ifitm1	protein_coding	interferon induced transmembrane protein 1 [Source:MGI Symbol;Acc:MGI:1915963]
ENSMUSG00000038580	Sct	protein_coding	secretin [Source:MGI Symbol;Acc:MGI:99466]
ENSMUSG00000025508	Rplp2	protein_coding	ribosomal protein, large P2 [Source:MGI Symbol;Acc:MGI:1914650]
ENSMUSG00000025515	Muc2	protein_coding	mucin 2 [Source:MGI Symbol;Acc:MGI:1339364]
ENSMUSG00000007891	Ctsd	protein_coding	cathepsin D [Source:MGI Symbol;Acc:MGI:88562]
ENSMUSG00000009545	Kcnq1	protein_coding	potassium voltage-gated channel, subfamily Q, member 1 [Source:MGI Symbol;Acc:MGI:108083]
ENSMUSG00000059119	Nap1l4	protein_coding	nucleosome assembly protein 1-like 4 [Source:MGI Symbol;Acc:MGI:1316687]
ENSMUSG00000025509	Pnpla2	protein_coding	patatin-like phospholipase domain containing 2 [Source:MGI Symbol;Acc:MGI:1914103]
ENSMUSG00000004626	Stxbp2	protein_coding	syntaxin binding protein 2 [Source:MGI Symbol;Acc:MGI:107370]
ENSMUSG00000003410	Elavl3	protein_coding	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 3 (Hu antigen C) [Source:MGI Symbol;Acc:MGI:109157]
ENSMUSG00000008206	Lass4	protein_coding	LAG1 homolog, ceramide synthase 4 [Source:MGI Symbol;Acc:MGI:1914510]
ENSMUSG00000048152	Gm1840	protein_coding	predicted gene 1840 [Source:MGI Symbol;Acc:MGI:3037693]
ENSMUSG00000032425	Arglu1	protein_coding	arginine and glutamate rich 1 [Source:MGI Symbol;Acc:MGI:2442581]
ENSMUSG00000045969	Ing1	protein_coding	inhibitor of growth family, member 1 [Source:MGI Symbol;Acc:MGI:1349481]
ENSMUSG00000031511	Arhgef7	protein_coding	Rho guanine nucleotide exchange factor (GEF7) [Source:MGI Symbol;Acc:MGI:1860495]
ENSMUSG00000074472	A230072I0	protein_coding	RIKEN cDNA A230072I06 gene [Source:MGI Symbol;Acc:MGI:2558221]
ENSMUSG00000031441	Atp11a	protein_coding	ATPase, class VI, type 11A [Source:MGI Symbol;Acc:MGI:1354735]
ENSMUSG00000031446	Cul4a	protein_coding	cullin 4A [Source:MGI Symbol;Acc:MGI:1914487]
ENSMUSG00000031447	Lamp1	protein_coding	lysosomal-associated membrane protein 1 [Source:MGI Symbol;Acc:MGI:96745]
ENSMUSG00000038506	Dcun1d2	protein_coding	DCN1, defective in cullin neddylation 1, domain containing 2 (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2142792]
ENSMUSG00000007425	Dlgap3	protein_coding	discs, large (Drosophila) homolog-associated protein 3 [Source:MGI Symbol;Acc:MGI:2443181]
ENSMUSG00000031480	Thsd1	protein_coding	thrombospondin, type I, domain 1 [Source:MGI Symbol;Acc:MGI:1925098]
ENSMUSG00000031540	Myst3	protein_coding	MYST histone acetyltransferase (monocytic leukemia) 3 [Source:MGI Symbol;Acc:MGI:2442415]
ENSMUSG00000031543	Ank1	protein_coding	ankyrin 1, erythroid [Source:MGI Symbol;Acc:MGI:88024]
ENSMUSG00000037492	Zmat4	protein_coding	zinc finger, matrin type 4 [Source:MGI Symbol;Acc:MGI:2442497]
ENSMUSG00000031557	Plekha2	protein_coding	pleckstrin homology domain-containing, family A (phosphoinositide binding specific) member 2 [Source:MGI Symbol;Acc:MGI:1928144]
ENSMUSG00000065954	Tacc1	protein_coding	transforming, acidic coiled-coil containing protein 1 [Source:MGI Symbol;Acc:MGI:2443510]
ENSMUSG00000054823	Whsc1l1	protein_coding	Wolf-Hirschhorn syndrome candidate 1-like 1 (human) [Source:MGI Symbol;Acc:MGI:2142581]
ENSMUSG00000031490	Eif4ebp1	protein_coding	eukaryotic translation initiation factor 4E binding protein 1 [Source:MGI Symbol;Acc:MGI:103267]
ENSMUSG00000031577	Tti2	protein_coding	TELO2 interacting protein 2 [Source:MGI Symbol;Acc:MGI:2384570]
ENSMUSG00000031586	Rbpms	protein_coding	RNA binding protein gene with multiple splicing [Source:MGI Symbol;Acc:MGI:1334446]

ENSMUSG00000031516	Dctn6	protein_coding	dynactin 6 [Source:MGI Symbol;Acc:MGI:1343154]
ENSMUSG00000031530	Dusp4	protein_coding	dual specificity phosphatase 4 [Source:MGI Symbol;Acc:MGI:2442191]
ENSMUSG00000031529	Tnks	protein_coding	tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase [Source:MGI Symbol;Acc:MGI:1341087]
ENSMUSG00000031523	Dlc1	protein_coding	deleted in liver cancer 1 [Source:MGI Symbol;Acc:MGI:1354949]
ENSMUSG00000022481	Mtmr7	protein_coding	myotubularin related protein 7 [Source:MGI Symbol;Acc:MGI:1351658]
ENSMUSG00000092083	Gm8120	protein_coding	predicted pseudogene 8120 [Source:MGI Symbol;Acc:MGI:3643273]
ENSMUSG00000032251	Snx25	protein_coding	sorting nexin 25 [Source:MGI Symbol;Acc:MGI:2142610]
ENSMUSG00000031633	Slc25a4	protein_coding	solute carrier family 25 (mitochondrial carrier, adenine nucleotide translocator), member 4 [Source:MGI Symbol;Acc:MGI:1353495]
ENSMUSG00000031608	Galnt7	protein_coding	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 [Source:MGI Symbol;Acc:MGI:1349449]
ENSMUSG00000031642	Sh3rf1	protein_coding	SH3 domain containing ring finger 1 [Source:MGI Symbol;Acc:MGI:1913066]
ENSMUSG00000031604	Sc4mol	protein_coding	sterol-C4-methyl oxidase-like [Source:MGI Symbol;Acc:MGI:1915434]
ENSMUSG00000036356	Csgalnact1	protein_coding	chondroitin sulfate N-acetylgalactosaminyltransferase 1 [Source:MGI Symbol;Acc:MGI:2442354]
ENSMUSG00000031188	Atp6v1b2	protein_coding	ATPase, H+ transporting, lysosomal V1 subunit B2 [Source:MGI Symbol;Acc:MGI:109618]
ENSMUSG00000031630	Gatad2a	protein_coding	GATA zinc finger domain containing 2A [Source:MGI Symbol;Acc:MGI:2384585]
ENSMUSG00000031823	Homer3	protein_coding	homer homolog 3 (Drosophila) [Source:MGI Symbol;Acc:MGI:1347359]
ENSMUSG00000057788	Ddx49	protein_coding	DEAD (Asp-Glu-Ala-Asp) box polypeptide 49 [Source:MGI Symbol;Acc:MGI:2136689]
ENSMUSG00000058301	Upf1	protein_coding	UPF1 regulator of nonsense transcripts homolog (yeast) [Source:MGI Symbol;Acc:MGI:107995]
ENSMUSG00000070002	Ell	protein_coding	elongation factor RNA polymerase II [Source:MGI Symbol;Acc:MGI:109377]
ENSMUSG00000019139	Isyna1	protein_coding	myo-inositol 1-phosphate synthase A1 [Source:MGI Symbol;Acc:MGI:1919030]
ENSMUSG00000071076	Jund	protein_coding	jun proto-oncogene related gene d [Source:MGI Symbol;Acc:MGI:96648]
ENSMUSG00000060928	Gm11172	protein_coding	predicted gene 11172 [Source:MGI Symbol;Acc:MGI:3650923]
ENSMUSG00000031833	Mast3	protein_coding	microtubule associated serine/threonine kinase 3 [Source:MGI Symbol;Acc:MGI:2683541]
ENSMUSG00000019261	Map1s	protein_coding	microtubule-associated protein 1S [Source:MGI Symbol;Acc:MGI:2443304]
ENSMUSG00000004677	Myo9b	protein_coding	myosin IXb [Source:MGI Symbol;Acc:MGI:106624]
ENSMUSG00000031805	Jak3	protein_coding	Janus kinase 3 [Source:MGI Symbol;Acc:MGI:99928]
ENSMUSG00000000767	Rab3a	protein_coding	RAB3A, member RAS oncogene family [Source:MGI Symbol;Acc:MGI:97843]
ENSMUSG00000003039	Fam32a	protein_coding	family with sequence similarity 32, member A [Source:MGI Symbol;Acc:MGI:1915072]
ENSMUSG00000001281	Slc35e1	protein_coding	solute carrier family 35, member E1 [Source:MGI Symbol;Acc:MGI:2144460]
ENSMUSG00000031622	Sin3b	protein_coding	transcriptional regulator, SIN3B (yeast) [Source:MGI Symbol;Acc:MGI:107158]
ENSMUSG00000004263	Large	protein_coding	like-glycosyltransferase [Source:MGI Symbol;Acc:MGI:1342270]
ENSMUSG00000005410	Mcm5	protein_coding	minichromosome maintenance deficient 5, cell division cycle 46 (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:103197]
ENSMUSG00000031684	Slc10a7	protein_coding	solute carrier family 10 (sodium/bile acid cotransporter family), member 7 [Source:MGI Symbol;Acc:MGI:1914635]
ENSMUSG00000031681	Smad1	protein_coding	MAD homolog 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:109452]
ENSMUSG00000032253	Abca1	protein_coding	ATP-binding cassette, sub-family A (ABC1), member 1 [Source:MGI Symbol;Acc:MGI:1155498]
ENSMUSG00000031715	Smarca5	protein_coding	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5 [Source:MGI Symbol;Acc:MGI:1935129]
ENSMUSG00000038250	Usp38	protein_coding	ubiquitin specific peptidase 38 [Source:MGI Symbol;Acc:MGI:1922030]
ENSMUSG00000037940	Inpp4b	protein_coding	inositol polyphosphate-4-phosphatase, type II [Source:MGI Symbol;Acc:MGI:2158925]
ENSMUSG00000031708	Tecr	protein_coding	trans-2,3-enoyl-CoA reductase [Source:MGI Symbol;Acc:MGI:1915408]
ENSMUSG00000019433	Gipc1	protein_coding	GIPC PDZ domain containing family, member 1 [Source:MGI Symbol;Acc:MGI:1926252]
ENSMUSG00000019464	Ptger1	protein_coding	prostaglandin E receptor 1 (subtype EP1) [Source:MGI Symbol;Acc:MGI:97793]
ENSMUSG00000005481	Ddx39	protein_coding	DEAD (Asp-Glu-Ala-Asp) box polypeptide 39 [Source:MGI Symbol;Acc:MGI:1915528]
ENSMUSG00000013033	Lphn1	protein_coding	latrophilin 1 [Source:MGI Symbol;Acc:MGI:1929461]
ENSMUSG00000074313	Gm10644	protein_coding	predicted gene 10644 [Source:MGI Symbol;Acc:MGI:3704314]
ENSMUSG00000075902	Samd1	protein_coding	sterile alpha motif domain containing 1 [Source:MGI Symbol;Acc:MGI:2143453]
ENSMUSG00000031706	Rfx1	protein_coding	regulatory factor X, 1 (influences HLA class II expression) [Source:MGI Symbol;Acc:MGI:105982]
ENSMUSG00000037102	Dcaf15	protein_coding	DDB1 and CUL4 associated factor 15 [Source:MGI Symbol;Acc:MGI:2684420]
ENSMUSG00000004996	Mri1	protein_coding	methylthioribose-1-phosphate isomerase homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1915132]
ENSMUSG00000053560	Ier2	protein_coding	immediate early response 2 [Source:MGI Symbol;Acc:MGI:104815]
ENSMUSG00000001910	Nacc1	protein_coding	nucleus accumbens associated 1, BEN and BTB (POZ) domain containing [Source:MGI Symbol;Acc:MGI:1914080]
ENSMUSG00000001911	Nfix	protein_coding	nuclear factor I/X [Source:MGI Symbol;Acc:MGI:97311]
ENSMUSG00000034041	Lyl1	protein_coding	lymphoblastomic leukemia 1 [Source:MGI Symbol;Acc:MGI:96891]
ENSMUSG00000003814	Calr	protein_coding	calreticulin [Source:MGI Symbol;Acc:MGI:88252]
ENSMUSG00000003808	Farsa	protein_coding	phenylalanyl-tRNA synthetase, alpha subunit [Source:MGI Symbol;Acc:MGI:1913840]
ENSMUSG00000005161	Prdx2	protein_coding	peroxiredoxin 2 [Source:MGI Symbol;Acc:MGI:109486]
ENSMUSG00000041205	2810025M1	protein_coding	RIKEN cDNA 2810025M15 gene [Source:MGI Symbol;Acc:MGI:1922885]
ENSMUSG00000031691	Tnpo2	protein_coding	transportin 2 (importin 3, karyopherin beta 2b) [Source:MGI Symbol;Acc:MGI:2384849]
ENSMUSG00000005142	Man2b1	protein_coding	mannosidase 2, alpha B1 [Source:MGI Symbol;Acc:MGI:107286]
ENSMUSG00000074194	Zfp791	protein_coding	zinc finger protein 791 [Source:MGI Symbol;Acc:MGI:2444978]
ENSMUSG00000031701	Dnaja2	protein_coding	DnaJ (Hsp40) homolog, subfamily A, member 2 [Source:MGI Symbol;Acc:MGI:1931882]
ENSMUSG00000031652	N4bp1	protein_coding	NEDD4 binding protein 1 [Source:MGI Symbol;Acc:MGI:2136825]
ENSMUSG00000031659	Adcy7	protein_coding	adenylate cyclase 7 [Source:MGI Symbol;Acc:MGI:102891]
ENSMUSG00000055932	Fto	protein_coding	fat mass and obesity associated [Source:MGI Symbol;Acc:MGI:1347093]
ENSMUSG00000031751	Amfr	protein_coding	autocrine motility factor receptor [Source:MGI Symbol;Acc:MGI:1345634]
ENSMUSG00000031774	Fam192a	protein_coding	family with sequence similarity 192, member A [Source:MGI Symbol;Acc:MGI:1919037]
ENSMUSG00000031776	Arl2bp	protein_coding	ADP-ribosylation factor-like 2 binding protein [Source:MGI Symbol;Acc:MGI:1929452]
ENSMUSG00000031785	Gpr56	protein_coding	G protein-coupled receptor 56 [Source:MGI Symbol;Acc:MGI:1340051]
ENSMUSG00000048920	Zfp612	protein_coding	zinc finger protein 612 [Source:MGI Symbol;Acc:MGI:1920612]
ENSMUSG00000036550	Cnot1	protein_coding	CCR4-NOT transcription complex, subunit 1 [Source:MGI Symbol;Acc:MGI:2442402]
ENSMUSG00000031672	Got2	protein_coding	glutamate oxaloacetate transaminase 2, mitochondrial [Source:MGI Symbol;Acc:MGI:95792]
ENSMUSG00000014859	E2f4	protein_coding	E2F transcription factor 4 [Source:MGI Symbol;Acc:MGI:103012]
ENSMUSG00000036604	Fam96b	protein_coding	family with sequence similarity 96, member B [Source:MGI Symbol;Acc:MGI:1915287]
ENSMUSG00000005698	Ctcf	protein_coding	CCCTC-binding factor [Source:MGI Symbol;Acc:MGI:109447]
ENSMUSG00000037415	Ranbp10	protein_coding	RAN binding protein 10 [Source:MGI Symbol;Acc:MGI:1921584]
ENSMUSG00000036442	Thap11	protein_coding	THAP domain containing 11 [Source:MGI Symbol;Acc:MGI:1930954]
ENSMUSG00000006410	Nutf2	protein_coding	nuclear transport factor 2 [Source:MGI Symbol;Acc:MGI:1913901]
ENSMUSG00000040810	Pskh1	protein_coding	protein serine kinase H1 [Source:MGI Symbol;Acc:MGI:2157220]
ENSMUSG00000017765	Slc12a4	protein_coding	solute carrier family 12, member 4 [Source:MGI Symbol;Acc:MGI:1309465]
ENSMUSG00000031904	Slc7a6	protein_coding	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6 [Source:MGI Symbol;Acc:MGI:2142590]
ENSMUSG00000040591	Chtf8	protein_coding	CTF8, chromosome transmission fidelity factor 8 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2445270]
ENSMUSG00000031913	Vps4a	protein_coding	vacuolar protein sorting 4a (yeast) [Source:MGI Symbol;Acc:MGI:1890520]
ENSMUSG00000031916	Cog8	protein_coding	component of oligomeric golgi complex 8 [Source:MGI Symbol;Acc:MGI:2142885]
ENSMUSG00000031921	Terf2	protein_coding	telomeric repeat binding factor 2 [Source:MGI Symbol;Acc:MGI:1195972]
ENSMUSG00000031924	Cyb5b	protein_coding	cytochrome b5 type B [Source:MGI Symbol;Acc:MGI:1913677]
ENSMUSG00000008348	Nob1	protein_coding	NIN1/RPN12 binding protein 1 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1914869]
ENSMUSG00000039067	Psmd7	protein_coding	proteasome (prosome, macropain) 26S subunit, non-ATPase, 7 [Source:MGI Symbol;Acc:MGI:1351511]
ENSMUSG00000037993	Dhx38	protein_coding	DEAH (Asp-Glu-Ala-His) box polypeptide 38 [Source:MGI Symbol;Acc:MGI:1927237]
ENSMUSG00000046027	Pkd1l3	protein_coding	polycystic kidney disease 1 like 3 [Source:MGI Symbol;Acc:MGI:2664670]
ENSMUSG00000031729	2400003C14	protein_coding	RIKEN cDNA 2400003C14 gene [Source:MGI Symbol;Acc:MGI:1919703]
ENSMUSG00000069035	Atxn1l	protein_coding	ataxin 1-like [Source:MGI Symbol;Acc:MGI:2684797]
ENSMUSG00000031731	Ap1g1	protein_coding	adaptor protein complex AP-1, gamma 1 subunit [Source:MGI Symbol;Acc:MGI:101919]
ENSMUSG00000059854	Hydin	protein_coding	HYDIN, axonemal central pair apparatus protein [Source:MGI Symbol;Acc:MGI:2389007]
ENSMUSG00000033732	Sf3b3	protein_coding	splicing factor 3b, subunit 3 [Source:MGI Symbol;Acc:MGI:1289341]
ENSMUSG00000031749	St3gal2	protein_coding	ST3 beta-galactoside alpha-2,3-sialyltransferase 2 [Source:MGI Symbol;Acc:MGI:99427]
ENSMUSG00000015023	Ddx19a	protein_coding	DEAD (Asp-Glu-Ala-Asp) box polypeptide 19a [Source:MGI Symbol;Acc:MGI:1913826]
ENSMUSG00000031960	Aars	protein_coding	alanyl-tRNA synthetase [Source:MGI Symbol;Acc:MGI:2384560]
ENSMUSG00000036024	Pdpr	protein_coding	pyruvate dehydrogenase phosphatase regulatory subunit [Source:MGI Symbol;Acc:MGI:2443128]
ENSMUSG00000033545	Znrf1	protein_coding	zinc and ring finger 1 [Source:MGI Symbol;Acc:MGI:2177508]
ENSMUSG00000031948	Kars	protein_coding	lysyl-tRNA synthetase [Source:MGI Symbol;Acc:MGI:1934754]
ENSMUSG00000073900	Mon1b	protein_coding	MON1 homolog b (yeast) [Source:MGI Symbol;Acc:MGI:1923203]
ENSMUSG00000004637	Wwox	protein_coding	WW domain-containing oxidoreductase [Source:MGI Symbol;Acc:MGI:1931237]
ENSMUSG00000034390	A930038C0	protein_coding	RIKEN cDNA A930038C07 gene [Source:MGI Symbol;Acc:MGI:1921890]
ENSMUSG00000034330	Plcg2	protein_coding	phospholipase C, gamma 2 [Source:MGI Symbol;Acc:MGI:97616]
ENSMUSG00000031841	Cdh13	protein_coding	cadherin 13 [Source:MGI Symbol;Acc:MGI:99551]
ENSMUSG00000031837	Necab2	protein_coding	N-terminal EF-hand calcium binding protein 2 [Source:MGI Symbol;Acc:MGI:2152211]
ENSMUSG00000031835	Mbtps1	protein_coding	membrane-bound transcription factor peptidase, site 1 [Source:MGI Symbol;Acc:MGI:1927235]
ENSMUSG00000031833	Taf1c	protein_coding	TATA box binding protein (Tbp)-associated factor, RNA polymerase I, C [Source:MGI Symbol;Acc:MGI:109578]
ENSMUSG00000034105	4832415K1	protein_coding	RIKEN cDNA 4832415K11 gene [Source:MGI Symbol;Acc:MGI:1921320]

ENSMUSG00000031827	Cotl1	protein_coding	coactosin-like 1 (Dictyostelium) [Source:MGI Symbol;Acc:MGI:1919292]
ENSMUSG00000031826	Usp10	protein_coding	ubiquitin specific peptidase 10 [Source:MGI Symbol;Acc:MGI:894652]
ENSMUSG00000092329	Gm20388	protein_coding	predicted gene 20388 [Source:MGI Symbol;Acc:MGI:5141853]
ENSMUSG00000031835	Zdhhc7	protein_coding	zinc finger, DHHC domain containing 7 [Source:MGI Symbol;Acc:MGI:2142662]
ENSMUSG00000031822	Gse1	protein_coding	genetic suppressor element 1 [Source:MGI Symbol;Acc:MGI:1098272]
ENSMUSG00000031821	Gins2	protein_coding	GINS complex subunit 2 (Psf2 homolog) [Source:MGI Symbol;Acc:MGI:1921019]
ENSMUSG00000031818	Cox4i1	protein_coding	cytochrome c oxidase subunit IV isoform 1 [Source:MGI Symbol;Acc:MGI:88473]
ENSMUSG00000031812	Map1lc3b	protein_coding	microtubule-associated protein 1 light chain 3 beta [Source:MGI Symbol;Acc:MGI:1914693]
ENSMUSG00000040010	Slc7a5	protein_coding	solute carrier family 7 (cationic amino acid transporter, y+ system), member 5 [Source:MGI Symbol;Acc:MGI:1298205]
ENSMUSG00000025316	Banp	protein_coding	BTG3 associated nuclear protein [Source:MGI Symbol;Acc:MGI:1889023]
ENSMUSG00000049577	Zfpm1	protein_coding	zinc finger protein, multitype 1 [Source:MGI Symbol;Acc:MGI:1095400]
ENSMUSG00000017478	Zc3h18	protein_coding	zinc finger CCCH-type containing 18 [Source:MGI Symbol;Acc:MGI:1922284]
ENSMUSG00000014444	Fam38a	protein_coding	family with sequence similarity 38, member A [Source:MGI Symbol;Acc:MGI:3603204]
ENSMUSG00000006585	Cdt1	protein_coding	chromatin licensing and DNA replication factor 1 [Source:MGI Symbol;Acc:MGI:1914427]
ENSMUSG00000006589	Aprt	protein_coding	adenine phosphoribosyl transferase [Source:MGI Symbol;Acc:MGI:88061]
ENSMUSG00000006362	Cbfa2t3	protein_coding	core-binding factor, runt domain, alpha subunit 2, translocated to, 3 (human) [Source:MGI Symbol;Acc:MGI:1338013]
ENSMUSG00000035569	Ankrd11	protein_coding	ankyrin repeat domain 11 [Source:MGI Symbol;Acc:MGI:1924337]
ENSMUSG00000000740	Rpl13	protein_coding	ribosomal protein L13 [Source:MGI Symbol;Acc:MGI:105922]
ENSMUSG00000032815	Fanca	protein_coding	Fanconi anemia, complementation group A [Source:MGI Symbol;Acc:MGI:1341823]
ENSMUSG00000001472	Tcf25	protein_coding	transcription factor 25 (basic helix-loop-helix) [Source:MGI Symbol;Acc:MGI:1914105]
ENSMUSG00000019478	Rab4a	protein_coding	RAB4A, member RAS oncogene family [Source:MGI Symbol;Acc:MGI:105068]
ENSMUSG00000031974	Abcb10	protein_coding	ATP-binding cassette, sub-family B (MDR/TAP), member 10 [Source:MGI Symbol;Acc:MGI:1860508]
ENSMUSG00000026837	Taf5l	protein_coding	TAF5-like RNA polymerase II, p300/CBP-associated factor (PCAF)-associated factor [Source:MGI Symbol;Acc:MGI:1919039]
ENSMUSG00000031976	Urb2	protein_coding	URB2 ribosome biogenesis 2 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2681124]
ENSMUSG00000020704	Galnt2	protein_coding	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 [Source:MGI Symbol;Acc:MGI:894694]
ENSMUSG00000074030	Exoc8	protein_coding	exocyst complex component 8 [Source:MGI Symbol;Acc:MGI:2142527]
ENSMUSG00000031987	Egln1	protein_coding	EGL nine homolog 1 (C. elegans) [Source:MGI Symbol;Acc:MGI:1932286]
ENSMUSG00000031832	BC031781	protein_coding	cDNA sequence BC031781 [Source:MGI Symbol;Acc:MGI:2385207]
ENSMUSG00000051495	Irf2bp2	protein_coding	interferon regulatory factor 2 binding protein 2 [Source:MGI Symbol;Acc:MGI:2443921]
ENSMUSG00000093904	Tomm20	protein_coding	translocase of outer mitochondrial membrane 20 homolog (yeast) [Source:MGI Symbol;Acc:MGI:1915202]
ENSMUSG00000042249	4930428N1	protein_coding	RIKEN cDNA 4930428N13 gene [Source:MGI Symbol;Acc:MGI:3142748]
ENSMUSG00000025898	Cwf19l2	protein_coding	CWF19-like 2, cell cycle control (S. pombe) [Source:MGI Symbol;Acc:MGI:1918035]
ENSMUSG00000025893	Kbtbd3	protein_coding	kelch repeat and BTB (POZ) domain containing 3 [Source:MGI Symbol;Acc:MGI:2141529]
ENSMUSG00000013076	Amotl1	protein_coding	angiomotin-like 1 [Source:MGI Symbol;Acc:MGI:1922973]
ENSMUSG00000031939	Taf1d	protein_coding	TATA box binding protein (Tbp)-associated factor, RNA polymerase I, D [Source:MGI Symbol;Acc:MGI:1921508]
ENSMUSG00000048113	1500041K0	protein_coding	RIKEN cDNA 1500041K0 gene [Source:MGI Symbol;Acc:MGI:2447521]
ENSMUSG00000060510	Zfp260	protein_coding	zinc finger protein 260 [Source:MGI Symbol;Acc:MGI:1929703]
ENSMUSG00000004099	Dnmt1	protein_coding	DNA methyltransferase (cytosine-5) 1 [Source:MGI Symbol;Acc:MGI:94912]
ENSMUSG00000010205	Raver1	protein_coding	ribonucleoprotein, PTB-binding 1 [Source:MGI Symbol;Acc:MGI:1919010]
ENSMUSG00000019471	Cdc37	protein_coding	cell division cycle 37 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:109531]
ENSMUSG00000003308	Keap1	protein_coding	kelch-like ECH-associated protein 1 [Source:MGI Symbol;Acc:MGI:1858732]
ENSMUSG00000002820	Atg4d	protein_coding	autophagy-related 4D (yeast) [Source:MGI Symbol;Acc:MGI:2444308]
ENSMUSG00000035947	Kri1	protein_coding	KRI1 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2384895]
ENSMUSG00000032178	Ilf3	protein_coding	interleukin enhancer binding factor 3 [Source:MGI Symbol;Acc:MGI:1339973]
ENSMUSG00000032185	Carm1	protein_coding	coactivator-associated arginine methyltransferase 1 [Source:MGI Symbol;Acc:MGI:1913208]
ENSMUSG00000032187	Smarca4	protein_coding	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 [Source:MGI Symbol;Acc:MGI:88192]
ENSMUSG00000032193	Ldlr	protein_coding	low density lipoprotein receptor [Source:MGI Symbol;Acc:MGI:96765]
ENSMUSG00000003402	Prkcsh	protein_coding	protein kinase C substrate 80K-H [Source:MGI Symbol;Acc:MGI:107877]
ENSMUSG00000031963	Bmper	protein_coding	BMP-binding endothelial regulator [Source:MGI Symbol;Acc:MGI:1920480]
ENSMUSG00000062257	Opcml	protein_coding	opioid binding protein/cell adhesion molecule-like [Source:MGI Symbol;Acc:MGI:97397]
ENSMUSG00000031996	Aplp2	protein_coding	amyloid beta (A4) precursor-like protein 2 [Source:MGI Symbol;Acc:MGI:88047]
ENSMUSG00000016087	Fli1	protein_coding	Friend leukemia integration 1 [Source:MGI Symbol;Acc:MGI:95554]
ENSMUSG00000032036	Kirrel3	protein_coding	kin of IRRE like 3 (Drosophila) [Source:MGI Symbol;Acc:MGI:1914953]
ENSMUSG00000032118	Fez1	protein_coding	fasciculation and elongation protein zeta 1 (zygin I) [Source:MGI Symbol;Acc:MGI:2670976]
ENSMUSG00000032064	Pknox2	protein_coding	Pbx/knotted 1 homeobox 2 [Source:MGI Symbol;Acc:MGI:2445415]
ENSMUSG00000032210	Nrgn	protein_coding	neurogranin [Source:MGI Symbol;Acc:MGI:1927184]
ENSMUSG00000040111	Gramd1b	protein_coding	GRAM domain containing 1B [Source:MGI Symbol;Acc:MGI:1925037]
ENSMUSG00000032020	Ubash3b	protein_coding	ubiquitin associated and SH3 domain containing, B [Source:MGI Symbol;Acc:MGI:1920078]
ENSMUSG00000032017	Grik4	protein_coding	glutamate receptor, ionotropic, kainate 4 [Source:MGI Symbol;Acc:MGI:95817]
ENSMUSG00000034342	Cbl	protein_coding	Casitas B-lineage lymphoma [Source:MGI Symbol;Acc:MGI:88279]
ENSMUSG00000049932	H2afx	protein_coding	H2A histone family, member X [Source:MGI Symbol;Acc:MGI:102688]
ENSMUSG00000063382	Bcl9l	protein_coding	B cell CLL/lymphoma 9-like [Source:MGI Symbol;Acc:MGI:1933114]
ENSMUSG00000032097	Ddx6	protein_coding	DEAD (Asp-Glu-Ala-Asp) box polypeptide 6 [Source:MGI Symbol;Acc:MGI:104976]
ENSMUSG00000034908	Sidt2	protein_coding	SID1 transmembrane family, member 2 [Source:MGI Symbol;Acc:MGI:2446134]
ENSMUSG00000003131	Pafah1b2	protein_coding	platelet-activating factor acetylhydrolase, isoform 1b, subunit 2 [Source:MGI Symbol;Acc:MGI:108415]
ENSMUSG00000034135	Sik3	protein_coding	SIK family kinase 3 [Source:MGI Symbol;Acc:MGI:2446296]
ENSMUSG00000032076	Cadm1	protein_coding	cell adhesion molecule 1 [Source:MGI Symbol;Acc:MGI:1889272]
ENSMUSG00000066687	Zbtb16	protein_coding	zinc finger and BTB domain containing 16 [Source:MGI Symbol;Acc:MGI:103222]
ENSMUSG00000032058	Ppp2r1b	protein_coding	protein phosphatase 2 (formerly 2A), regulatory subunit A (PR 65), beta isoform [Source:MGI Symbol;Acc:MGI:1920949]
ENSMUSG00000032050	Rdx	protein_coding	radixin [Source:MGI Symbol;Acc:MGI:97887]
ENSMUSG00000034218	Atm	protein_coding	ataxia telangiectasia mutated homolog (human) [Source:MGI Symbol;Acc:MGI:107202]
ENSMUSG00000074505	C230081A1	protein_coding	RIKEN cDNA C230081A13 gene [Source:MGI Symbol;Acc:MGI:2443548]
ENSMUSG00000032329	Hmg20a	protein_coding	high mobility group 20A [Source:MGI Symbol;Acc:MGI:1914117]
ENSMUSG00000032288	Imp3	protein_coding	IMP3, U3 small nucleolar ribonucleoprotein, homolog (yeast) [Source:MGI Symbol;Acc:MGI:1916133]
ENSMUSG00000032300	1700017B0	protein_coding	RIKEN cDNA 1700017B05 gene [Source:MGI Symbol;Acc:MGI:1921483]
ENSMUSG00000032312	Csk	protein_coding	c-src tyrosine kinase [Source:MGI Symbol;Acc:MGI:88537]
ENSMUSG00000032340	Neo1	protein_coding	neogenin [Source:MGI Symbol;Acc:MGI:1097159]
ENSMUSG00000025234	Arih1	protein_coding	ariadne ubiquitin-conjugating enzyme E2 binding protein homolog 1 (Drosophila) [Source:MGI Symbol;Acc:MGI:1344363]
ENSMUSG00000032294	Pkm2	protein_coding	pyruvate kinase, muscle [Source:MGI Symbol;Acc:MGI:97591]
ENSMUSG00000032280	Tle3	protein_coding	transducin-like enhancer of split 3, homolog of Drosophila E(spl) [Source:MGI Symbol;Acc:MGI:104634]
ENSMUSG00000007892	Rplp1	protein_coding	ribosomal protein, large, P1 [Source:MGI Symbol;Acc:MGI:1927099]
ENSMUSG00000032244	Fem1b	protein_coding	feminization 1 homolog b (C. elegans) [Source:MGI Symbol;Acc:MGI:1335087]
ENSMUSG00000032399	Rpl4	protein_coding	ribosomal protein L4 [Source:MGI Symbol;Acc:MGI:1915141]
ENSMUSG00000032397	Tipin	protein_coding	timeless interacting protein [Source:MGI Symbol;Acc:MGI:1921571]
ENSMUSG00000004771	Rab11a	protein_coding	RAB11A, member RAS oncogene family [Source:MGI Symbol;Acc:MGI:1858202]
ENSMUSG00000064203	2010321M	protein_coding	RIKEN cDNA 2010321M09 gene [Source:MGI Symbol;Acc:MGI:1917133]
ENSMUSG00000032392	Parp16	protein_coding	poly (ADP-ribose) polymerase family, member 16 [Source:MGI Symbol;Acc:MGI:2446133]
ENSMUSG00000050721	Plekho2	protein_coding	pleckstrin homology domain containing, family O member 2 [Source:MGI Symbol;Acc:MGI:2145132]
ENSMUSG00000040524	Zfp609	protein_coding	zinc finger protein 609 [Source:MGI Symbol;Acc:MGI:2674092]
ENSMUSG00000032384	Csnk1g1	protein_coding	casein kinase 1, gamma 1 [Source:MGI Symbol;Acc:MGI:2660884]
ENSMUSG00000038664	Herc1	protein_coding	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1 [Source:MGI Symbol;Acc:MGI:2384589]
ENSMUSG00000032366	Tpm1	protein_coding	tropomyosin 1, alpha [Source:MGI Symbol;Acc:MGI:98809]
ENSMUSG00000052698	Tln2	protein_coding	talin 2 [Source:MGI Symbol;Acc:MGI:1917799]
ENSMUSG00000032238	Rora	protein_coding	RAR-related orphan receptor alpha [Source:MGI Symbol;Acc:MGI:104661]
ENSMUSG00000032220	Myo1e	protein_coding	myosin IE [Source:MGI Symbol;Acc:MGI:106621]
ENSMUSG00000054693	Adam10	protein_coding	a disintegrin and metallopeptidase domain 10 [Source:MGI Symbol;Acc:MGI:109548]
ENSMUSG00000032199	Polr2m	protein_coding	polymerase (RNA) II (DNA directed) polypeptide M [Source:MGI Symbol;Acc:MGI:1097262]
ENSMUSG00000050187	Gcom1	protein_coding	GRINL1A complex locus [Source:MGI Symbol;Acc:MGI:3041187]
ENSMUSG00000041361	Myzap	protein_coding	myocardial zonula adherens protein [Source:MGI Symbol;Acc:MGI:2142008]
ENSMUSG00000032228	Tcf12	protein_coding	transcription factor 12 [Source:MGI Symbol;Acc:MGI:101877]
ENSMUSG00000037674	Rfx7	protein_coding	regulatory factor X, 7 [Source:MGI Symbol;Acc:MGI:2442275]
ENSMUSG00000032216	Nedd4	protein_coding	neural precursor cell expressed, developmentally down-regulated 4 [Source:MGI Symbol;Acc:MGI:97297]
ENSMUSG00000062151	Unc13c	protein_coding	unc-13 homolog C (C. elegans) [Source:MGI Symbol;Acc:MGI:2149021]
ENSMUSG00000007656	Arpp19	protein_coding	cAMP-regulated phosphoprotein 19 [Source:MGI Symbol;Acc:MGI:1891691]
ENSMUSG00000034593	Myo5a	protein_coding	myosin VA [Source:MGI Symbol;Acc:MGI:105976]
ENSMUSG00000042688	Mapk6	protein_coding	mitogen-activated protein kinase 6 [Source:MGI Symbol;Acc:MGI:1354946]
ENSMUSG00000032359	2510006D	protein_coding	RIKEN cDNA 2510006D16 gene [Source:MGI Symbol;Acc:MGI:1914553]

ENSMUSG00000037742	Eef1a1	protein_coding	eukaryotic translation elongation factor 1 alpha 1 [Source:MGI Symbol;Acc:MGI:1096881]
ENSMUSG00000034712	Senp8	protein_coding	SUMO/sentrin specific peptidase 8 [Source:MGI Symbol;Acc:MGI:1922075]
ENSMUSG00000040789	Mei4	protein_coding	meiosis-specific, MEI4 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1922700]
ENSMUSG00000032255	Phip	protein_coding	pleckstrin homology domain interacting protein [Source:MGI Symbol;Acc:MGI:1932404]
ENSMUSG00000032265	Fam46a	protein_coding	family with sequence similarity 46, member A [Source:MGI Symbol;Acc:MGI:2670964]
ENSMUSG00000035941	Ibtk	protein_coding	inhibitor of Bruton agammaglobulinemia tyrosine kinase [Source:MGI Symbol;Acc:MGI:1918677]
ENSMUSG00000092341	Gm20387	protein_coding	predicted gene 20387 [Source:MGI Symbol;Acc:MGI:5142002]
ENSMUSG00000032423	Syncrip	protein_coding	synaptotagmin binding, cytoplasmic RNA interacting protein [Source:MGI Symbol;Acc:MGI:1891690]
ENSMUSG00000032407	2610101N10Rik	protein_coding	RIKEN cDNA 2610101N10 gene [Source:MGI Symbol;Acc:MGI:1919208]
ENSMUSG00000032411	Tfdp2	protein_coding	transcription factor Dp 2 [Source:MGI Symbol;Acc:MGI:107167]
ENSMUSG00000032412	Atp1b3	protein_coding	ATPase, Na+/K+ transporting, beta 3 polypeptide [Source:MGI Symbol;Acc:MGI:107788]
ENSMUSG00000032413	Rasa2	protein_coding	RAS p21 protein activator 2 [Source:MGI Symbol;Acc:MGI:2149960]
ENSMUSG00000068415	Msl2	protein_coding	male-specific lethal 2 homolog (Drosophila) [Source:MGI Symbol;Acc:MGI:1925100]
ENSMUSG00000032803	Cdv3	protein_coding	carnitine deficiency-associated gene expressed in ventricle 3 [Source:MGI Symbol;Acc:MGI:2446715]
ENSMUSG00000032564	Cpne4	protein_coding	copine IV [Source:MGI Symbol;Acc:MGI:1921270]
ENSMUSG00000032571	Pik3r4	protein_coding	phosphatidylinositol 3 kinase, regulatory subunit, polypeptide 4, p150 [Source:MGI Symbol;Acc:MGI:1922919]
ENSMUSG00000032537	Wdr22	protein_coding	WD repeat domain containing 22 [Source:MGI Symbol;Acc:MGI:1924133]
ENSMUSG00000032377	Twf2	protein_coding	twinfilin, actin-binding protein, homolog 2 (Drosophila) [Source:MGI Symbol;Acc:MGI:1346078]
ENSMUSG00000040661	Rad54l2	protein_coding	RAD54 like 2 (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1933196]
ENSMUSG00000032575	Manf	protein_coding	mesencephalic astrocyte-derived neurotrophic factor [Source:MGI Symbol;Acc:MGI:1922090]
ENSMUSG00000045503	Rbm15b	protein_coding	RNA binding motif protein 15B [Source:MGI Symbol;Acc:MGI:1923358]
ENSMUSG00000010066	Cacna2d2	protein_coding	calcium channel, voltage-dependent, alpha 2/delta subunit 2 [Source:MGI Symbol;Acc:MGI:1929813]
ENSMUSG00000032562	Gnai2	protein_coding	guanine nucleotide binding protein (G protein), alpha inhibiting 2 [Source:MGI Symbol;Acc:MGI:95772]
ENSMUSG00000032580	Rbm5	protein_coding	RNA binding motif protein 5 [Source:MGI Symbol;Acc:MGI:1933204]
ENSMUSG00000032586	Traip	protein_coding	TRAF-interacting protein [Source:MGI Symbol;Acc:MGI:1096377]
ENSMUSG00000072532	Cdhr4	protein_coding	cadherin-related family member 4 [Source:MGI Symbol;Acc:MGI:1918840]
ENSMUSG00000042106	8430427H17Rik	protein_coding	RIKEN cDNA 8430427H17 gene [Source:MGI Symbol;Acc:MGI:1915420]
ENSMUSG00000039952	Dag1	protein_coding	dystroglycan 1 [Source:MGI Symbol;Acc:MGI:101864]
ENSMUSG00000007815	Rhoa	protein_coding	ras homolog gene family, member A [Source:MGI Symbol;Acc:MGI:1096342]
ENSMUSG00000063856	Gpx1	protein_coding	glutathione peroxidase 1 [Source:MGI Symbol;Acc:MGI:104887]
ENSMUSG00000032605	Ccdc71	protein_coding	coiled-coil domain containing 71 [Source:MGI Symbol;Acc:MGI:1918794]
ENSMUSG00000006673	Qrich1	protein_coding	glutamine-rich 1 [Source:MGI Symbol;Acc:MGI:1918483]
ENSMUSG00000032257	Wdr6	protein_coding	WD repeat domain 6 [Source:MGI Symbol;Acc:MGI:1930140]
ENSMUSG00000032479	Map4	protein_coding	microtubule-associated protein 4 [Source:MGI Symbol;Acc:MGI:97178]
ENSMUSG00000032480	Dhx30	protein_coding	DEAH (Asp-Glu-Ala-His) box polypeptide 30 [Source:MGI Symbol;Acc:MGI:1920081]
ENSMUSG00000032481	Smarcc1	protein_coding	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1 [Source:MGI Symbol;Acc:MGI:1203524]
ENSMUSG00000056724	Nbeal2	protein_coding	neurobeachin-like 2 [Source:MGI Symbol;Acc:MGI:2448554]
ENSMUSG00000032504	Pdcd6ip	protein_coding	programmed cell death 6 interacting protein [Source:MGI Symbol;Acc:MGI:1333753]
ENSMUSG00000032507	Fbxl2	protein_coding	F-box and leucine-rich repeat protein 2 [Source:MGI Symbol;Acc:MGI:1919429]
ENSMUSG00000032498	Cmtm7	protein_coding	CKLF-like MARVEL transmembrane domain containing 7 [Source:MGI Symbol;Acc:MGI:2447166]
ENSMUSG00000032437	Stt3b	protein_coding	STT3, subunit of the oligosaccharyltransferase complex, homolog B (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:1915542]
ENSMUSG00000039607	Rbms3	protein_coding	RNA binding motif, single stranded interacting protein [Source:MGI Symbol;Acc:MGI:2444477]
ENSMUSG00000047409	Ctdspl	protein_coding	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase-like [Source:MGI Symbol;Acc:MGI:1916224]
ENSMUSG00000052336	Cx3cr1	protein_coding	chemokine (C-X3-C) receptor 1 [Source:MGI Symbol;Acc:MGI:1333815]
ENSMUSG00000032518	Rpsa	protein_coding	ribosomal protein SA [Source:MGI Symbol;Acc:MGI:105381]
ENSMUSG00000038941	Eif1b	protein_coding	eukaryotic translation initiation factor 1B [Source:MGI Symbol;Acc:MGI:1916312]
ENSMUSG00000006932	Ctnnb1	protein_coding	catenin (cadherin associated protein), beta 1 [Source:MGI Symbol;Acc:MGI:88276]
ENSMUSG00000032525	Nktr	protein_coding	natural killer tumor recognition sequence [Source:MGI Symbol;Acc:MGI:97346]
ENSMUSG00000025786	Zdhhc3	protein_coding	zinc finger, DHHC domain containing 3 [Source:MGI Symbol;Acc:MGI:1926134]

TABLE S4

Table S4. Percentages of human donor derived chimerism used to calculate CRU

Primary LDA

	Percentage of hCD45+ GFP+ cells in TNC
Control 50K	1.20%
	1.11%
	0.85%
	4.29%
Control 20K	1.66%
	1.51%
	1.47%
	2.10%
	7.37%
YTHDF2 KD 50K	67.90%
	22.80%
	21.00%
	12.30%
YTHDF2 KD 20K	8.23%
	4.57%
	1.53%
	0.17%
Control 10K *	0.46%
	1.00%
	0.65%
	1.23%
	2.51%
YTHDF2 KD 20K	1.60%
	1.28%
	1.40%
	1.66%
	3.07%
	0.95%

* Control 10K group also transplanted 7 mice. However, 2 mice were dead before the time point of analysis partially due to the deficiency in hematopoietic recovery.

TABLE S4 (con't)

Secondary LDA

	Percentage of hCD45+ GFP+ cells in TNC
Control 12E+6	0.27%
	0.26%
	0.35%
Control 8E+6	0.02%
	0.01%
	7.57E-05
Control 4E+6	0.03%
	0.02%
	0.01%
YTHDF2 KD 12E+6	0.02%
	0.92%
	1.13%
	1.45%
YTHDF2 KD 8E+6	0.38%
	0.37%
	0.72%
YTHDF2 KD 4E+6	0.27%
	0.29%
	0.19%
	0.44%

TABLE S5

Table S5. qPCR primers used to verify the expressional levels of transcription factors in *wt* and *Ythdf2* KO HSPCs.

mouse Tal1 qPCR primer F	CGCTGCTCTATAGCCTTAGCC
mouse Tal1 qPCR primer R	CTCTTCACCCGGTTGTTGTT
mouse Gata2 qPCR primer F	CAACCCTTACTACGCCAACC
mouse Gata2 qPCR primer R	GCTGTGCAACAAGTGTGGTC
mouse Runx1 qPCR primer F	CCAGCCTCTCTGCAGAACTT
mouse Runx1 qPCR primer R	GGAGATGGACGGCAGAGTAG
mouse Stat5a qPCR primer F	AGAAGCAAGTGTCCCTGGAG
mouse Stat5a qPCR primer R	GTCGTCCAGGATGATGGTCT
mouse Actb qPCR primer F	TGTCACCAACTGGGACGATA
mouse Actb qPCR primer R	ACCCTCATAGATGGGCACAG

What is claimed is:

1. A method for expanding a population of stem cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the population of stem cells, to expand the number of stem cells.

2. The method according to claim 1, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells that results in modulation of a molecule in the m^6A mRNA modification pathway or contacting the stem cell with a modulator of a molecule in the m^6A mRNA modification pathway selected from the group consisting of a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

3. The method according to claim 2, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

4. The method according to claim 3, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, and a m^6A mRNA eraser.

5. The method according to claim 4, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader.

6. The method according to claim 5, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

7. The method according to claim 6, wherein the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2.

8. The method according to claim 4, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser.

9. The method according to claim 8, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser selected from the group consisting of FTO and ALKBH5.

10. The method according to claim 4, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer.

11. The method according to claim 10, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP and KIAA1429.

12. The method according to claim 3, wherein modulating the m^6A mRNA modification pathway comprises exposing the stem cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway.

13. The method according to claim 3, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation that incorporates shRNA into the stem cells to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

14. The method according to claim 13, wherein the shRNA is introduced by exposing the stem cells to a lentivirus to deliver the shRNA.

15. The method according to claim 1, wherein modulating the m^6A mRNA modification pathway comprises down-regulating a m^6A mRNA modification reader.

16. The method according to claim 15, wherein the m^6A mRNA modification reader is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

17. The method according to claim 16, wherein the m^6A mRNA modification reader comprises Ythdf2.

18. The method according to claim 15, wherein down-regulating the m^6A mRNA modification reader comprises contacting the stem cells with an inhibitor of the m^6A mRNA modification reader selected from the group consisting of selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-

30e; (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p; (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p,

hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262; (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-

655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p

(MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296: (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t, hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262.

19. The method according to claim 1, wherein the expansion of the stem cells is by a factor of at least 2 fold.

20. The method according to claim 19, wherein the expansion of the stem cells is by a factor of at least 4 fold.

21. The method according to claim 20, wherein the expansion of the stem cells is by a factor of at least 5 fold.

22. The method according to claim 21, wherein the expansion of the stem cells is by a factor of at least 8 fold.

23. The method according to claim 22, wherein the expansion of the stem cells is by a factor of at least 10 fold.

24. The method according to claim 1, wherein the stem cells are selected from the group consisting of hematopoietic stem cells (HSCs), hematopoietic stem and progenitor cells (HSPCs), endothelial progenitor cells (EPCs), mesenchymal stem cells (MSCs), cardiac stem cells (CSCs), neuronal stem cells (NSCs), and combinations thereof.

25. The method according to claim 24, wherein the stem cells are HSCs.

26. The method according to claim 1, wherein the expanded cells have at least a 5 fold increase in total colony-forming units (CFU).

27. The method according to claim 1, wherein the expanded cells have at least a 3.8 fold increase in CFU-granulocyte erythrocyte monocyte megakaryocyte (GEMM) colonies.

28. A method for ex vivo expansion of a substantially undifferentiated stem cell population comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the undifferentiated stem cell population to expand the number of undifferentiated stem cells without significant differentiation of the stem cell population.

29. A method for ex vivo expansion of an hematopoietic stem cell (HSC) population obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the HSC population to expand the HSC population to a sufficient quantity while maintaining a multilineage differentiation potential in the HSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

30. The method according to claim 29, wherein the subject is a human.

31. The method according to any of claims 28 or 29, wherein:

modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells that results in modulation of a molecule in the m^6A mRNA modification pathway or contacting the stem cell with a modulator of a molecule in the m^6A mRNA modification pathway selected from the group consisting of a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

32. The method according to claim 31, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

33. The method according to claim 32, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, and a m^6A mRNA eraser.

34. The method according to claim 33, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader.

35. The method according to claim 34, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

36. The method according to claim 35, wherein the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2.

37. The method according to claim 33, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser.

38. The method according to claim 37, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser selected from the group consisting of FTO and ALKBH5.

39. The method according to claim 33, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer.

40. The method according to claim 39, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP and KIAA1429.

41. The method according to claim 31, wherein modulating the m^6A mRNA modification pathway comprises exposing the stem cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway.

42. The method according to claim 31, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation that incorporates shRNA into the stem cells to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

43. The method according to claim 42, wherein the shRNA is introduced by exposing the stem cells to a lentivirus to deliver the shRNA.

44. The method according to claim 29, wherein modulating the m^6A mRNA modification pathway comprises down-regulating a m^6A mRNA modification reader.

45. The method according to claim 44, wherein the m^6A mRNA modification reader is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

46. The method according to claim 45, wherein the m^6A mRNA modification reader comprises Ythdf2.

47. The method according to claim 44, wherein down-regulating the m^6A mRNA modification reader comprises contacting the stem cells with an inhibitor of the m^6A mRNA modification reader selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-

505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e; (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-

3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p; (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d,

hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262; (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p

(MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296: (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-

200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t, hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262.

48. The method according to claim 28, wherein the stem cell is selected from the group consisting of hematopoietic stem cells (HSCs), hematopoietic stem and progenitor cells (HSPCs), endothelial progenitor cells (EPCs), mesenchymal stem cells (MSCs), cardiac stem cells (CSCs), neuronal stem cells (NSCs), and combinations thereof.

49. The method according to claim 48, wherein the stem cell is a hematopoietic stem cell (HSC).

50. The method according to claim 49, wherein the HSC is obtained from mammalian tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

51. The method according to claim 31, wherein the expansion of the number of stem cells is by a factor selected from the group consisting of at least 2-fold, at least 4-fold, at least 5-fold, at least 8-fold and at least 10-fold.

52. An expanded, substantially undifferentiated stem cell population made by the process according to claim 28.

53. An expanded HSC population made by the process according to claim 29.

54. A method for ex vivo expansion of hematopoietic stem cells (HSCs) by at least 2-fold, the expanded HSCs being competent to reconstitute an HSC lineage upon transplantation into a mammal in need thereof, the method comprising introducing a mutation into the stem cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of HSCs in a suitable culture medium.

55. The method according to claim 54, wherein the HSCs are obtained from a mammalian tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

56. The method according to claim 54, wherein the mammal is a human.

57. The method according to claim 54, wherein the mutation deletes, replaces or reduces expression of a gene expressing Ythdf2.

58. The method according to claim 54, wherein the mutation is introduced by exposing the stem cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader.

59. The method according to claim 54, wherein the mutation incorporates shRNA into the stem cells to reduce expression of a gene that expresses a m^6A mRNA modification reader.

60. The method according to claim 54, wherein the expansion of the number of HSCs is by a factor selected from the group consisting of at least 2-fold, at least 4-fold, at least 5-fold, at least 8-fold and at least 10-fold.

61. A kit for expanding an hematopoietic stem cell population (HSC) population for subsequent transplantation into a subject in need thereof, the kit comprising a system for introducing a mutation into the HSC population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

62. The kit according to claim 61, wherein the system for introducing a mutation into the HSC population includes one or more reagents capable of introducing a mutation into the HSC population that results in deletion, replacement or reduced expression of a gene expressing Ythdf2.

63. The kit according to claim 62, wherein the system for introducing a mutation into the HSC population comprises a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader.

64. The kit according to claim 62, wherein the system for introducing a mutation into the HSC population comprises reagents for delivering a lentivirus that incorporates shRNA into the HSC population to reduce expression of a gene that expresses a m^6A mRNA modification reader.

65. A kit for expanding an hematopoietic stem cell population (HSC) population for subsequent transplantation into a subject in need thereof, the kit comprising an inhibitor of a m^6A mRNA modification reader, and instructions for use thereof.

66. A method for administering an hematopoietic stem cell (HSC) to a subject in need thereof, the method comprising:

(a) introducing, into a sample containing an HSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader,

(b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject; and

(c) administering the HSCs to the subject.

67. The method according to claim 66, wherein the HSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

68. The method according to claim 66, wherein the mutation results in deletion a gene expressing Ythdf2.

69. The method according to claim 66, wherein the mutation results in incorporation of shRNA into the HSC population that reduces expression of a gene expressing Ythdf2.

70. A method for administering an hematopoietic stem cell (HSC) to a subject in need thereof, the method comprising:

(a) culturing, in a suitable culture media, a sample containing an HSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject;

(b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and

(c) administering the HSCs to the subject.

71. The method according to claim 70, wherein the HSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

72. The method according to claim 70, wherein the inhibitor of the m^6A mRNA modification reader inhibits Ythfd2.

73. The method according to claim 70, wherein the subject is a human.

74. A method for reconstituting bone marrow in a subject in need thereof, comprising:

(a) introducing, into a sample containing an HSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader,

(b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject;

(c) administering the HSCs to the subject.

75. The method according to claim 74, wherein the HSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

76. A method for reconstituting bone marrow in a subject in need thereof, comprising:

(a) culturing, in a suitable culture media, a sample containing an HSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of HSCs in the sample to a number sufficient to transplant into the subject;

(b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and

(c) administering the HSCs to the subject.

77. The method according to claim 76, wherein the HSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

78. A method for expanding a population of hematopoietic cells (HSCs) comprising culturing the population of HSCs under conditions sufficient to result in an expansion of the HSC population by at least 2-fold, wherein the expanded population of HSCs is suitable for transplantation into a mammal in need thereof.

79. The method according to claim 78, wherein the expansion of the HSC population is at least 4-fold.

80. The method according to claim 79, wherein the expansion of the HSC population is at least 5-fold.

81. The method according to claim 80, wherein the expansion of the HSC population is at least 8-fold.

82. The method according to claim 81, wherein the expansion of the HSC population is at least 10-fold.

83. The method according to claim 82, wherein the mammal is a human.

84. The method according to claim 83, wherein the human requires a transplant selected from the group consisting of a bone marrow transplant, a peripheral blood transplant, and an umbilical cord blood transplant.

85. A method for treating a subject in need of a transplant, selected from the group consisting of a bone marrow transplant, a peripheral blood transplant and an umbilical cord blood transplant comprising administering to the subject a population of HSCs obtained by the method of claim 78.

86. A method for expanding a population of hematopoietic stem cells (HSCs) comprising:

(a) obtaining from a mammal a tissue sample comprising an HSC population;

(b) expanding, in vitro, the HSC population from the sample, wherein:

(i) the HSC population expands by at least 2-fold; and

(ii) the expanded HSC population has at least a 5-fold increase in total colony-forming units.

87. The method according to claim 86, wherein the expansion of the HSC population is at least 4-fold.

88. The method according to claim 87, wherein the expansion of the HSC population is at least 5-fold.

89. The method according to claim 88, wherein the expansion of the HSC population is at least 8-fold.

90. The method according to claim 89, wherein the expansion of the HSC population is at least 10-fold.

91. The method according to claim 86, wherein the mammal is a human.

92. The method according to claim 91, wherein the human requires a bone marrow transplant.

93. The method according to claim 92, wherein the tissue sample is obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

94. A method for reconstituting a hematopoietic stem cell lineage in a subject in need thereof, the method comprising:

(a) obtaining from a mammal a tissue sample comprising an HSC population;

(b) expanding, in vitro, the HSC population from the sample, wherein:

(i) the HSC population expands by at least 2-fold; and

(ii) the expanded HSC population has at least a 5-fold increase in total colony-forming units; and

(c) transplanting the expanded HSC population into a subject in need thereof.

95. The method according to claim 94, wherein the expansion of the HSC population is at least 4-fold.

96. The method according to claim 95, wherein the expansion of the HSC population is at least 5-fold.

97. The method according to claim 96, wherein the expansion of the HSC population is at least 8-fold.

98. The method according to claim 97, wherein the expansion of the HSC population is at least 10-fold.

99. The method according to claim 94, wherein the mammal is a human.

100. The method according to claim 99, wherein the human requires a bone marrow transplant.

101. The method according to claim 100, wherein the tissue sample is obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

102. The method according to claim 101, wherein the sample is from an autologous or allogeneic source.

103. The method according to claim 102, wherein the sample is from an autologous source.

104. A method for expanding a hematopoietic stem cell population in a mammal in need of such expansion comprising administering to the mammal a therapeutically effective amount of a modulator of a N^6-Methyladenosine (m^6A) mRNA modification pathway for a period of time sufficient to expand the HSC population by at least 2-fold with HSCs that possess the ability to reconstitute a hematopoietic lineage in the mammal.

105. The method according to claim 104, wherein the modulator comprises a system for introducing a mutation into the HSC population the deletes, replaces, or reduces expression of a gene expressing a N^6-Methyladenosine (m^6A) mRNA modification reader.

106. The method according to claim 105, wherein the modulator comprises a system for introducing a mutation into the HSC population that deletes, replaces or reduces expression of a gene expressing Ythdf2.

107. The method according to claim 104, wherein the modulator comprising an inhibitor of a N^6-Methyladenosine (m^6A) mRNA modification reader.

108. The method according to claim 107, wherein the modulator comprises an inhibitor of Ythdf2.

109. The method according to claim 104, wherein the mammal is a human.

110. A method for ex vivo expansion of a substantially undifferentiated mesenchymal stem cell (MSC) population, comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the undifferentiated MSC population to expand the number of undifferentiated MSCs without significant differentiation of the MSCs.

111. The method according to claim 110, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

112. The method according to claim 111, wherein the MSC population comprises N-cadherin+ MSCs.

113. A method for ex vivo expansion of a mesenchymal stem cell (MSC) population obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the MSC population to expand the MSC population to a sufficient quantity while maintaining a multilineage differentiation potential in the MSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

114. The method according to claim 113, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

115. The method according to claim 113, wherein the MSC population comprises N-cadherin+ MSCs.

116. The method according to claim 113, wherein the subject is a human.

117. The method according to any of claims 110 or 113, wherein:

modulating the m^6A mRNA modification pathway comprises introducing a mutation into the MSCs that results in modulation of a molecule in the m^6A mRNA modification pathway or contacting the stem cell with a modulator of a molecule in the m^6A mRNA modification pathway selected from the group consisting of a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

118. The method according to claim 117, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

119. The method according to claim 118, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, and a m^6A mRNA eraser.

120. The method according to claim 119, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader.

121. The method according to claim 120, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

122. The method according to claim 121, wherein the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2.

123. The method according to claim 119, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser.

124. The method according to claim 123, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser selected from the group consisting of FTO and ALKBH5.

125. The method according to claim 119, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer.

126. The method according to claim 125, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP and KIAA1429.

127. The method according to claim 119, wherein modulating the m^6A mRNA modification pathway comprises exposing the MSCs to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway.

128. The method according to claim 119, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation that incorporates

shRNA into the MSCs to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

129. The method according to claim 128, wherein the shRNA is introduced by exposing the stem cells to a lentivirus to deliver the shRNA.

130. The method according to claim 119, wherein modulating the m^6A mRNA modification pathway comprises down-regulating a m^6A mRNA modification reader.

131. The method according to claim 130, wherein the m^6A mRNA modification reader is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

132. The method according to claim 131, wherein the m^6A mRNA modification reader comprises Ythdf2.

133. The method according to claim 130, wherein down-regulating the m^6A mRNA modification reader comprises contacting the MSCs with an inhibitor of the m^6A mRNA modification reader selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p,

hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e; (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-

miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p; (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262; (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-

520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424,

hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296: (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t,

hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262.

134. The method according to claim 113, wherein the MSC is obtained from mammalian tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

135. The method according to claim 134, wherein the expansion of the number of stem cells is by a factor selected from the group consisting of at least 2-fold, at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold and at least 8-fold.

136. An expanded, substantially undifferentiated mesenchymal cell population made by the process according to claim 110.

137. An expanded MSC population made by the process according to claim 113.

138. A method for ex vivo expansion of mesenchymal stem cells (MSCs) by at least 2-fold, the expanded MSCs being competent to reconstitute an MSC lineage upon transplantation into a mammal in need thereof, the method comprising introducing a mutation into the stem cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of HSCs in a suitable culture medium.

139. The method according to claim 138, wherein the MSC population comprises at least one selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

140. The method according to claim 138, wherein the MSCs are obtained from a mammalian tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

141. The method according to claim 138, wherein the mammal is a human.

142. The method according to claim 138, wherein the mutation deletes, replaces or reduces expression of a gene expressing Ythdf2.

143. The method according to claim 138, wherein the mutation is introduced by exposing the MSCs to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader.

144. The method according to claim 138, wherein the mutation incorporates shRNA into the MSCs to reduce expression of a gene that expresses a m^6A mRNA modification reader.

145. The method according to claim 138, wherein the expansion of the number of MSCs is by a factor selected from the group consisting of at least 2-fold, at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold and at least 8-fold.

146. A kit for expanding a mesenchymal stem cell population (MSC) population for subsequent transplantation into a subject in need thereof, the kit comprising a system for introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

147. The kit according to claim 146, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

148. The kit according to claim 146, wherein the system for introducing a mutation into the MSC population includes one or more reagents capable of

introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing Ythdf2.

149. The kit according to claim 146, wherein the system for introducing a mutation into the MSC population comprises a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader.

150. The kit according to claim 146, wherein the system for introducing a mutation into the MSC population comprises reagents for delivering a lentivirus that incorporates shRNA into the HSC population to reduce expression of a gene that expresses a m^6A mRNA modification reader.

151. A kit for expanding an mesenchymal stem cell population (MSC) population for subsequent transplantation into a subject in need thereof, the kit comprising an inhibitor of a m^6A mRNA modification reader, and instructions for use thereof.

152. The kit according to claim 151, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

153. A method for administering mesenchymal stem cells (MSCs) to a subject in need thereof, the method comprising:

(a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader,

(b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject; and

(c) administering the MSCs to the subject.

154. The method according to claim 153, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

155. The method according to claim 153, wherein the MSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

156. The method according to claim 153, wherein the mutation results in deletion a gene expressing Ythdf2.

157. The method according to claim 153, wherein the mutation results in incorporation of shRNA into the HSC population that reduces expression of a gene expressing Ythdf2.

159. A method for administering mesenchymal stem cells (MSCs) to a subject in need thereof, the method comprising:

(a) culturing, in a suitable culture media, a sample containing an MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject;

(b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and

(c) administering the MSCs to the subject.

160. The method according to claim 159, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

161. The method according to claim 159, wherein the MSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

162. The method according to claim 159, wherein the inhibitor of the m^6A mRNA modification reader inhibits Ythfd2.

163. The method according to claim 159, wherein the subject is a human.

164. A method for reconstituting bone marrow in a subject in need thereof, comprising:

(a) introducing, into a sample containing a MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader,

(b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject;

(c) administering the MSCs to the subject.

165. The method according to claim 164, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

166. The method according to claim 164, wherein the MSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

167. A method for reconstituting bone marrow in a subject in need thereof, comprising:

(a) culturing, in a suitable culture media, a sample containing an MSC population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject;

(b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and

(c) administering the MSCs to the subject.

168. The method according to claim 167, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

169. The method according to claim 167, wherein the MSCs are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

170. A method for expanding a population of mesenchymal stem cells (MSCs) comprising culturing the population of MSCs under conditions sufficient to result in an expansion of the MSC population by at least 2-fold, wherein the expanded population of MSCs is suitable for transplantation into a mammal in need thereof.

171. The method according to claim 170, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

172. The method according to claim 170, wherein the expansion of the MSC population is at least 2.5-fold.

173. The method according to claim 172, wherein the expansion of the MSC population is at least 3-fold.

174. The method according to claim 173, wherein the expansion of the MSC population is at least 3.5-fold.

175. The method according to claim 174, wherein the expansion of the MSC population is at least 4-fold.

176. The method according to claim 175, wherein the expansion of the MSC population is at least 8-fold.

177. The method according to claim 170, wherein the mammal is a human.

178. The method according to claim 177, wherein the human requires a transplant selected from the group consisting of a bone marrow transplant, a peripheral blood transplant, and an umbilical cord blood transplant.

179. A method for treating a subject in need of a transplant, selected from the group consisting of a bone marrow transplant, a peripheral blood transplant and an umbilical cord blood transplant comprising administering to the subject a population of MSCs obtained by the method of claim 170.

180. A method for expanding a population of mesenchymal stem cells (MSCs) comprising:

(a) obtaining from a mammal a tissue sample comprising a MSC population; and

(b) expanding, in vitro, the MSC population from the sample, wherein:

(i) the MSC population expands by at least 2-fold.

181. The method according to claim 180, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

182. The method according to claim 180, wherein the expansion of the MSC population is at least 2.5-fold.

183. The method according to claim 182, wherein the expansion of the MSC population is at least 3-fold.

184. The method according to claim 183, wherein the expansion of the MSC population is at least 3.5-fold.

185. The method according to claim 184, wherein the expansion of the MSC population is at least 4-fold.

186. The method according to claim 185, wherein the expansion of the MSC population is at least 8-fold.

187. The method according to claim 180, wherein the mammal is a human.

188. The method according to claim 187, wherein the human requires a bone marrow transplant.

189. The method according to claim 180, wherein the tissue sample is obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

190. A method for reconstituting a mesenchymal stem cell lineage in a subject in need thereof, the method comprising:

(a) obtaining from a mammal a tissue sample comprising a MSC population;

(b) expanding, in vitro, the MSC population from the sample, wherein:

(i) the MSC population expands by at least 2-fold; and

(c) transplanting the expanded MSC population into a subject in need thereof.

191. The method according to claim 190, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

192. The method according to claim 190, wherein the expansion of the MSC population is at least 2.5-fold.

193. The method according to claim 192, wherein the expansion of the MSC population is at least 3-fold.

194. The method according to claim 193, wherein the expansion of the MSC population is at least 3.5-fold.

195. The method according to claim 194, wherein the expansion of the MSC population is at least 4-fold.

196. The method according to claim 195, wherein the expansion of the MSC population is at least 8-fold.

197. The method according to claim 190, wherein the mammal is a human.

198. The method according to claim 197, wherein the human requires a bone marrow transplant.

199. The method according to claim 190, wherein the tissue sample is obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

200. The method according to claim 199, wherein the sample is from an autologous or allogeneic source.

201. The method according to claim 199, wherein the sample is from an autologous source.

202. A method for expanding a mesenchymal stem cell population in a mammal in need of such expansion comprising administering to the mammal a therapeutically effective amount of a modulator of a N^6-Methyladenosine (m^6A) mRNA modification pathway for a period of time sufficient to expand the MSC population by at least 2-fold with HSCs that possess the ability to reconstitute a mesenchymal lineage in the mammal.

203. The method according to claim 202, wherein the MSC population comprises at least one MSC selected from the group consisting of N-cadherin+ MSCs and CD105+ MSCs.

204. The method according to claim 202, wherein the modulator comprises a system for introducing a mutation into the MSC population the deletes, replaces, or reduces expression of a gene expressing a N^6-Methyladenosine (m^6A) mRNA modification reader.

205. The method according to claim 202, wherein the modulator comprises a system for introducing a mutation into the MSC population that deletes, replaces or reduces expression of a gene expressing Ythdf2.

206. The method according to claim 202, wherein the modulator comprising an inhibitor of a N^6-Methyladenosine (m^6A) mRNA modification reader.

207. The method according to claim 202, wherein the modulator comprises an inhibitor of Ythdf2.

208. The method according to claim 202, wherein the mammal is a human.

209. A method of isolating mesenchymal stem cells (MSCs) from a biological sample, the method comprising contacting the biological sample having a population of MSCs with one or more N-cadherin antibodies.

210. The method according to claim 209, wherein the biological sample comprises a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow.

211. The method according to claim 209, further comprising expanding the population of MSCs from the biological sample, by modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the population of MSCs, to expand the number of mesenchymal stem cells.

212. The method according to claim 211, wherein the population of MSCs is expanded after isolating from the biological sample.

213. The method according to claim 211, wherein the population of MSCs in the biological sample is expanded before isolation of the MSCs from the biological sample.

214. The method according to claim 211, wherein the MSC population is expanded to a sufficient quantity while maintaining a multilineage differentiation potential in the MSC population, which is sufficient for subsequent transplantation into a subject in need thereof.

215. The method according to claim 214, wherein the subject is a human.

216. The method according to claim 211, wherein:

modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells that results in modulation of a molecule in the m^6A mRNA modification pathway or contacting the stem cell with a modulator of a molecule in the m^6A mRNA modification pathway selected from the group consisting of a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

217. The method according to claim 216, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the stem cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

218. The method according to claim 217, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, and a m^6A mRNA eraser.

219. The method according to claim 218, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader.

220. The method according to claim 219, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

221. The method according to claim 220, wherein the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2.

222. The method according to claim 218, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser.

223. The method according to claim 218, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser selected from the group consisting of FTO and ALKBH5.

224. The method according to claim 218, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer.

225. The method according to claim 224, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP and KIAA1429.

226. The method according to claim 211, wherein modulating the m^6A mRNA modification pathway comprises exposing the stem cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway.

227. The method according to claim 211, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation that incorporates shRNA into the stem cells to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

228. The method according to claim 227, wherein the shRNA is introduced by exposing the stem cells to a lentivirus to deliver the shRNA.

229. The method according to claim 211, wherein modulating the m^6A mRNA modification pathway comprises down-regulating a m^6A mRNA modification reader.

230. The method according to claim 229, wherein the m^6A mRNA modification reader is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

231. The method according to claim 230, wherein the m^6A mRNA modification reader comprises Ythdf2.

232. The method according to claim 229, wherein down-regulating the m^6A mRNA modification reader comprises contacting the stem cells with an inhibitor of the m^6A mRNA modification reader selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224,

hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e; (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p; (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-

521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262; (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187,

hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-

mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296: (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t, hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611,

hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262.

233. An isolated population of mesenchymal stem cells made by the process according to claim 209.

234. An expanded, isolated population of mesenchymal stem cells made by the process of claim 211.

235. A kit for isolating a mesenchymal stem cell (MSC) population for subsequent transplantation into a subject in need thereof, the kit comprising a system for contacting a biological sample comprising MSCs with one or more N-cadherin antibodies, and instructions for use thereof.

236. The kit according to claim 235, further comprising a system for expanding the population of MSCs by introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

237. The kit according to claim 236, wherein the system for introducing a mutation into the MSC population includes one or more reagents capable of introducing a mutation into the MSC population that results in deletion, replacement or reduced expression of a gene expressing Ythdf2.

238. The kit according to claim 237, wherein the system for introducing a mutation into the MSC population comprises a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader.

239. The kit according to claim 237, wherein the system for introducing a mutation into the MSC population comprises reagents for delivering a lentivirus that incorporates shRNA into the MSC population to reduce expression of a gene that expresses a m^6A mRNA modification reader.

240. A method for administering a mesenchymal stem cell (MSC) to a subject in need thereof, the method comprising:

(a) isolating MSCs from a biological sample comprising a population of MSCs, by contacting the biological sample with one or more N-cadherin antibodies; and

(b) administering the isolated MSCs to the subject.

241. The method according to claim 240, further comprising introducing, into the biological sample containing the MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and culturing the biological sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject.

242. The method according to claim 240, wherein the MSCs are obtained from a biological sample comprising a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

243. The method according to claim 241, wherein the mutation results in deletion a gene expressing Ythdf2.

244. The method according to claim 241, wherein the mutation results in incorporation of shRNA into the HSC population that reduces expression of a gene expressing Ythdf2.

245. A method for reconstituting bone marrow in a subject in need thereof, comprising:

(a) isolating mesenchymal stem cells (MSCs) from a biological sample comprising a population of MSCs, by contacting the biological sample with one or more N-cadherin antibodies; and

(b) administering the isolated MSCs to the subject.

246. The method according to claim 245, further comprising introducing, into the biological sample containing the MSC population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and culturing the sample in a suitable culture media for a period of time sufficient to expand the number of MSCs in the sample to a number sufficient to transplant into the subject;

247. The method according to claim 245, wherein the MSCs are obtained from a biological sample comprising a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

248. A method for treating a subject in need of a transplant, selected from the group consisting of a bone marrow transplant, a peripheral blood transplant and an umbilical cord blood transplant comprising administering to the subject a population of isolated MSCs obtained by the method of claim 209.

249. The method according to claim 248, wherein the sample is from an autologous or allogeneic source.

250. The method according to claim 249, wherein the sample is from an autologous source.

251. A method for expanding a population of chimeric antigen receptor (CAR) T-cells prepared by modifying T-cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the population of CAR T-cells, to expand the number of CAR-T cells.

252. The method according to claim 251, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the CAR-T cells that results in modulation of a molecule in the m^6A mRNA modification pathway or contacting the CAR T-cell with a modulator of a molecule in the m^6A mRNA

modification pathway selected from the group consisting of a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

253. The method according to claim 252, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the CAR T-cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

254. The method according to claim 253, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, and a m^6A mRNA eraser.

255. The method according to claim 254, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader.

256. The method according to claim 255, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

257. The method according to claim 256, wherein the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2.

258. The method according to claim 254, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser.

259. The method according to claim 258, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser selected from the group consisting of FTO and ALKBH5.

260. The method according to claim 254, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer.

261. The method according to claim 260, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP and KIAA1429.

262. The method according to claim 253, wherein modulating the m^6A mRNA modification pathway comprises exposing the CAR T-cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway.

263. The method according to claim 253, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation that incorporates

shRNA into the CAR-T cells to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

264. The method according to claim 263, wherein the shRNA is introduced by exposing the CAR T-cells to a lentivirus to deliver the shRNA.

265. The method according to claim 251, wherein modulating the m^6A mRNA modification pathway comprises down-regulating a m^6A mRNA modification reader.

266. The method according to claim 265, wherein the m^6A mRNA modification reader is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

267. The method according to claim 266, wherein the m^6A mRNA modification reader comprises Ythdf2.

268. The method according to claim 265, wherein down-regulating the m^6A mRNA modification reader comprises contacting the CAR T-cells with an inhibitor of the m^6A mRNA modification reader selected from the group consisting of selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-

miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e; (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-

miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p; (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p (MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262; (inhibitors of Ythdf3) hsa-miR-

582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583, hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-

miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296: (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t,

hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262.

269. The method according to claim 251, wherein the expansion of the CAR T-cells is by a factor of at least 2 fold.

270. The method according to claim 269, wherein the expansion of the CAR T-cells is by a factor of at least 4 fold.

271. The method according to claim 270, wherein the expansion of the CAR T-cells is by a factor of at least 5 fold.

272. The method according to claim 271, wherein the expansion of the CAR T-cells is by a factor of at least 8 fold.

273. The method according to claim 272, wherein the expansion of the CAR T-cells is by a factor of at least 10 fold.

274. A method for ex vivo expansion of a chimeric antigen receptor (CAR) T-cell population comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the CAR T-cell population to expand the number of CAR T-cells.

275. A method for ex vivo expansion of a chimeric antigen receptor (CAR) T-cell population prepared by modifying T-cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood, and bone marrow, the method comprising modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the CAR T-cell population to expand the CAR T-cell population to a sufficient quantity which is sufficient for subsequent transplantation into a subject in need thereof.

276. The method according to claim 275, wherein the subject is a human.

277. The method according to claim 275, wherein the subject is suffering from cancer.

278. The method according to claim 275, wherein the subject is suffering from a blood cancer selected from the group consisting of leukemia and lymphoma.

279. The method according to any of claims 274 or 275, wherein:

modulating the m^6A mRNA modification pathway comprises introducing a mutation into the CAR T-cells that results in modulation of a molecule in the m^6A mRNA modification pathway or contacting the CAR T-cell with a modulator of a molecule in the m^6A mRNA modification pathway selected from the group consisting of a small molecule, a biologic, an antisense RNA, a small interfering RNA (siRNA), and combinations thereof.

280. The method according to claim 279, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation into the CAR T-cells to delete, replace, or reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

281. The method according to claim 280, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a molecule selected from the group consisting of a m^6A mRNA modification reader, a m^6A mRNA modification writer, and a m^6A mRNA eraser.

282. The method according to claim 281, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader.

283. The method according to claim 282, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification reader selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

284. The method according to claim 283, wherein the mutation deletes, replaces or reduces expression of a gene that expresses Ythdf2.

285. The method according to claim 280, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser.

286. The method according to claim 285, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification eraser selected from the group consisting of FTO and ALKBH5.

287. The method according to claim 280, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer.

288. The method according to claim 280, wherein the mutation deletes, replaces or reduces expression of a gene that expresses a m^6A mRNA modification writer selected from the group consisting of METTL3, METTL14, WTAP and KIAA1429.

289. The method according to claim 279, wherein modulating the m^6A mRNA modification pathway comprises exposing the CAR T-cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a molecule in the m^6A mRNA modification pathway.

290. The method according to claim 279, wherein modulating the m^6A mRNA modification pathway comprises introducing a mutation that incorporates shRNA into the CAR-T cells to reduce expression of a gene that expresses a molecule in the m^6A mRNA modification pathway.

291. The method according to claim 290, wherein the shRNA is introduced by exposing the CAR-T cells to a lentivirus to deliver the shRNA.

292. The method according to claim 275, wherein modulating the m^6A mRNA modification pathway comprises down-regulating a m^6A mRNA modification reader.

293. The method according to claim 292, wherein the m^6A mRNA modification reader is selected from the group consisting of Ythdf1, Ythdf2, Ythdf3, Ythdc1, Ythdc2, HNRNPC, HNRNPA2B1, and eIF3.

294. The method according to claim 293, wherein the m^6A mRNA modification reader comprises Ythdf2.

295. The method according to claim 292, wherein down-regulating the m^6A mRNA modification reader comprises contacting the stem cells with an inhibitor of the m^6A mRNA modification reader selected from the group consisting of: (inhibitors of HNRNPC) hsa-let-7e-5p (MIRT051596), hsa-mir-455-3p (MIRT037890), hsa-mir-30c-5p (MIRT047904), hsa-mir-186-5p (MIRT045150), hsa-mir-744-5p (MIRT037494), hsa-mir-18a-3p (MIRT040851), hsa-mir-484 (MIRT042196), hsa-mir-505-5p (MIRT037959), hsa-mir-615-3p (MIRT039991), hsa-mir-342-3p (MIRT043694), hsa-miR-3607-3p, hsa-miR-30d, hsa-miR-3916, hsa-miR-3162-5p, hsa-miR-1273d, hsa-miR-3161, hsa-miR-30a, hsa-miR-629, hsa-miR-208b, hsa-miR-489, hsa-miR-3148, hsa-miR-2113, hsa-miR-877, hsa-miR-455-5p, hsa-miR-186, hsa-miR-548o, hsa-miR-3139, hsa-miR-320a, hsa-miR-4311, hsa-miR-555, hsa-miR-3605-5p, hsa-miR-515-5p, hsa-miR-144, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-548x, hsa-miR-299-5p, hsa-miR-653, hsa-miR-576-5p, hsa-miR-548p, hsa-miR-586, hsa-miR-888, hsa-miR-3647-3p, hsa-miR-484, hsa-miR-320b, hsa-miR-620, hsa-miR-30b, hsa-miR-548q, hsa-miR-29b-1, hsa-miR-570, hsa-miR-183, hsa-miR-1276, hsa-miR-208a, hsa-miR-186, hsa-miR-28-5p, hsa-miR-330-3p, hsa-miR-548am, hsa-miR-320d, hsa-miR-3175, hsa-miR-3155, hsa-miR-548aa, hsa-miR-519e, hsa-miR-1270, hsa-miR-513b, hsa-miR-599, hsa-miR-518f, hsa-miR-4301, hsa-miR-30c, hsa-miR-3135, hsa-miR-4286, hsa-miR-202, hsa-miR-4263, hsa-miR-4299, hsa-miR-606, hsa-miR-3133, hsa-miR-583, hsa-miR-3125, hsa-miR-501-5p, hsa-miR-7-1, hsa-miR-514b-3p, hsa-miR-3155b, hsa-miR-548d-3p, hsa-miR-224, hsa-miR-7-2, hsa-miR-708, hsa-miR-3199, hsa-miR-514, hsa-miR-30e; (inhibitors of HNRNPA2B1) hsa-mir-92a-3p (MIRT049721), hsa-mir-30c-5p (MIRT048009), hsa-mir-191-5p (MIRT045809), hsa-let-7f-5p (MIRT051404), hsa-mir-27b-3p (MIRT046213), hsa-mir-877-3p (MIRT037116), hsa-mir-615-3p (MIRT040278), hsa-

mir-1260b (MIRT052680), hsa-mir-103a-3p (MIRT027027), hsa-mir-16-5p (MIRT031508), hsa-mir-1296-5p (MIRT036075), hsa-mir-197-3p (MIRT048098), hsa-miR-548j, hsa-miR-3678-3p, hsa-miR-607, hsa-miR-188-5p, hsa-miR-15a, hsa-miR-3653, hsa-miR-371-5p, hsa-miR-550a, hsa-miR-3622b-3p, hsa-miR-548a-5p, hsa-miR-3170, hsa-miR-3148, hsa-miR-556-3p, hsa-miR-490-3p, hsa-miR-559, hsa-miR-200c, hsa-miR-130a, hsa-miR-548y, hsa-miR-548o, hsa-miR-23c, hsa-miR-491-3p, hsa-miR-335, hsa-miR-3667-3p, hsa-miR-466, hsa-miR-23b, hsa-miR-4310, hsa-miR-127-5p, hsa-miR-548b-5p, hsa-miR-616, hsa-miR-16, hsa-miR-338-3p, hsa-miR-3200-5p, hsa-miR-362-3p, hsa-miR-448, hsa-miR-1306, hsa-miR-944, hsa-miR-3684, hsa-miR-373, hsa-miR-103a, hsa-miR-380, hsa-miR-499-5p, hsa-miR-1323, hsa-miR-323-5p, hsa-miR-3674, hsa-miR-1252, hsa-miR-33b, hsa-miR-580, hsa-miR-548c-3p, hsa-miR-103a-2, hsa-miR-548w, hsa-miR-600, hsa-miR-634, hsa-miR-586, hsa-miR-497, hsa-miR-720, hsa-miR-654-3p, hsa-miR-524-5p, hsa-miR-543, hsa-miR-548q, hsa-let-7f-2, hsa-miR-330-5p, hsa-miR-500a, hsa-miR-548l, hsa-miR-570, hsa-miR-374a, hsa-miR-1184, hsa-miR-649, hsa-miR-424, hsa-miR-3658, hsa-miR-186, hsa-miR-326, hsa-miR-548d-5p, hsa-miR-23a, hsa-miR-15b, hsa-miR-190, hsa-miR-203, hsa-miR-548h, hsa-miR-3136-5p, hsa-miR-618, hsa-miR-551b, hsa-miR-211, hsa-miR-1305, hsa-miR-513b, hsa-miR-96, hsa-miR-2117, hsa-miR-548n, hsa-miR-3910, hsa-miR-217, hsa-miR-892b, hsa-miR-502-5p, hsa-miR-548i, hsa-miR-520d-5p, hsa-miR-4299, hsa-miR-1285, hsa-miR-3133, hsa-miR-483-3p; (inhibitors of Ythdf1) hsa-miR-548g, hsa-miR-204, hsa-miR-3143, hsa-miR-521, hsa-miR-195, hsa-miR-3182, hsa-miR-3941, hsa-miR-34c-3p, hsa-miR-767-3p, hsa-miR-563, hsa-miR-548c-5p, hsa-miR-1911, hsa-miR-26b, hsa-miR-190b, hsa-miR-33a, hsa-miR-329, hsa-miR-221, hsa-miR-612, hsa-miR-3185, hsa-miR-3156-5p, hsa-miR-107, hsa-miR-664, hsa-miR-3657; (inhibitors of Ythdf2) hsa-mir-615-3p

(MIRT040054), hsa-mir-106b-5p (MIRT044257), hsa-mir-1 (MIRT023842), miR-145, hsa-miR-3607-3p, hsa-miR-200a, hsa-miR-301a, hsa-miR-519a, hsa-miR-141, hsa-miR-130b, hsa-miR-181b, hsa-miR-301b, hsa-miR-3117-3p, hsa-miR-1236, hsa-miR-181a, hsa-miR-519c-3p, hsa-miR-551b, hsa-miR-519e, hsa-miR-519b-3p, hsa-miR-19b, hsa-miR-1303, hsa-miR-608, hsa-miR-145, hsa-miR-130a, hsa-miR-181c, hsa-miR-323b-3p, hsa-miR-421, hsa-miR-515-5p, hsa-miR-3666, hsa-miR-181d, hsa-miR-146a, hsa-miR-4295, hsa-miR-454, hsa-miR-3919, hsa-miR-19a, hsa-miR-543, hsa-miR-4262; (inhibitors of Ythdf3) hsa-miR-582-3p, hsa-miR-579, hsa-miR-520e, hsa-miR-520f, hsa-miR-3152-3p, hsa-miR-106a, hsa-miR-30d, hsa-miR-30a, hsa-miR-93, hsa-miR-508-5p, hsa-miR-29a, hsa-miR-3148, hsa-miR-490-5p, hsa-miR-520b, hsa-miR-20a, hsa-miR-409-3p, hsa-miR-4255, hsa-let-7i, hsa-miR-373, hsa-let-7e, hsa-miR-520c-3p, hsa-miR-3920, hsa-miR-127-5p, hsa-miR-380, hsa-miR-616, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-let-7c, hsa-miR-340, hsa-miR-373, hsa-miR-520a-3p, hsa-miR-144, hsa-miR-1265, hsa-miR-548x, hsa-miR-362-5p, hsa-miR-33b, hsa-miR-26b, hsa-miR-17, hsa-miR-569, hsa-miR-3618, hsa-miR-576-5p, hsa-miR-922, hsa-miR-302a, hsa-miR-106b, hsa-miR-888, hsa-miR-484, hsa-let-7b, hsa-miR-582-5p, hsa-let-7f, hsa-miR-30b, hsa-miR-524-5p, hsa-miR-302d, hsa-let-7d, hsa-miR-513a-5p, hsa-miR-500a, hsa-miR-570, hsa-miR-548l, hsa-miR-105, hsa-miR-374c, hsa-let-7g hsa-miR-372, hsa-miR-3658, hsa-let-7a, hsa-miR-3908, hsa-miR-302b, hsa-miR-526b, hsa-miR-190, hsa-miR-181b, hsa-miR-433, hsa-miR-98, hsa-miR-3606, hsa-miR-595, hsa-miR-548am, hsa-miR-187, hsa-miR-561, hsa-miR-181a, hsa-miR-3155, hsa-miR-655, hsa-miR-302c, hsa-miR-195, hsa-miR-26a, hsa-miR-590-3p, hsa-miR-30c, hsa-miR-502-5p, hsa-miR-495, hsa-miR-137, hsa-miR-181c, hsa-miR-520d-5p, hsa-miR-3942-5p, hsa-miR-202, hsa-miR-302e, hsa-miR-513c, hsa-miR-885-5p, hsa-miR-520a-5p, hsa-miR-583,

hsa-miR-1297, hsa-miR-7-1, hsa-miR-520d-3p, hsa-miR-3155b, hsa-miR-3182, hsa-miR-519d, hsa-miR-550a, hsa-miR-7-2, hsa-miR-181d, hsa-miR-190b, hsa-miR-1912, hsa-miR-151-3p, hsa-miR-33a, hsa-miR-525-5p, hsa-miR-20b, hsa-miR-514b-5p, hsa-miR-30e, hsa-miR-4262, hsa-miR-636; (inhibitor of eIF3) hsa-mir-92b-3p (MIRT040734), hsa-mir-16-5p (MIRT031705), hsa-mir-18a-3p (MIRT040974), hsa-mir-155-5p (MIRT020771), hsa-mir-484 (MIRT042324), hsa-let-7c-5p (MIRT051776), hsa-miR-3910, hsa-miR-148b, hsa-miR-136, hsa-miR-15a, hsa-miR-488, hsa-miR-500a, hsa-miR-1297, hsa-miR-3159, hsa-miR-374c, hsa-miR-424, hsa-miR-7-1, hsa-miR-186, hsa-miR-195, hsa-miR-15b, hsa-miR-26b, hsa-miR-505, hsa-miR-1206, hsa-miR-653, hsa-miR-1283, hsa-miR-7-2, hsa-miR-196a, hsa-miR-497, hsa-miR-33a, hsa-miR-655, hsa-miR-26a hsa-miR-16, hsa-mir-151a-3p (MIRT043600), hsa-mir-92a-3p (MIRT049064), hsa-mir-615-3p (MIRT039779), hsa-mir-877-3p (MIRT036964), hsa-mir-222-3p (MIRT046746), hsa-mir-423-3p (MIRT042468), hsa-mir-324-3p (MIRT042887), hsa-mir-124-3p (MIRT022932), hsa-miR-3140-3p, hsa-miR-124, hsa-miR-198, hsa-miR-525-5p, hsa-miR-506, hsa-miR-520a-5p, hsa-miR-196a* hsa-miR-3117-3p, hsa-mir-342-5p (MIRT038210), hsa-mir-378a-5p (MIRT043981), hsa-mir-615-3p (MIRT040086), hsa-let-7b-5p (MIRT052211), hsa-mir-455-3p (MIRT037879), hsa-miR-4267, hsa-miR-590-3p, hsa-mir-106b-5p (MIRT044355), hsa-mir-320a (MIRT044466), hsa-mir-16-5p (MIRT032018), hsa-mir-155-5p (MIRT021009), hsa-miR-4302, hsa-mir-191-5p (MIRT045793), hsa-mir-1303 (MIRT035890), hsa-mir-193b-3p (MIRT016316), hsa-mir-222-3p (MIRT046640), hsa-mir-532-3p (MIRT037924), hsa-mir-18a-3p (MIRT040929), hsa-mir-92a-3p (MIRT049001), hsa-miR-582-3p, hsa-miR-4265, hsa-miR-218-2, hsa-miR-1271, hsa-miR-340, hsa-miR-221, hsa-miR-20b, hsa-miR-508-3p, hsa-miR-141, hsa-miR-4325, hsa-miR-889, hsa-miR-29a, hsa-miR-129-3p, hsa-

miR-129, hsa-miR-96, hsa-miR-3163, hsa-miR-187, hsa-miR-196a, hsa-miR-222, hsa-miR-1179, hsa-miR-182, hsa-miR-9* hsa-miR-32, hsa-miR-143, hsa-miR-4296: (inhibitors of YTHDC1) hsa-mir-20a-3p (MIRT038967), hsa-mir-103a-3p (MIRT027037), hsa-mir-1 (MIRT023492), hsa-mir-19b-3p (MIRT031105), hsa-mir-100-5p (MIRT048400), hsa-mir-93-5p (MIRT027989), hsa-mir-16-5p (MIRT031379), hsa-let-7b-5p (MIRT052150), hsa-miR-520f, hsa-miR-300, hsa-miR-15a, hsa-miR-200a, hsa-miR-605, hsa-miR-30d, hsa-miR-30a, hsa-miR-3613-3p, hsa-miR-509-3-5p, hsa-miR-34c-5p, hsa-miR-324-3p, hsa-miR-1248, hsa-miR-152, hsa-miR-548t, hsa-miR-4310, hsa-miR-145, hsa-miR-516a-3p, hsa-miR-16, hsa-miR-3668, hsa-miR-4277, hsa-miR-448, hsa-miR-16-2, hsa-miR-148b, hsa-miR-509-5p, hsa-miR-103a, hsa-miR-1265, hsa-miR-2115, hsa-miR-548c-3p, hsa-miR-148a, hsa-miR-548p, hsa-miR-513a-3p, hsa-miR-497, hsa-miR-3647-3p, hsa-miR-382, hsa-miR-30b, hsa-miR-543, hsa-let-7f-2, hsa-miR-1269, hsa-miR-3164, hsa-miR-503, hsa-miR-500a, hsa-miR-449a, hsa-miR-141, hsa-miR-424, hsa-miR-3908, hsa-miR-889, hsa-miR-2116, hsa-miR-330-3p, hsa-miR-15b, hsa-miR-181b, hsa-miR-187, hsa-miR-1237, hsa-miR-449b, hsa-miR-101, hsa-miR-381, hsa-miR-618, hsa-miR-222, hsa-miR-181a, hsa-miR-432, hsa-miR-96, hsa-miR-19b, hsa-miR-195, hsa-miR-548n, hsa-miR-485-5p, hsa-miR-217, hsa-miR-30c, hsa-miR-495, hsa-miR-137, hsa-miR-1288, hsa-miR-181c, hsa-miR-3942-5p, hsa-miR-548v, hsa-miR-487a, hsa-miR-221, hsa-miR-891b, hsa-miR-205, hsa-miR-195, hsa-miR-4271, hsa-miR-3611, hsa-miR-516b, hsa-miR-181d, hsa-miR-154, hsa-miR-646, hsa-miR-153, hsa-miR-34a, hsa-miR-19a, hsa-miR-107, hsa-miR-30e and hsa-miR-4262.

296. The method according to claim 274, wherein the CAR T-cell is prepared by modifying a T-cell obtained from mammalian tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

297. The method according to claim 279, wherein the expansion of the number of CAR T-cells is by a factor selected from the group consisting of at least 2-fold, at least 4-fold, at least 5-fold, at least 8-fold and at least 10-fold.

298. An expanded CAR T-cell population made by the process according to claim 274.

299. An expanded CAR T-cell population made by the process according to claim 275.

291. A method for ex vivo expansion of chimeric antigen receptor (CAR) T-cells, the expanded CAR T-cells being competent to treat a cancer and/or blood disorder upon transplantation into a mammal in need thereof, the method comprising introducing a mutation into the CAR T-cells that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader and culturing the population of CAR T-cells in a suitable culture medium.

292. The method according to claim 291, wherein the CAR T-cells are obtained by modifying T-cells from a mammalian tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

293. The method according to claim 291, wherein the mammal is a human.

294. The method according to claim 291, wherein the mammal is suffering from cancer.

295. The method according to claim 294, wherein the cancer comprises a blood cancer selected from the group consisting of leukemia and lymphoma.

296. The method according to claim 291, wherein the mutation deletes, replaces or reduces expression of a gene expressing Ythdf2.

297. The method according to claim 291, wherein the mutation is introduced by exposing the CAR T-cells to a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader.

298. The method according to claim 296, wherein the mutation incorporates shRNA into the stem cells to reduce expression of a gene that expresses a m^6A mRNA modification reader.

299. The method according to claim 291, wherein the expansion of the number of CAR T-cells is by a factor selected from the group consisting of at least 2-fold, at least 4-fold, at least 5-fold, at least 8-fold and at least 10-fold.

300. A kit for expanding a chimeric antigen receptor (CAR) T-cell (HSC) population for subsequent transplantation into a subject in need thereof, the kit

comprising a system for introducing a mutation into the CAR T-cell population that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader, and instructions for use thereof.

301. The kit according to claim 300, wherein the system for introducing a mutation into the CAR T-cell population includes one or more reagents capable of introducing a mutation into the CAR T-cell population that results in deletion, replacement or reduced expression of a gene expressing Ythdf2.

302. The kit according to claim 301, wherein the system for introducing a mutation into the CAR T-cell population comprises a Mx1-Cre targeting system that inactivates or deletes at least a portion of a gene that expresses a m^6A mRNA modification reader.

303. The kit according to claim 301, wherein the system for introducing a mutation into the CAR T-cell population comprises reagents for delivering a lentivirus that incorporates shRNA into the CAR T-cell population to reduce expression of a gene that expresses a m^6A mRNA modification reader.

304. A kit for expanding chimeric antigen receptor (CAR) T-cell population for subsequent transplantation into a subject in need thereof, the kit comprising an inhibitor of a m^6A mRNA modification reader, and instructions for use thereof.

305. A method for administering chimeric antigen receptor (CAR) T-cell to a subject in need thereof, the method comprising:

(a) introducing, into a sample containing CAR T-cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader,

(b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject; and

(c) administering the CAR T-cells to the subject.

306. The method according to claim 305, wherein the CAR T-cells are obtained by modifying T-cells obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

307. The method according to claim 305, wherein the mutation results in deletion a gene expressing Ythdf2.

308. The method according to claim 305, wherein the mutation results in incorporation of shRNA into the CAR T-cell population that reduces expression of a gene expressing Ythdf2.

309. A method for administering a CAR T-cell to a subject in need thereof, the method comprising:

(a) culturing, in a suitable culture media, a sample containing a CAR T-cell population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject;

(b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and

(c) administering the CAR T-cells to the subject.

310. The method according to claim 309, wherein the CAR T-cells are obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

311. The method according to claim 309, wherein the inhibitor of the m^6A mRNA modification reader inhibits Ythfd2.

312. The method according to claim 309, wherein the subject is a human.

313. A method for treating cancer and/or a blood disorder in a subject in need thereof, comprising:

(a) introducing, into a sample containing a CAR T-cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m^6A mRNA modification reader,

(b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject;

(c) administering the CAR T-cells to the subject.

314. The method according to claim 313, wherein the CAR T-cells are obtained by modifying T-cells obtained a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

315. The method according to claim 313 wherein the subject is suffering from cancer.

316. The method according to claim 315 wherein the subject is suffering from a blood cancer selected from the group consisting of leukemia and lymphoma.

371. A method for treating cancer and/or a blood disorder in a subject in need thereof, comprising:

(a) culturing, in a suitable culture media, a sample containing a CAR T-cell population in the presence of an inhibitor of a m^6A mRNA modification reader, for a period of time sufficient to expand the number of CAR T-cells in the sample to a number sufficient to transplant into the subject;

(b) removing from the culture the inhibitor of the m^6A mRNA modification reader; and

(c) administering the CAR T-cells to the subject.

372. The method according to claim 371, wherein the CAR T-cells are obtained by modifying T-cells obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

373. A method for expanding a population of chimeric antigen receptor (CAR) T-cells comprising culturing the population of CAR T-cells under conditions sufficient to result in an expansion of the CAR T-cell population by at least 2-fold, wherein the expanded population of CAR T-cells is suitable for transplantation into a mammal in need thereof.

374. The method according to claim 373, wherein the expansion of the CAR T-cell population is at least 4-fold.

375. The method according to claim 374, wherein the expansion of the CAR T-cell population is at least 5-fold.

376. The method according to claim 375, wherein the expansion of the CAR T-cell population is at least 8-fold.

377. The method according to claim 376, wherein the expansion of the CAR T-cell population is at least 10-fold.

378. The method according to claim 377, wherein the mammal is a human.

379. The method according to claim 378, wherein the human is suffering from cancer and/or a blood disorder.

380. A method for treating a subject suffering from cancer and/or a blood disorder, comprising administering to the subject a population of CAR T-cells obtained by the method of claim 373.

381. A method for expanding a population of chimeric antigen receptor (CAR) T-cells comprising:

(a) obtaining from a mammal a tissue sample comprising a T-cell population;

(b) modifying the T-cell population with chimeric antigen receptors to provide CAR T-cell population; and

(c) expanding, in vitro, the CAR T-cell population from the sample, wherein:

(i) the CAR T-cell population expands by at least 2-fold.

382. The method according to claim 381, wherein the expansion of the CAR T-cell population is at least 4-fold.

383. The method according to claim 382, wherein the expansion of the CAR T-cell population is at least 5-fold.

384. The method according to claim 383, wherein the expansion of the CAR T-cell population is at least 8-fold.

385. The method according to claim 384, wherein the expansion of the CAR T-cell population is at least 10-fold.

386. The method according to claim 381, wherein the mammal is a human.

387. The method according to claim 386, wherein the human is suffering from cancer and/or a blood disorder.

388. The method according to claim 387, wherein the tissue sample is obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

389. A method for treating a subject suffering from cancer and/or a blood disorder, the method comprising:

(a) obtaining from a mammal a tissue sample comprising a T-cell population;

(b) modifying the T-cell population with a chimeric antigen receptor (CAR) to form a CAR T-cell population

(c) expanding, in vitro, the CAR T-cell population from the sample, wherein:

(i) the CAR T-cell population expands by at least 2-fold; and

(d) transplanting the expanded CAR T-cell population into the subject.

390. The method according to claim 389, wherein the expansion of the HSC population is at least 4-fold.

391. The method according to claim 390, wherein the expansion of the HSC population is at least 5-fold.

392. The method according to claim 391, wherein the expansion of the HSC population is at least 8-fold.

393. The method according to claim 392, wherein the expansion of the HSC population is at least 10-fold.

394. The method according to claim 389, wherein the mammal is a human.

395. The method according to claim 394, wherein the human is suffering from at least one cancer selected from the group consisting of leukemia and lymphoma.

396. The method according to claim 394, wherein the tissue sample is obtained from a tissue selected from the group consisting of cord blood, peripheral blood, and bone marrow.

397. The method according to claim 396, wherein the sample is from an autologous or allogeneic source.

398. The method according to claim 397, wherein the sample is from an autologous source.

399. A method for expanding a chimeric antigen receptor (CAR) T-cell population in a mammal in need of such expansion comprising administering to the mammal a therapeutically effective amount of a modulator of a N^6-Methyladenosine

(m^6A) mRNA modification pathway for a period of time sufficient to expand the CAR T-cell population by at least 2-fold with CAR T-cells that possess the ability to treat cancer and/or a blood disorder in the mammal.

400. The method according to claim 399, wherein the modulator comprises a system for introducing a mutation into the CAR T-cell population the deletes, replaces, or reduces expression of a gene expressing a N^6-Methyladenosine (m^6A) mRNA modification reader.

401. The method according to claim 400, wherein the modulator comprises a system for introducing a mutation into the CAR T-cell population that deletes, replaces or reduces expression of a gene expressing Ythdf2.

402. The method according to claim 399, wherein the modulator comprising an inhibitor of a N^6-Methyladenosine (m^6A) mRNA modification reader.

403. The method according to claim 402, wherein the modulator comprises an inhibitor of Ythdf2.

404. The method according to claim 403, wherein the mammal is a human.

405. A method of treating a subject suffering from a blood disorder, the method comprising:

(a) obtaining a population of cells selected from the group consisting of stem cells and T-cells, from a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow;

(b) optionally, in a case where the population of cells comprises T-cells, modifying the T-cells with a chimeric antigen receptor (CAR) to provide CAR T-cells;

(c) expanding the population of cells by modulating a N^6-Methyladenosine (m^6A) mRNA modification pathway in the cells, to expand the number of cells; and

(d) transplanting the expanded cells to the subject to treat the blood disorder.

406. The method of claim 405, wherein the blood disorder comprises leukemia.

407. The method of claim 405, wherein the population of cells comprises cells selected from the group consisting of HSCs and MSCs.

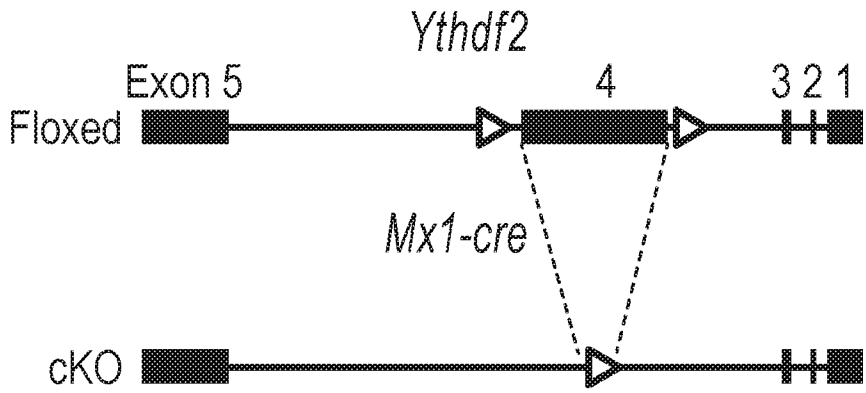


FIG. 1A

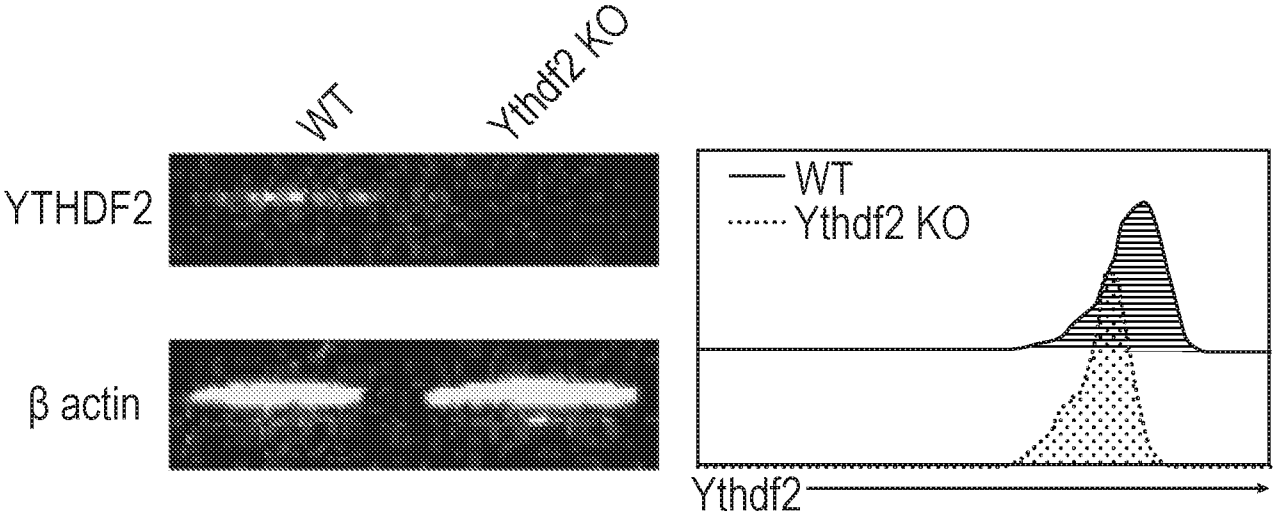

WT
Ythdf2 KO
YTHDF2
β actin
WT
Ythdf2 KO
Ythdf2

FIG. 1B

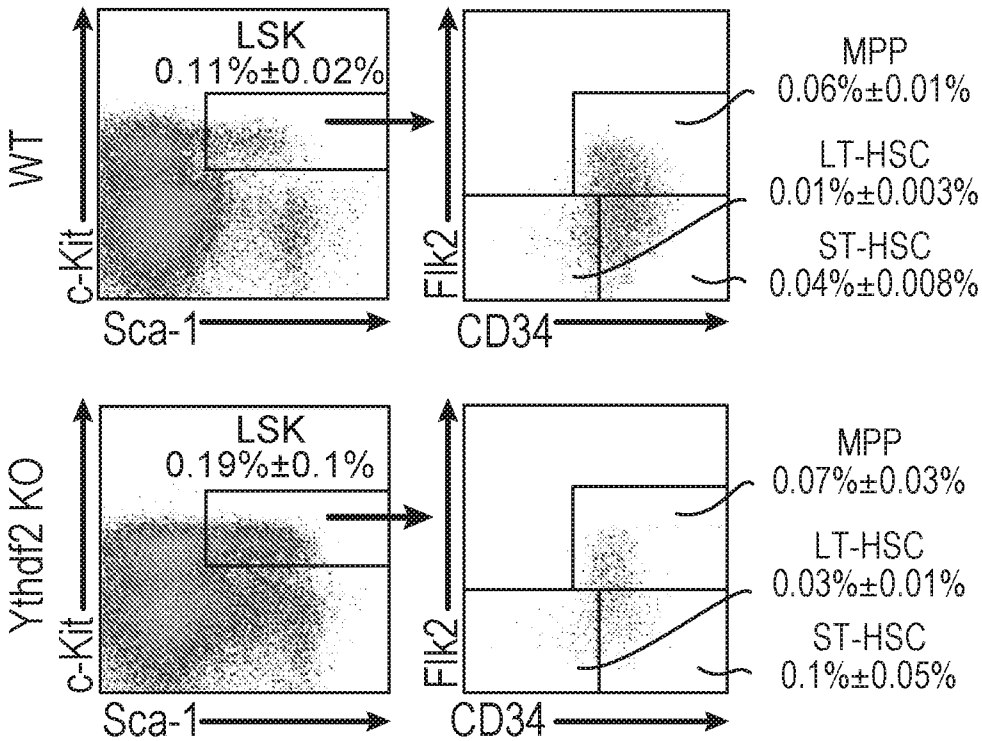

WT
c-Kit
Sca-1
LSK
0.11%±0.02%
Flk2
CD34
MPP
0.06%±0.01%
LT-HSC
0.01%±0.003%
ST-HSC
0.04%±0.008%
Ythdf2 KO
c-Kit
Sca-1
LSK
0.19%±0.1%
Flk2
CD34
MPP
0.07%±0.03%
LT-HSC
0.03%±0.01%
ST-HSC
0.1%±0.05%

FIG. 1C

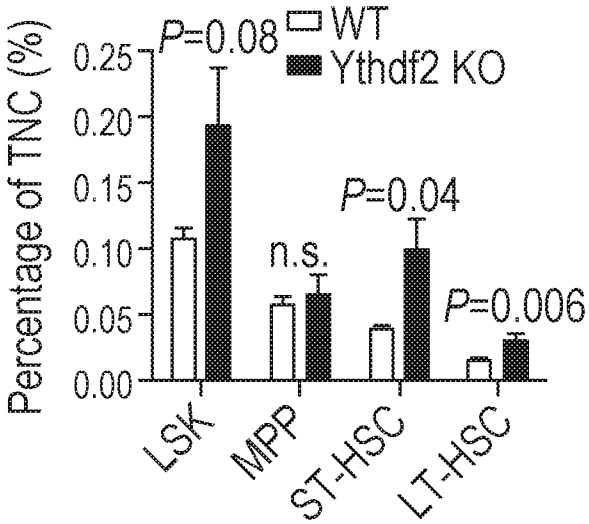


FIG. 1D

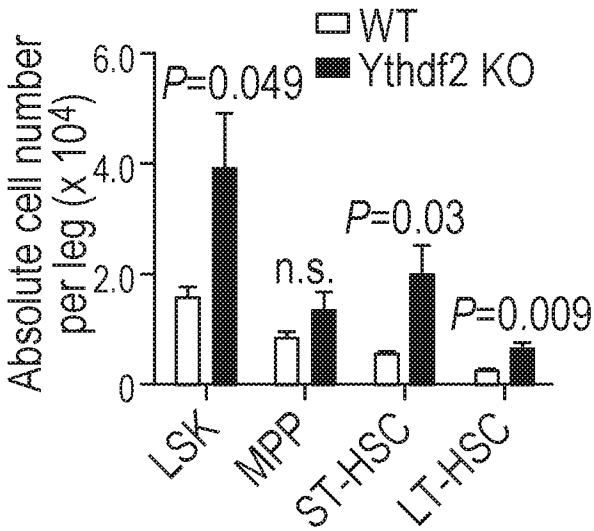


FIG. 1E

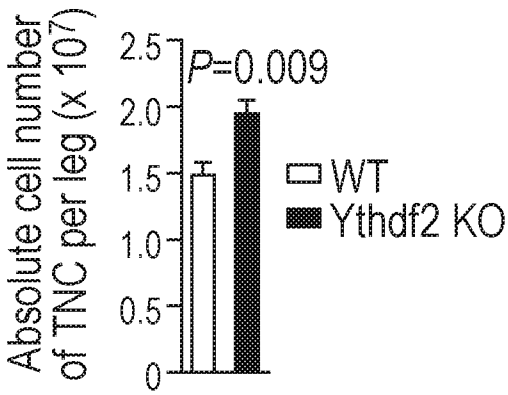


FIG. 1F

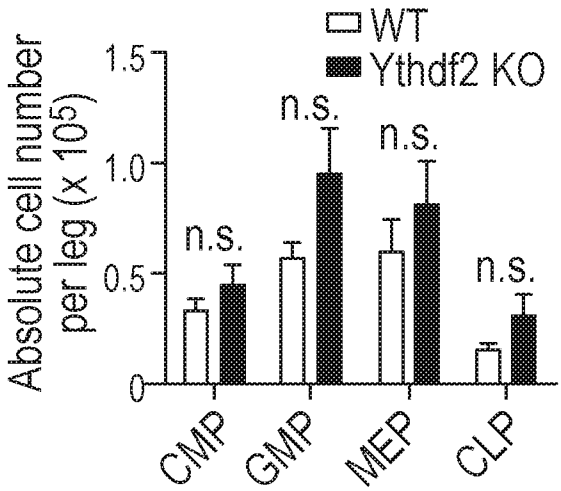


FIG. 1G

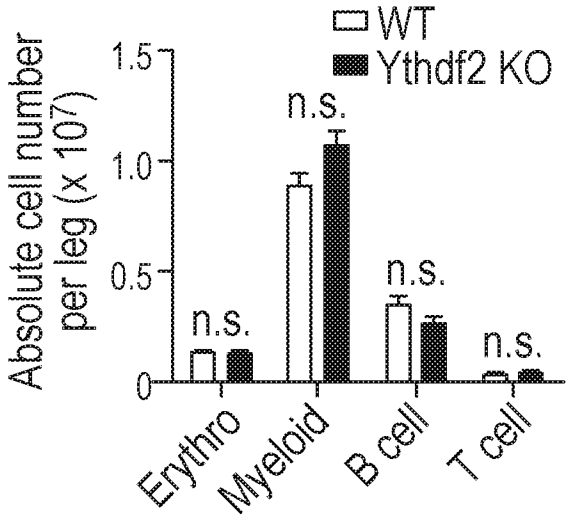


FIG. 1H

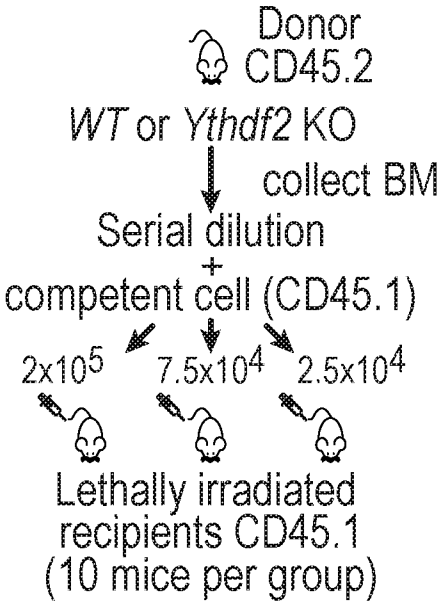


FIG. 2A

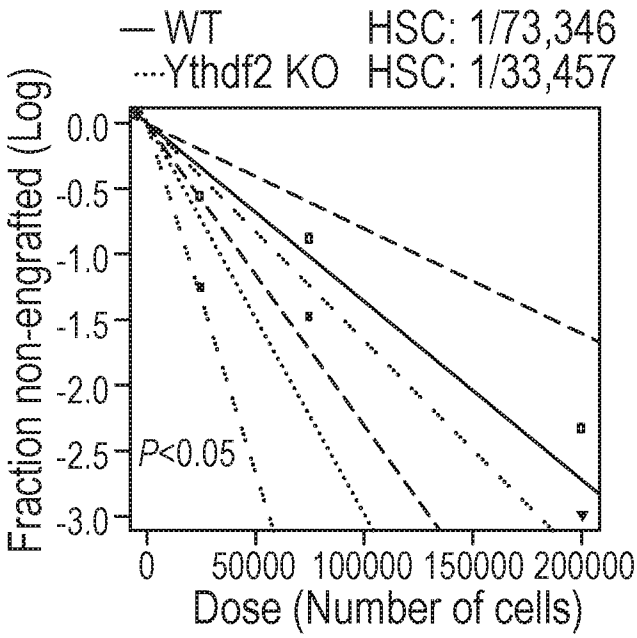


FIG. 2B

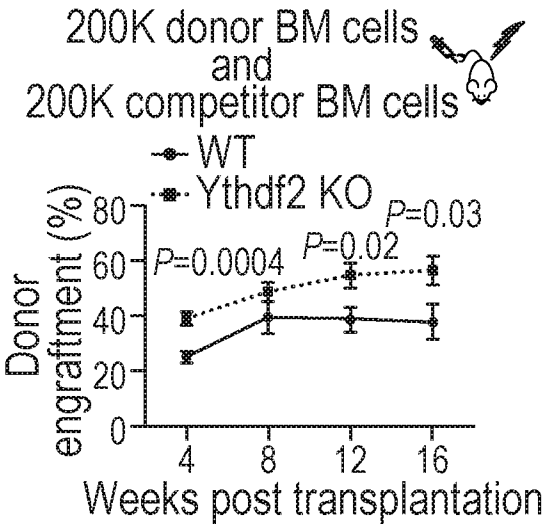


FIG. 2C

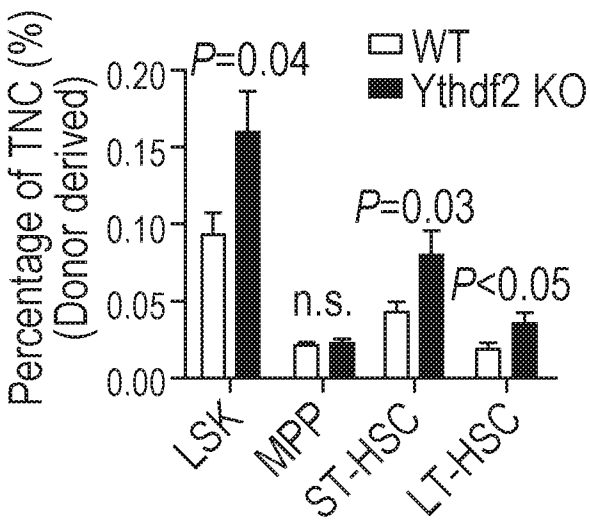


FIG. 2D

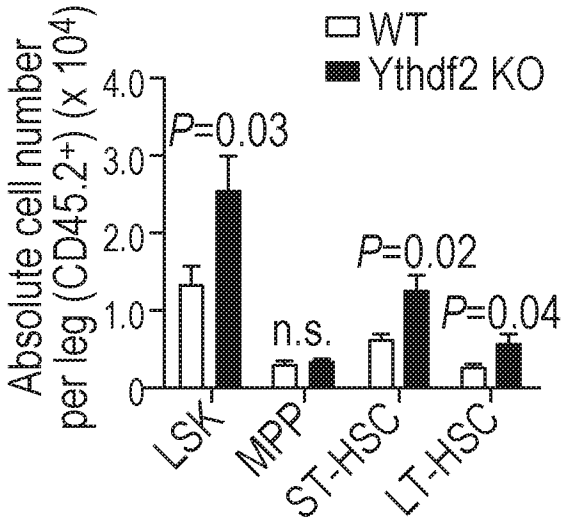


FIG. 2E

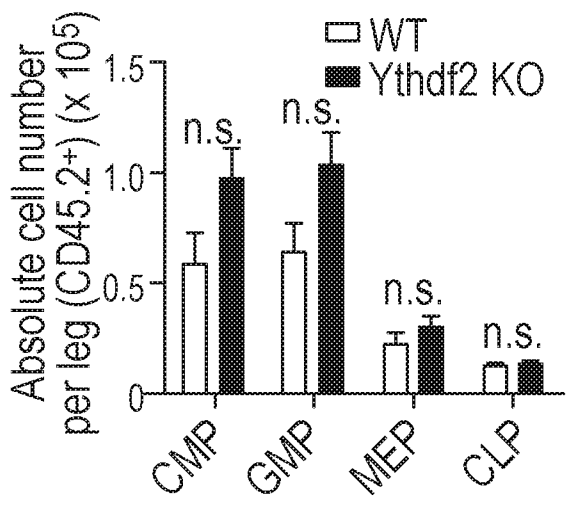


FIG. 2F

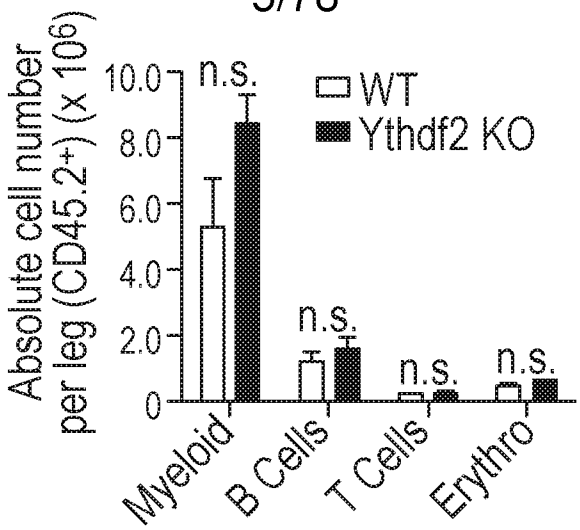


FIG. 2G

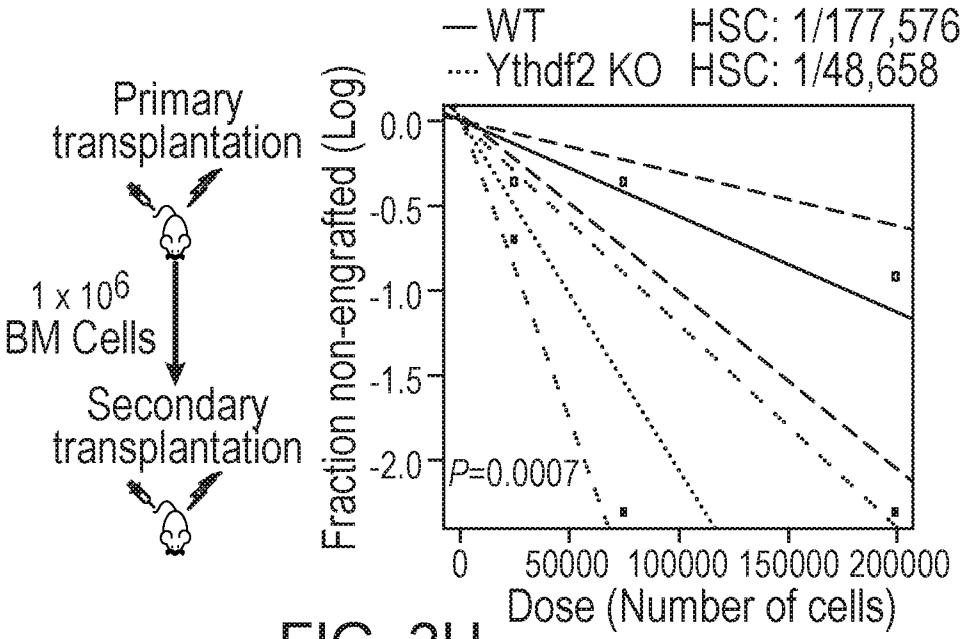


FIG. 2H

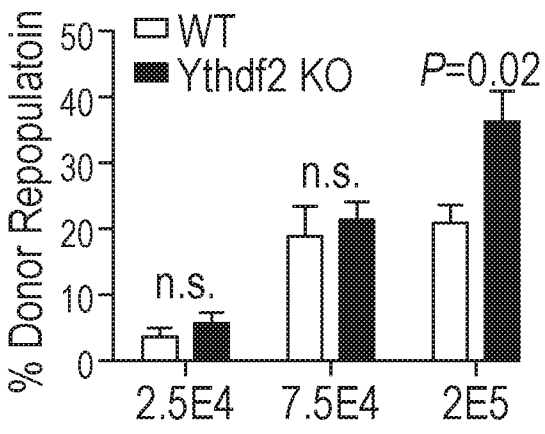


FIG. 2I

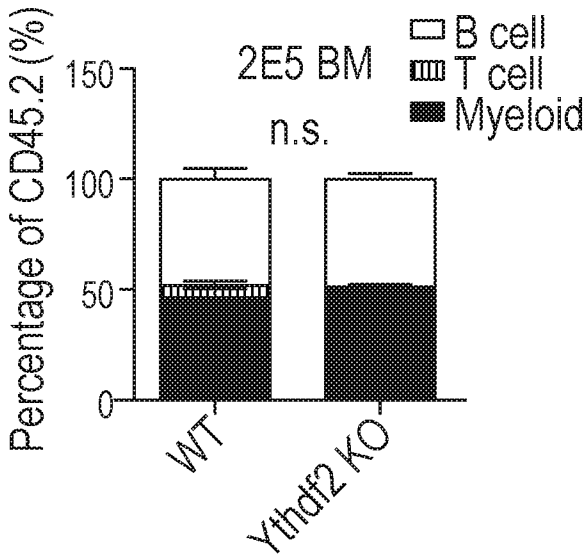


FIG. 2J

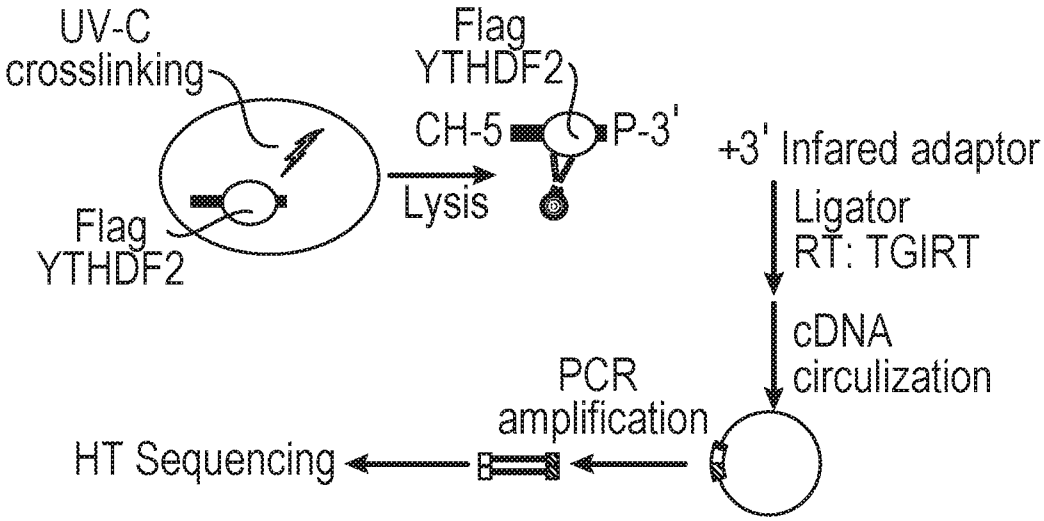


FIG. 3A

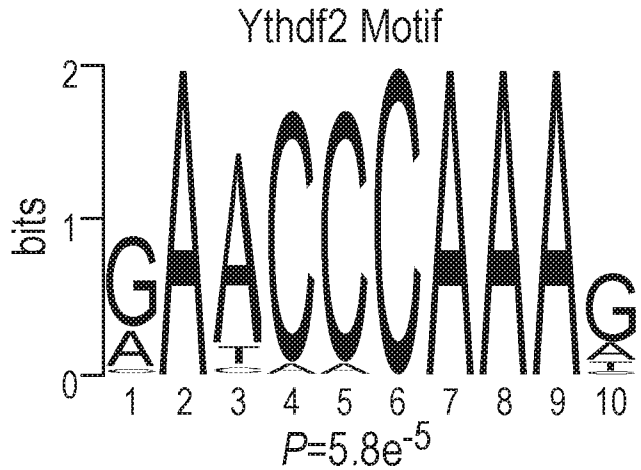


FIG. 3B

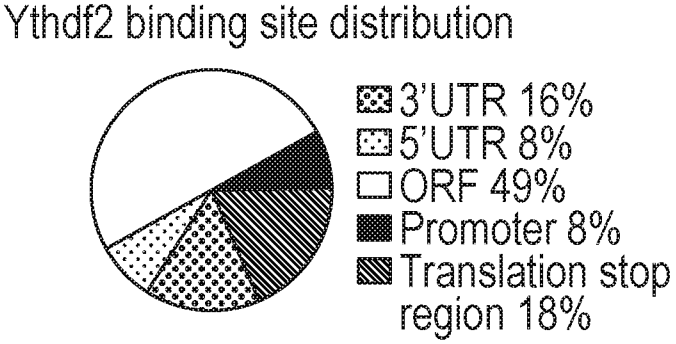


FIG. 3C

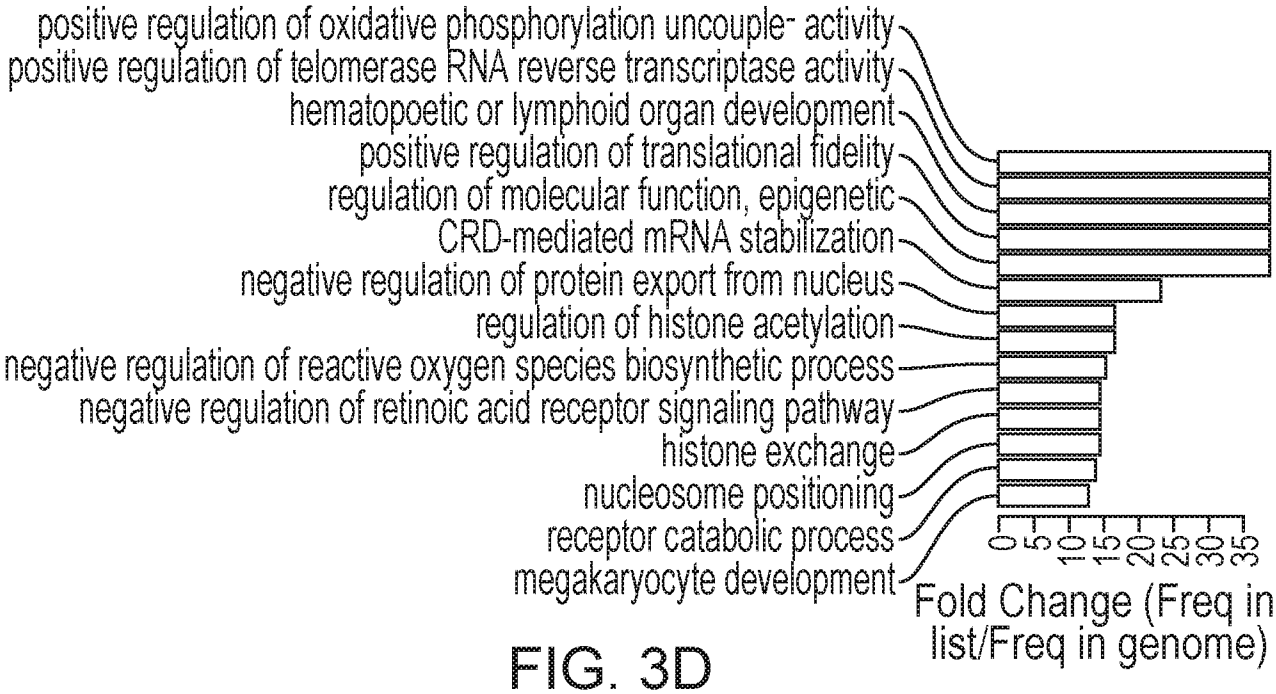


FIG. 3D

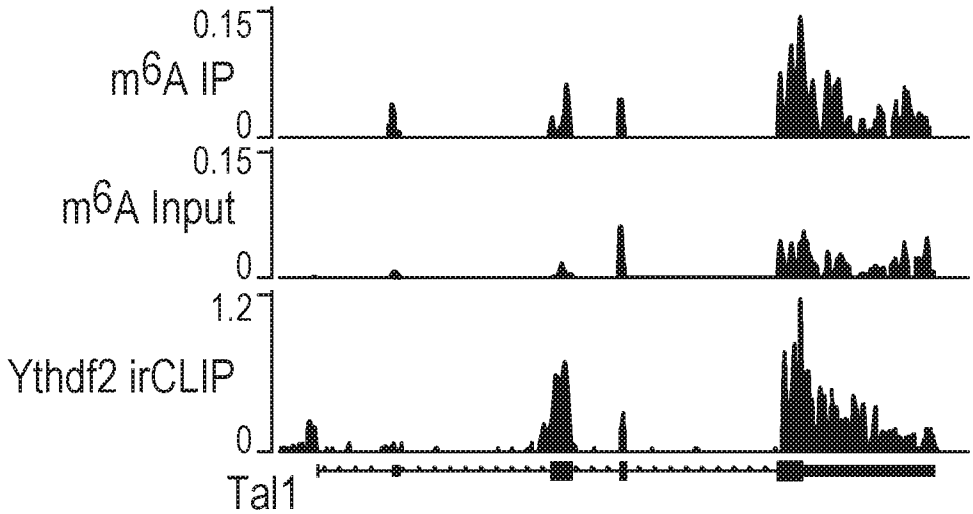


FIG. 3E

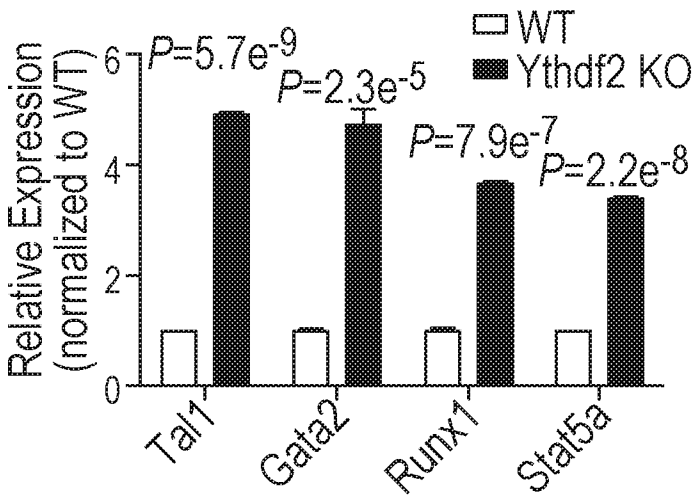


FIG. 3F

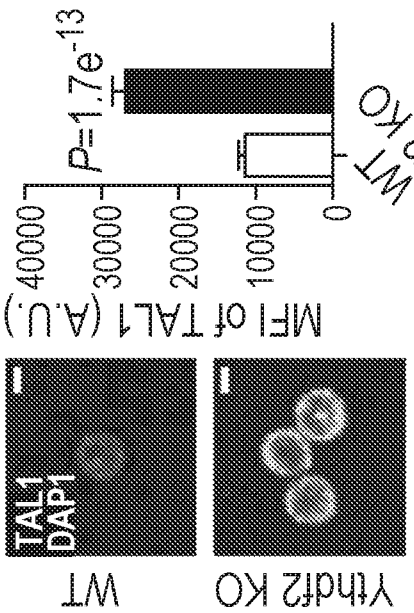

TAL1
DAP1
WT
Ythdf2 KO
MFI of TAL1 (A.U.)
40000
30000
20000
10000
0
P=1.7e-13
WT
Ythdf2 KO

FIG. 3G

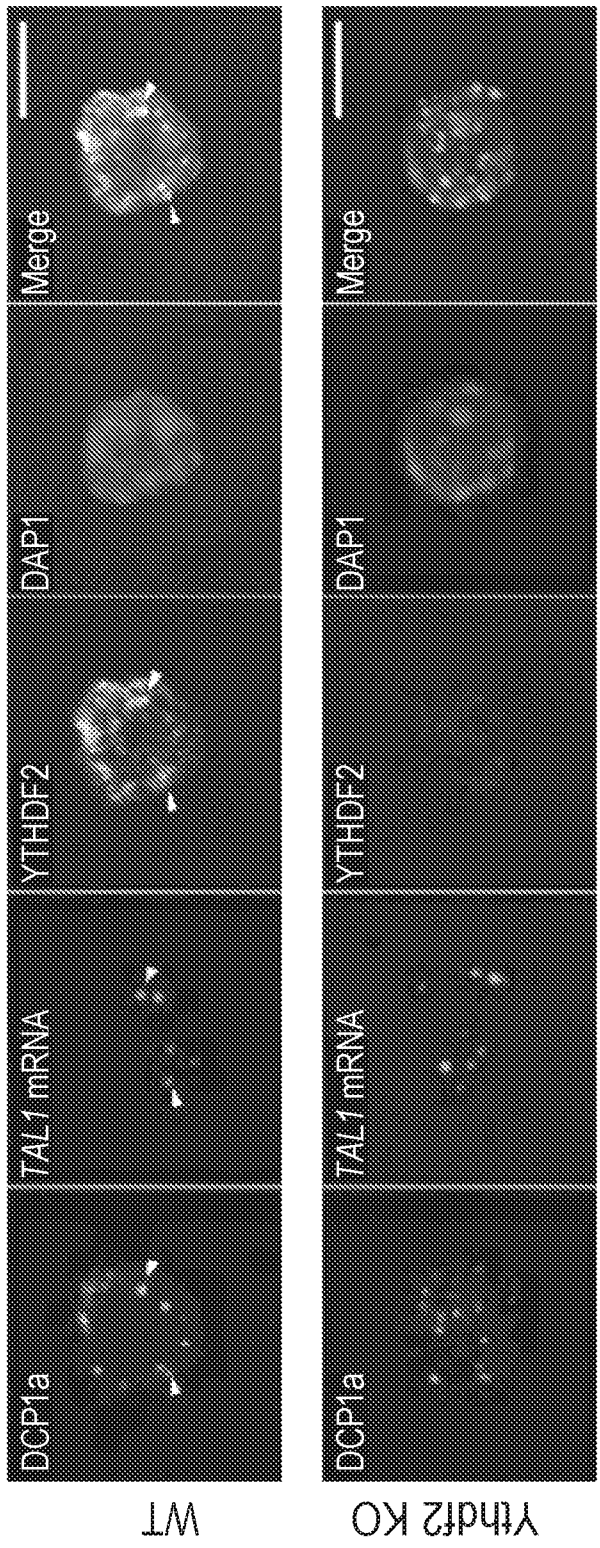

DCP1a
TAL1 mRNA
YTHDF2
DAP1
Merge
WT
Ythdf2 KO

FIG. 3H

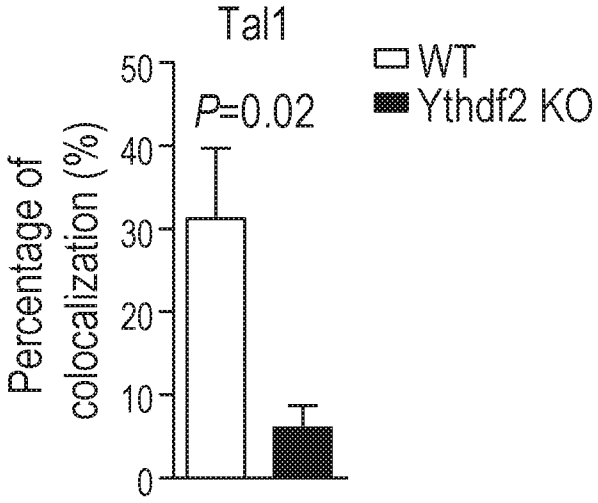


FIG. 3I

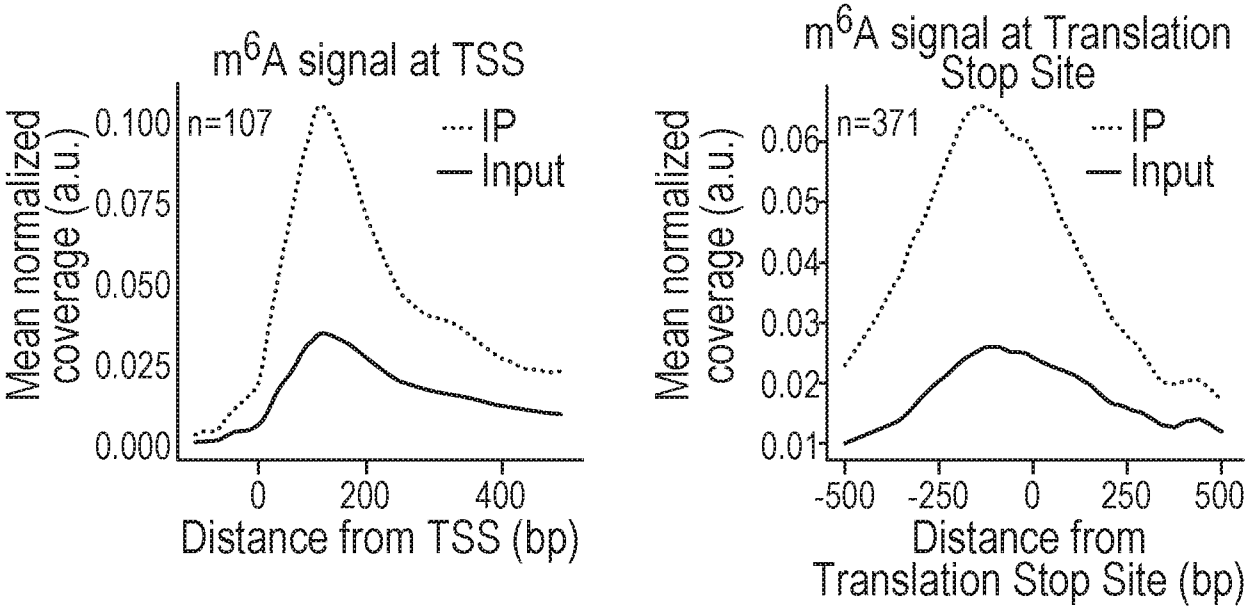


FIG. 4A

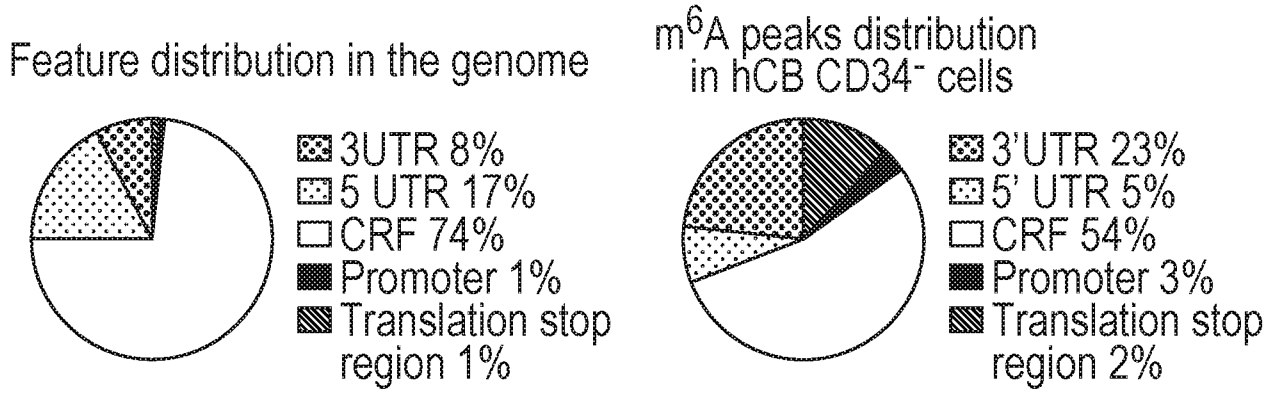


FIG. 4B

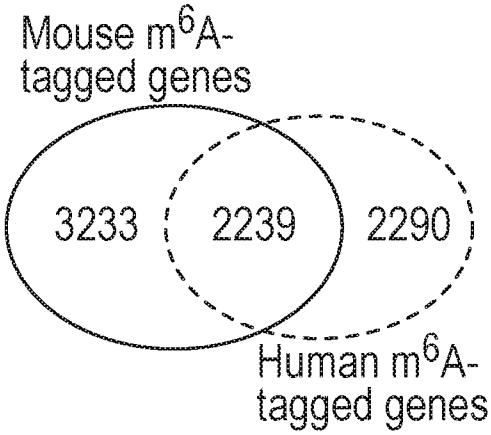


FIG. 4C

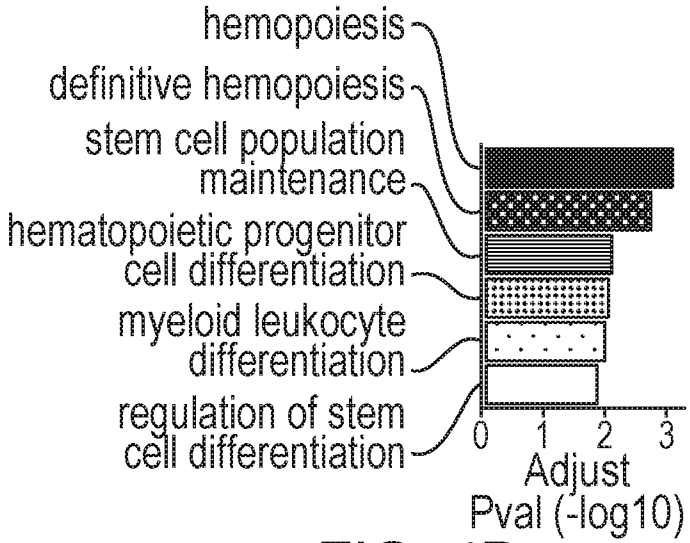


FIG. 4D

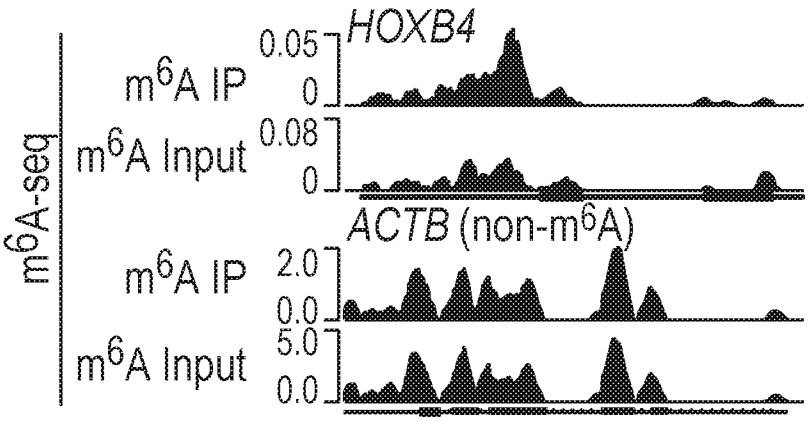


FIG. 4E

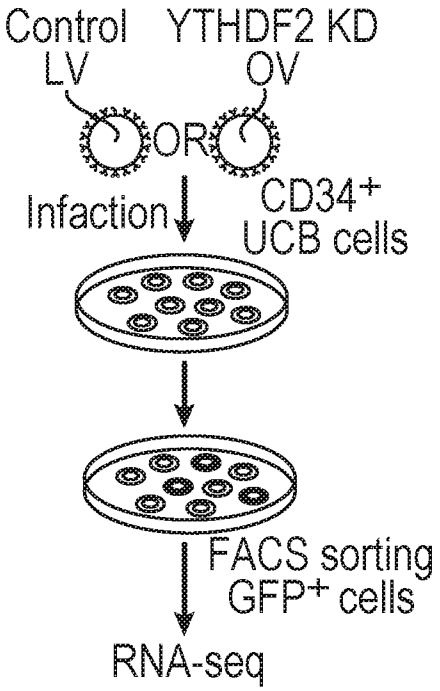


FIG. 4F

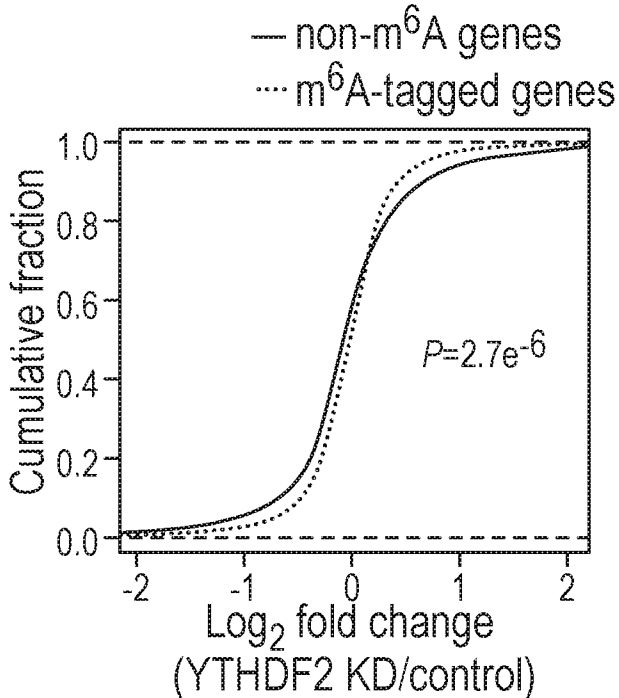


FIG. 4G

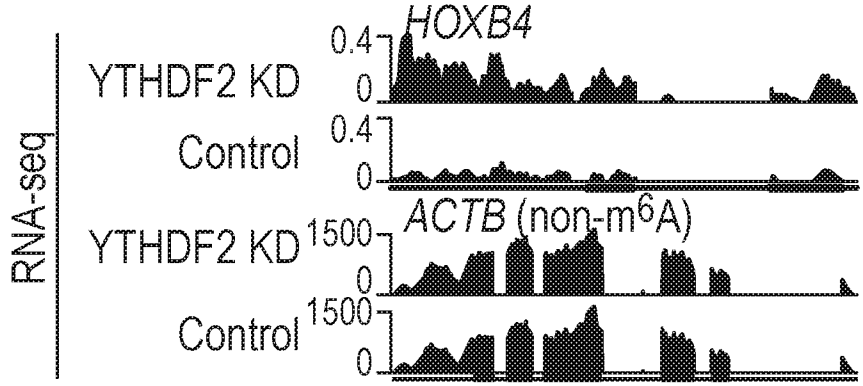


FIG. 4H

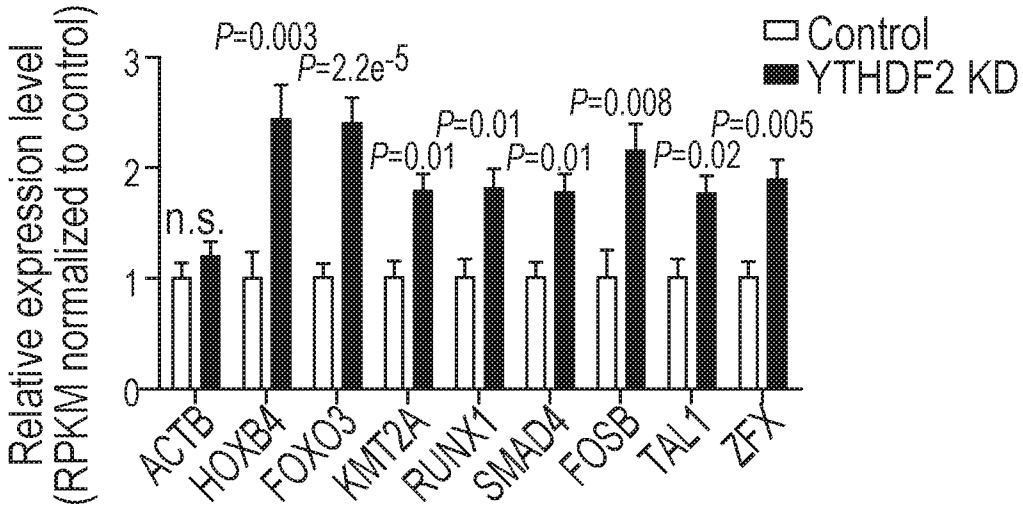


FIG. 4I

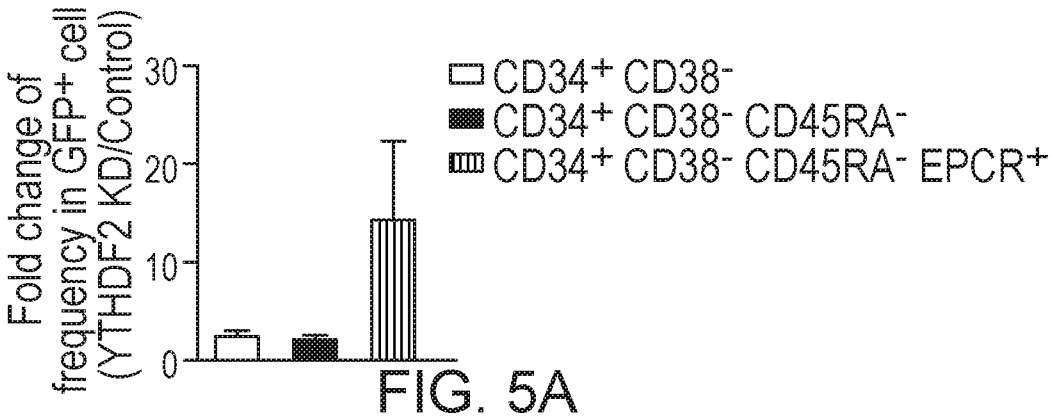


FIG. 5A

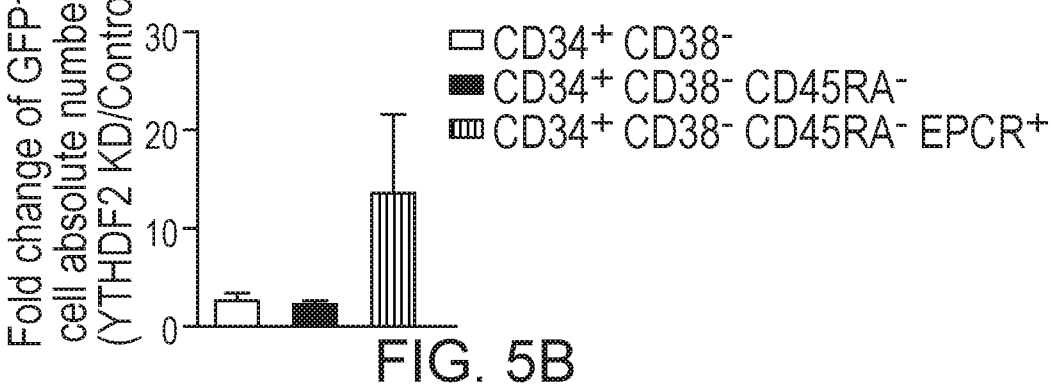


FIG. 5B

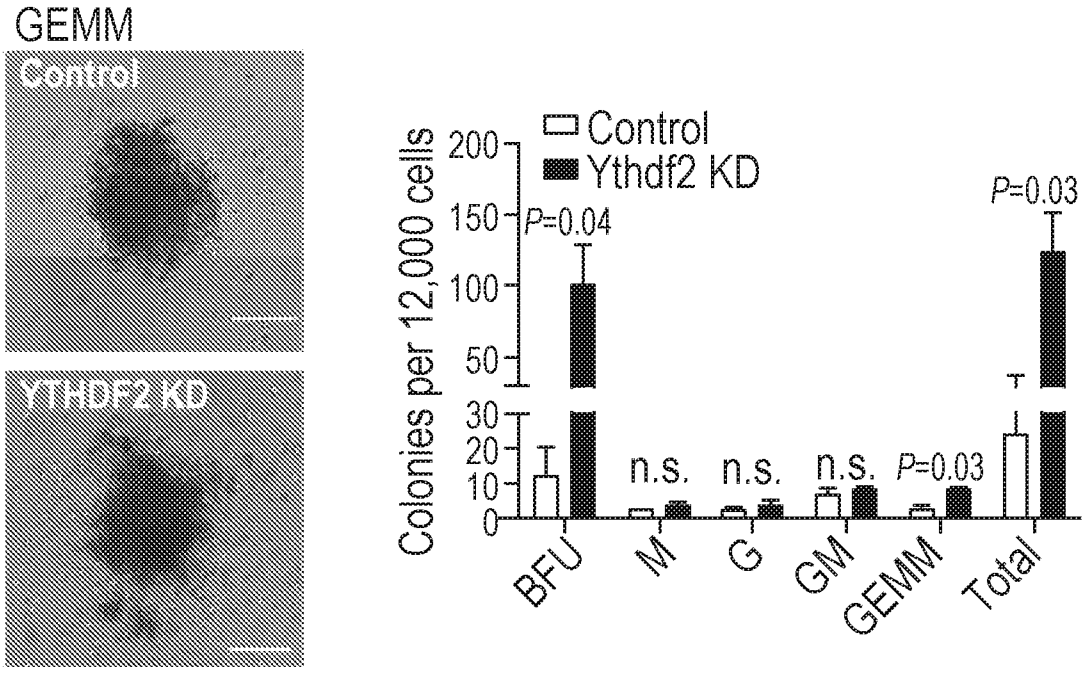


FIG. 5C

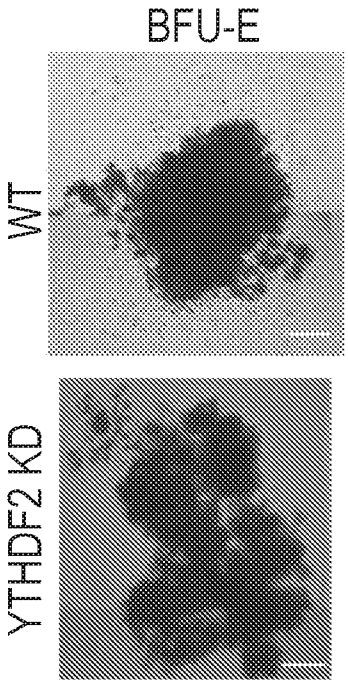


FIG. 5D

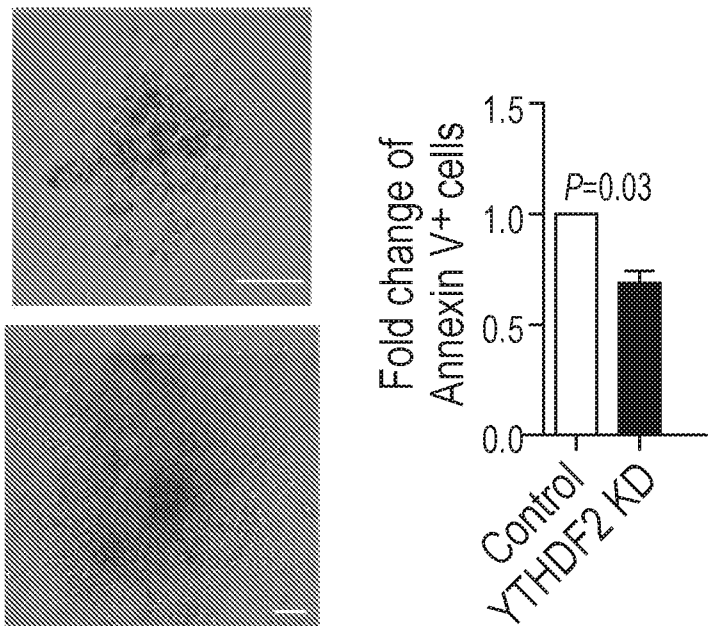


FIG. 5E

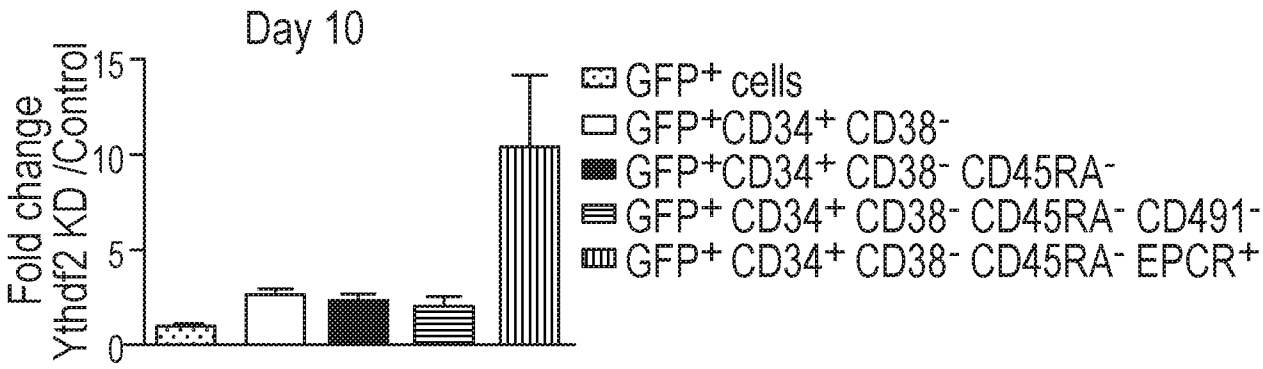

Day 10
Fold change Ythdf2 KD /Control
15
10
5
0
GFP+ cells
GFP+CD34+ CD38-
GFP+CD34+ CD38- CD45RA-
GFP+ CD34+ CD38- CD45RA- CD491-
GFP+ CD34+ CD38- CD45RA- EPCR+

FIG. 5F

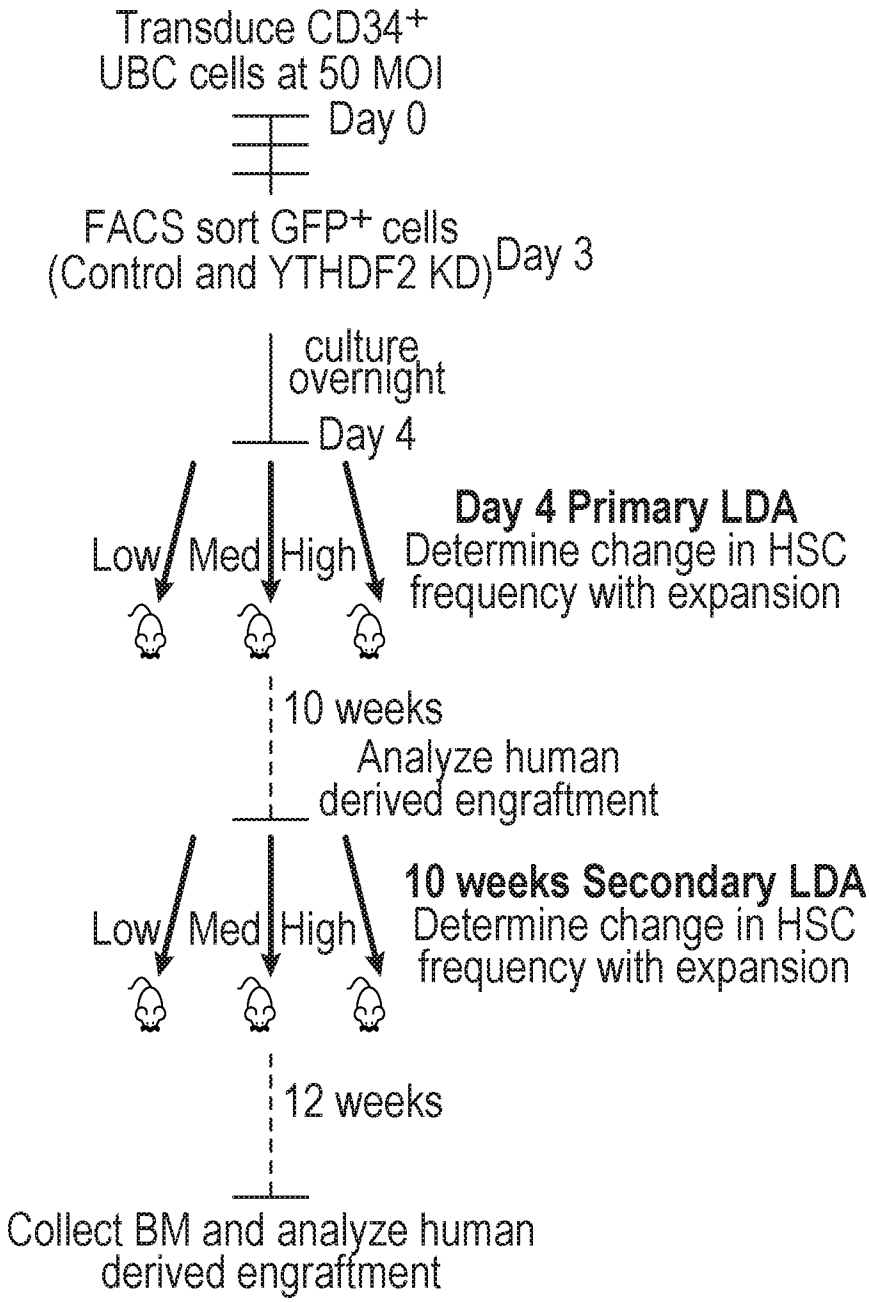

Transduce CD34+
UBC cells at 50 MOI
Day 0
FACS sort GFP+ cells
(Control and YTHDF2 KD)
Day 3
culture
overnight
Day 4
Low
Med
High
Day 4 Primary LDA
Determine change in HSC
frequency with expansion
10 weeks
Analyze human
derived engraftment
Low
Med
High
10 weeks Secondary LDA
Determine change in HSC
frequency with expansion
12 weeks
Collect BM and analyze human
derived engraftment

FIG. 6A

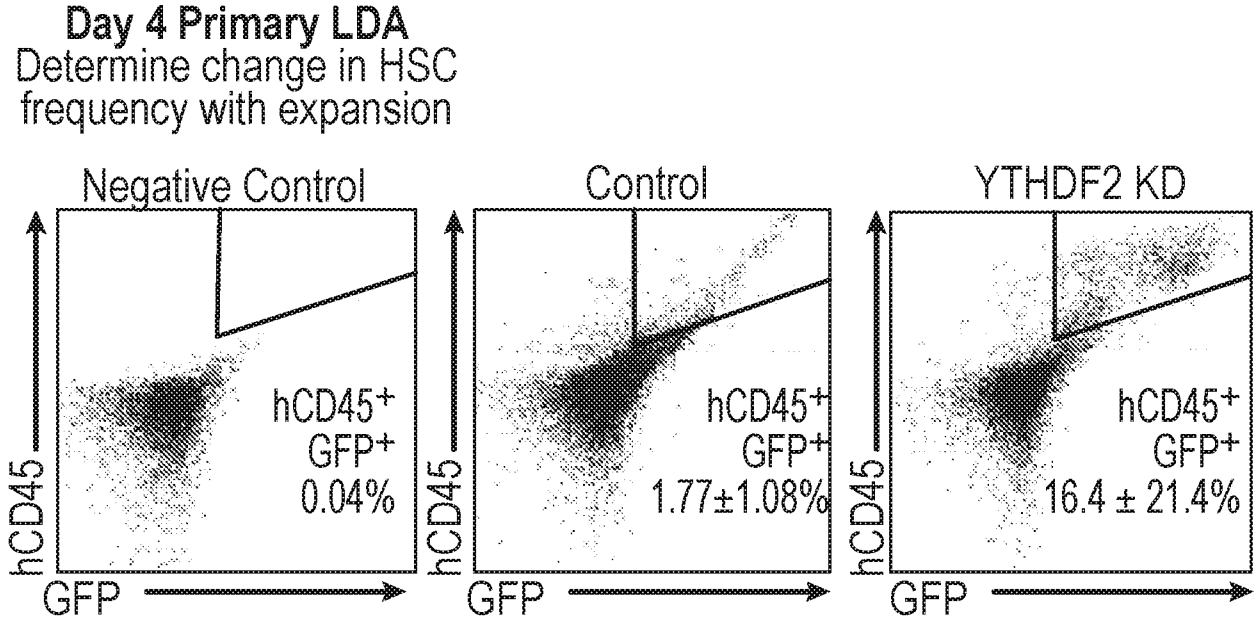


FIG. 6B

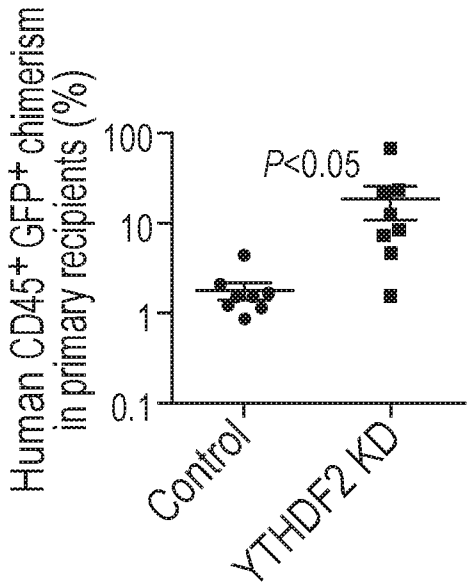


FIG. 6C

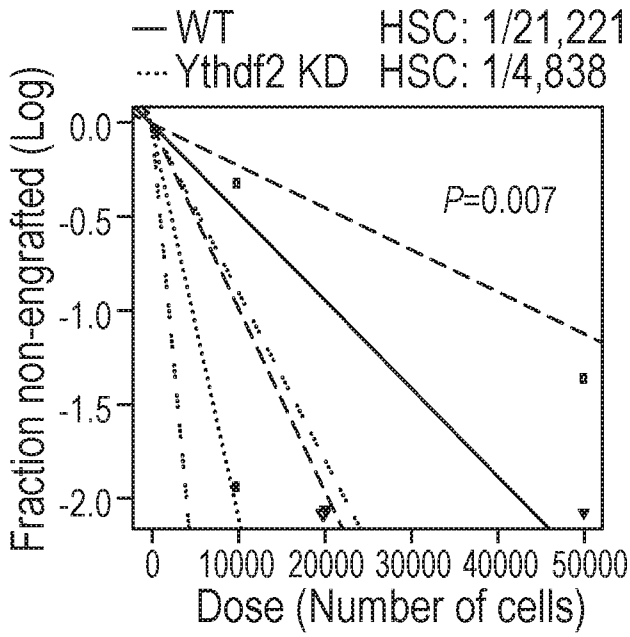


FIG. 6D

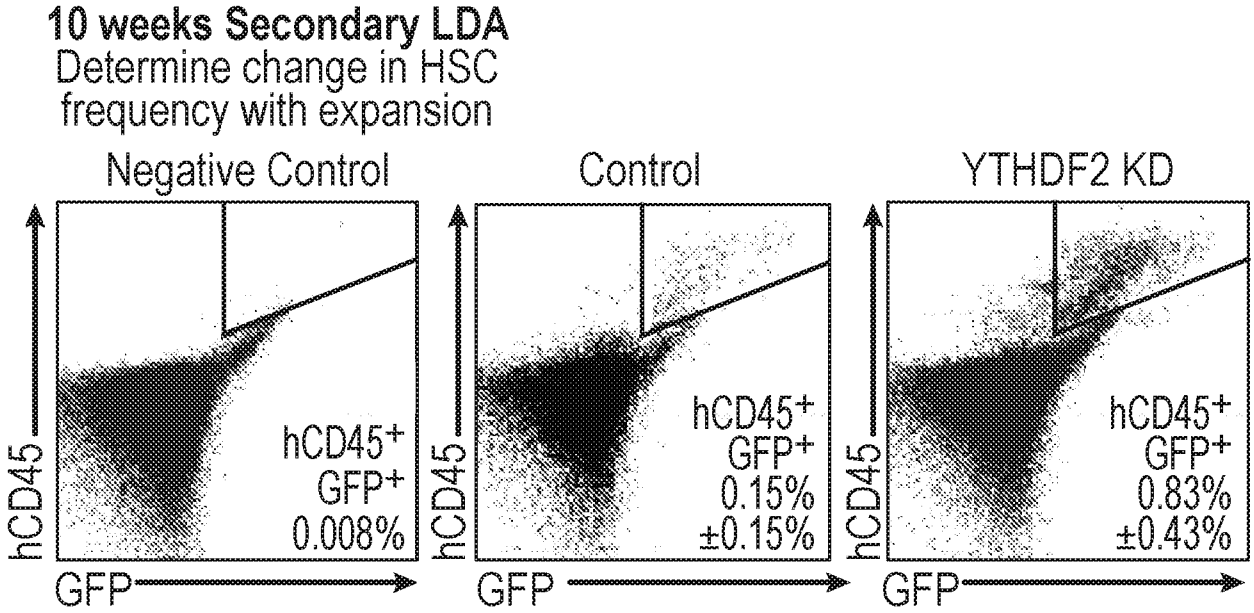


FIG. 6E

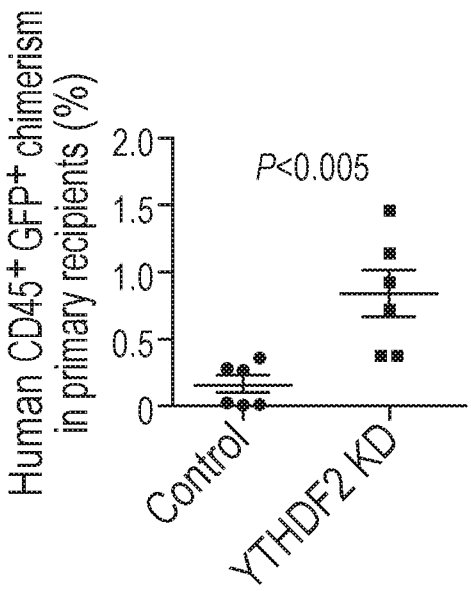


FIG. 6F

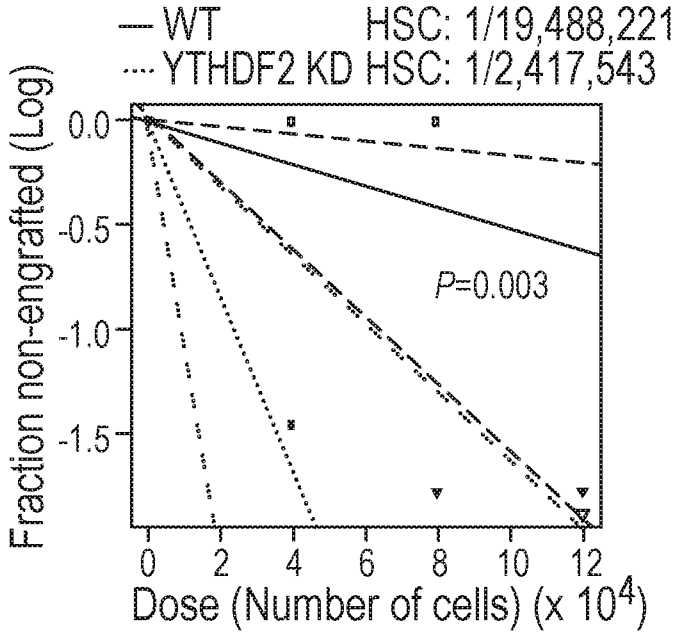


FIG. 6G

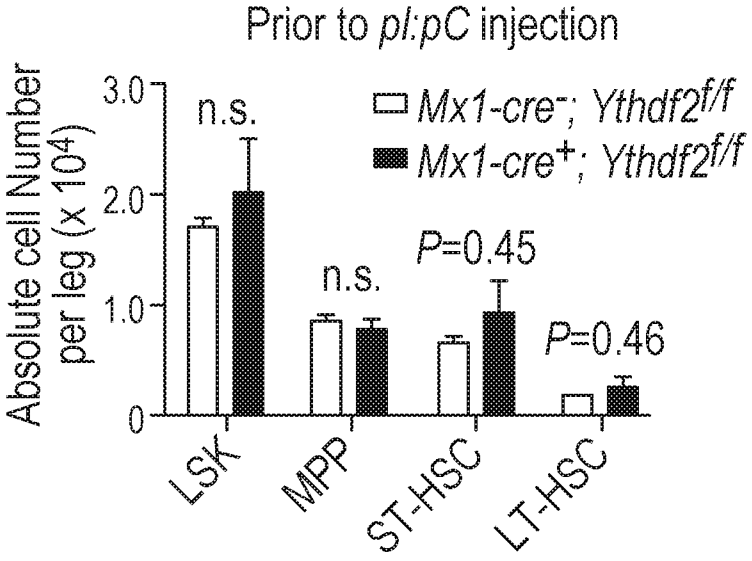


FIG. 7A

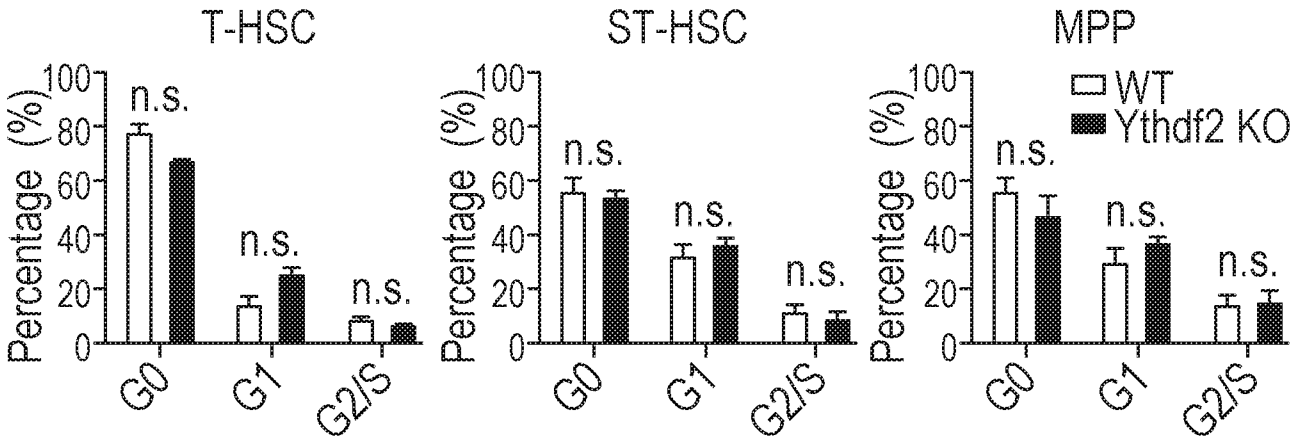


FIG. 7B

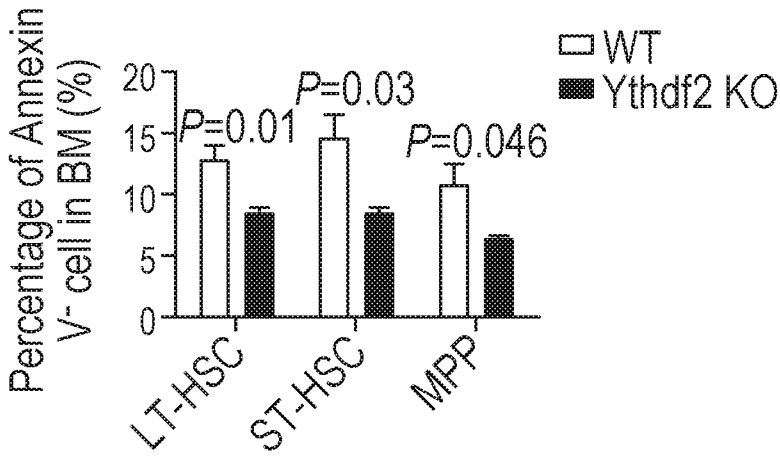


FIG. 7C

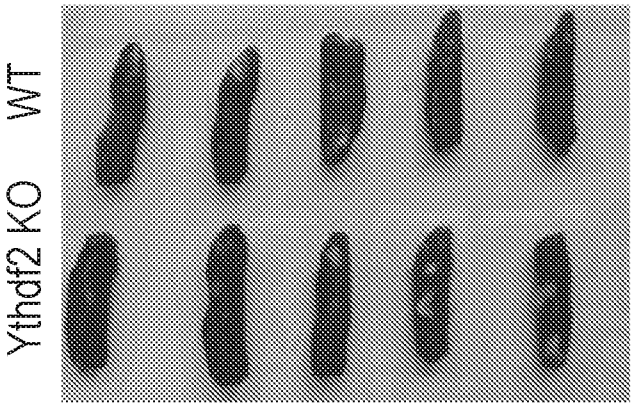


FIG. 7D

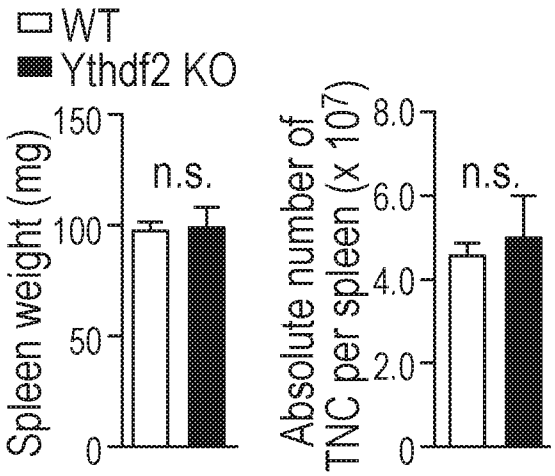


FIG. 7E

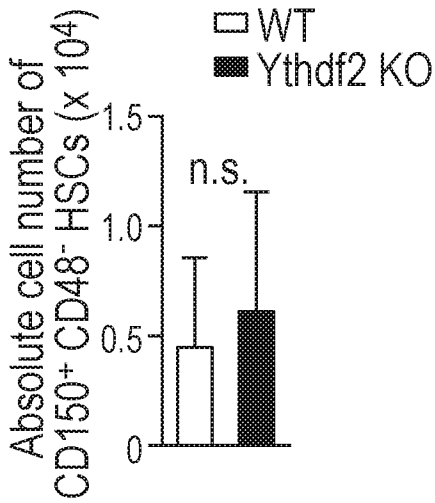


FIG. 7F

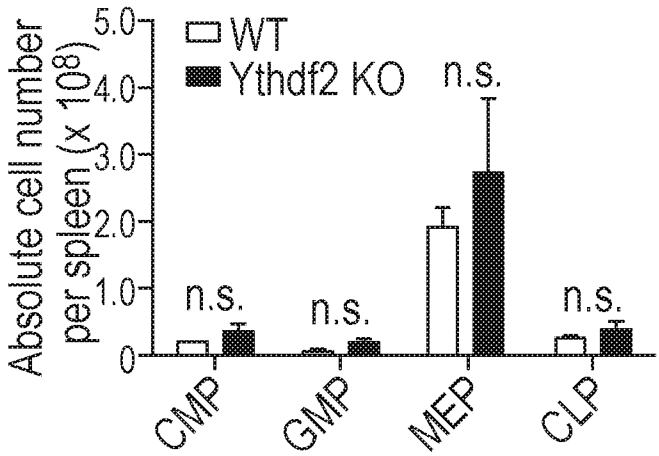


FIG. 7G

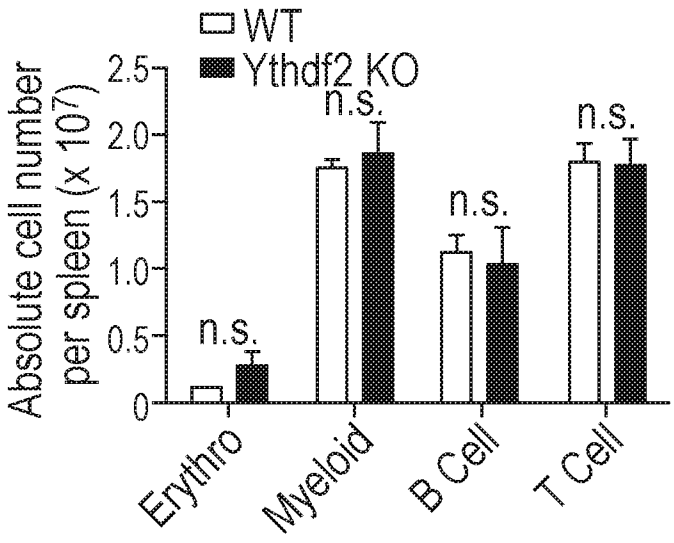


FIG. 7H

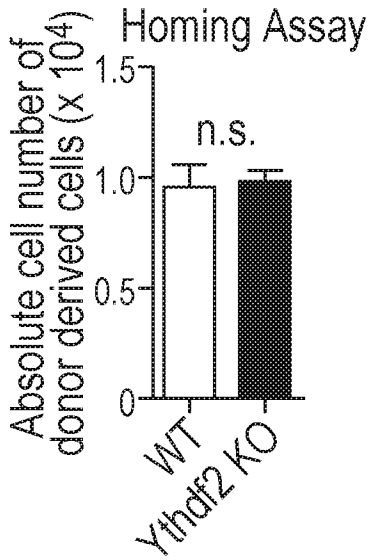


FIG. 7I

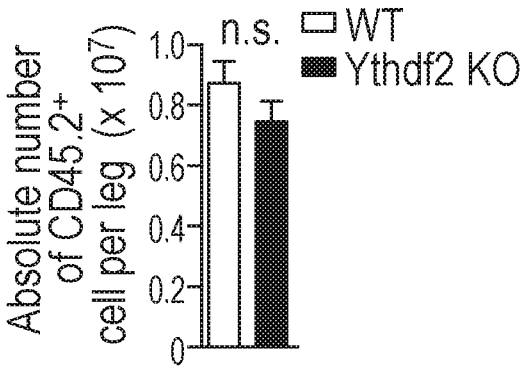


FIG. 8A

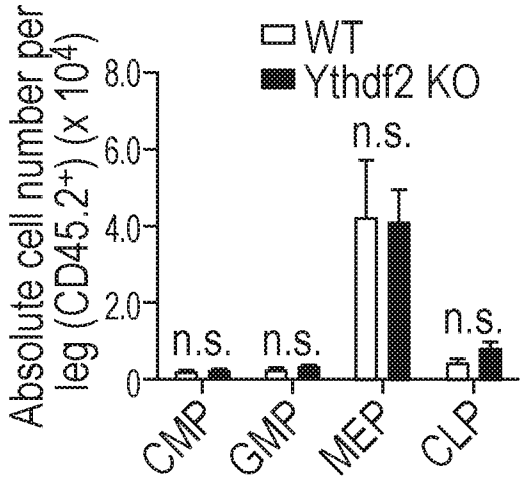


FIG. 8B

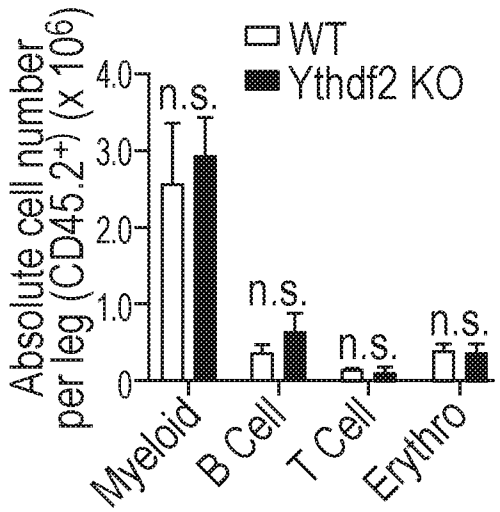


FIG. 8C

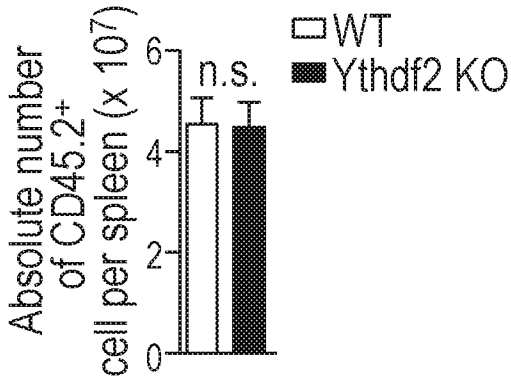


FIG. 8D

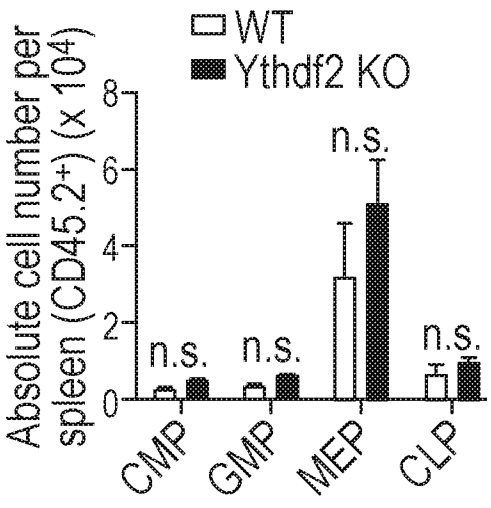


FIG. 8E

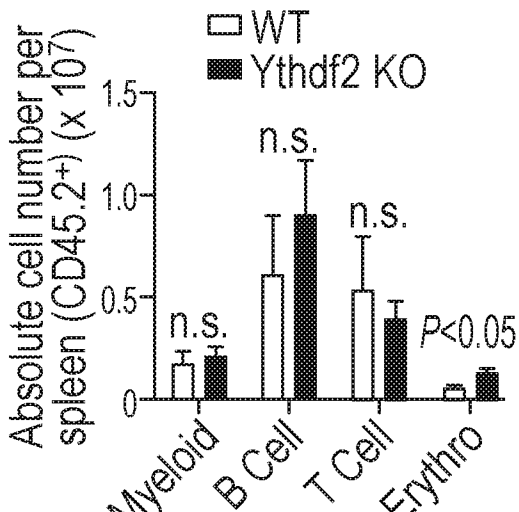


FIG. 8F

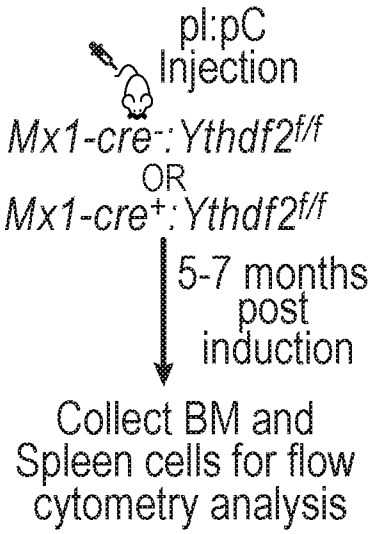


FIG. 9A

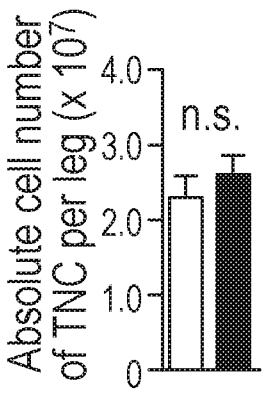


FIG. 9B

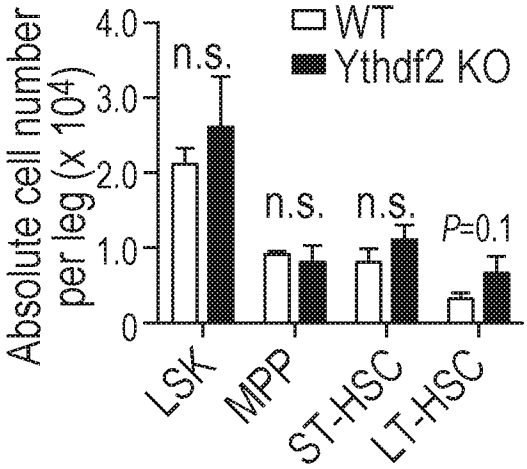


FIG. 9C

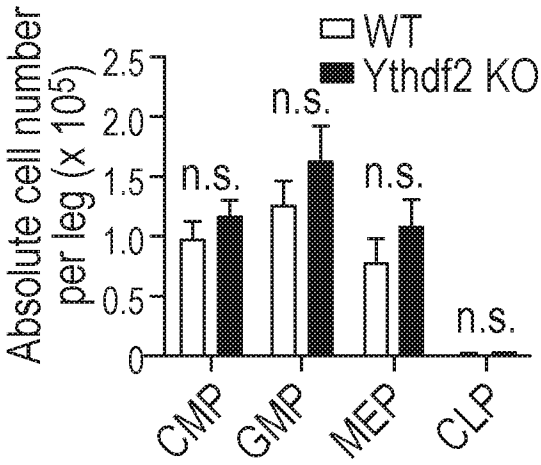


FIG. 9D

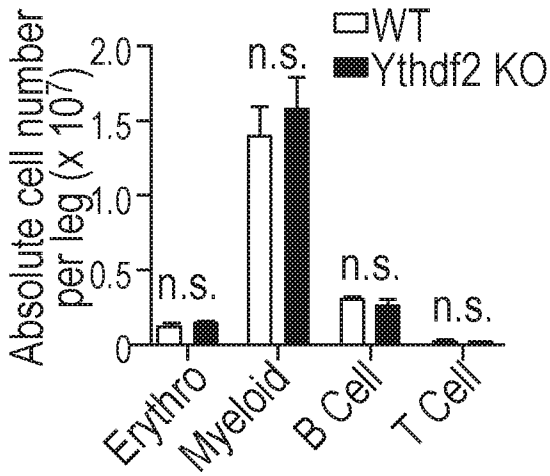


FIG. 9E

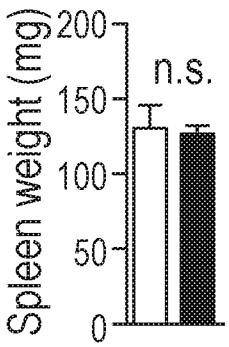


FIG. 9F

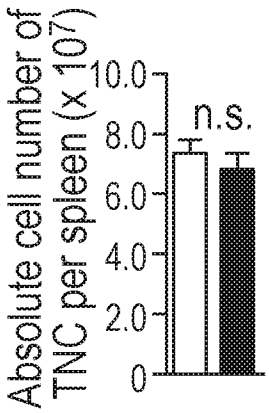


FIG. 9G

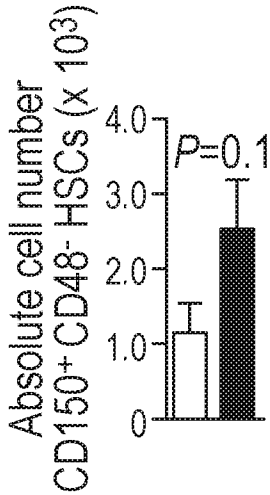


FIG. 9H

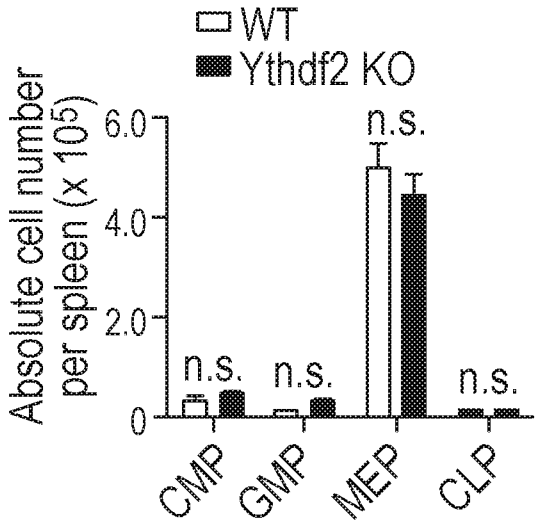


FIG. 9I

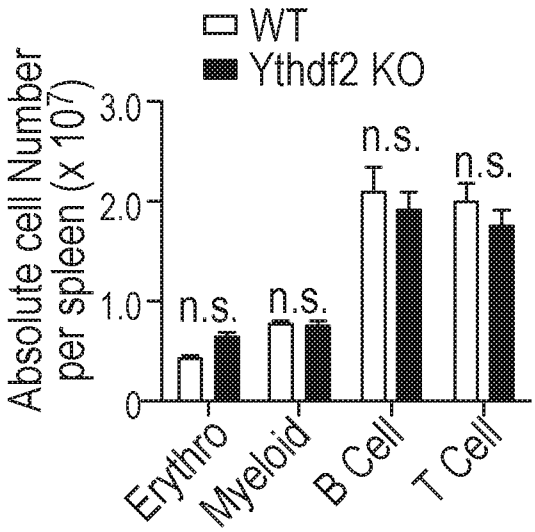
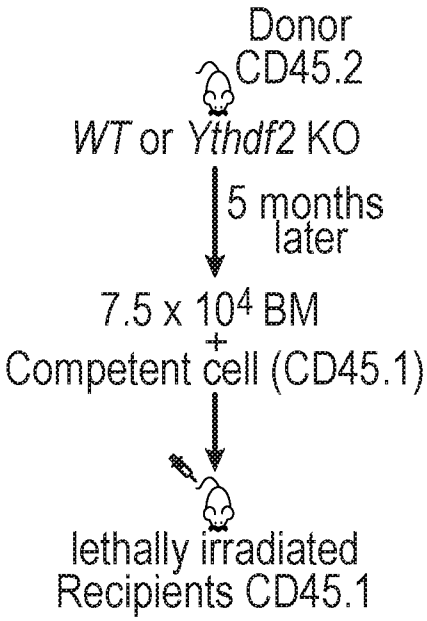


FIG. 9J



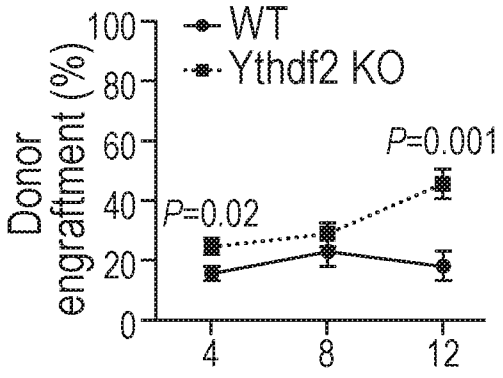


FIG. 9K

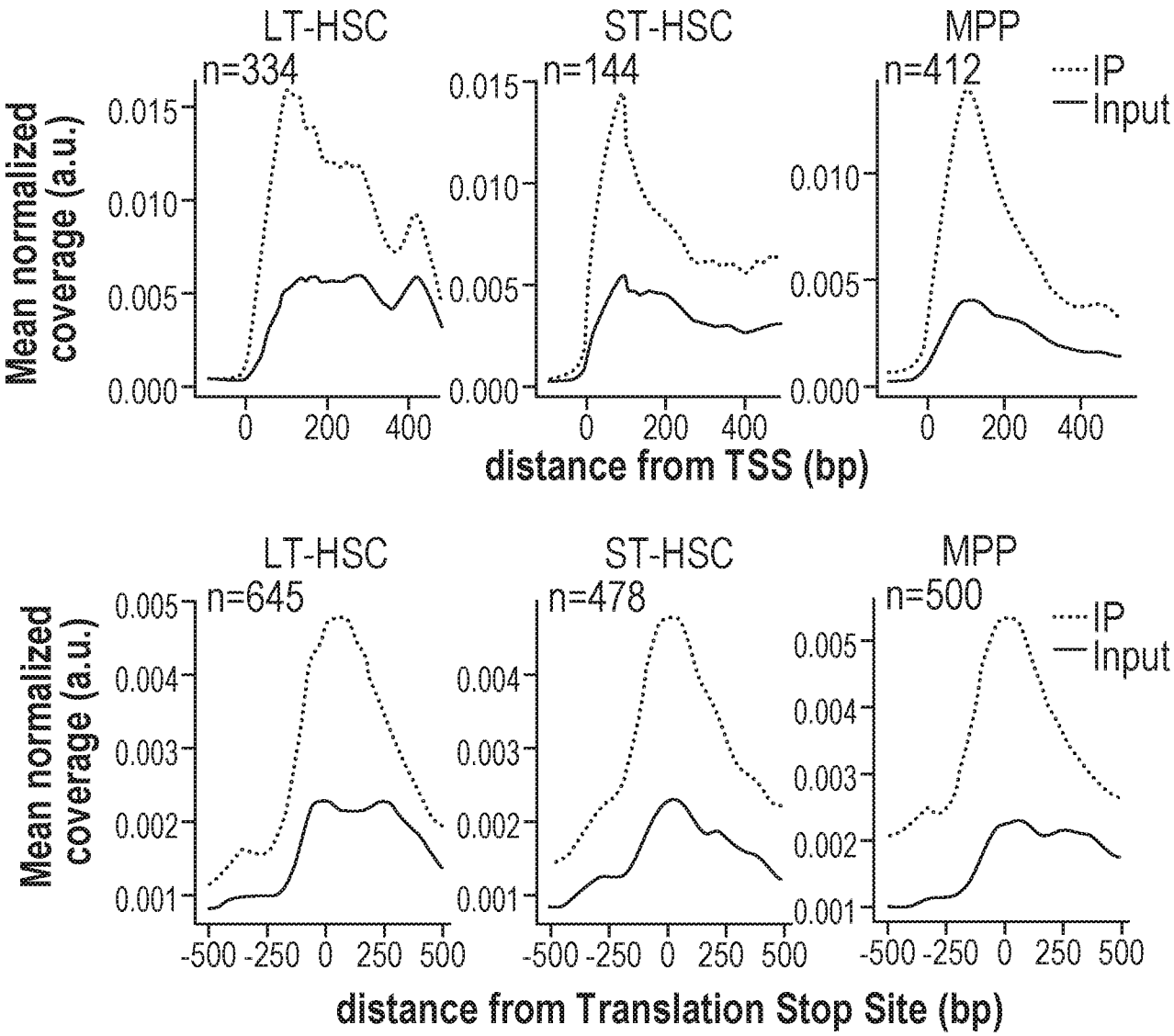

LT-HSC
n=334
ST-HSC
n=144
MPP
n=412
IP
Input
Mean normalized coverage (a.u.)
0.015
0.010
0.005
0.000
0
200
400
distance from TSS (bp)
LT-HSC
n=645
ST-HSC
n=478
MPP
n=500
0.005
0.004
0.003
0.002
0.001
-500 -250 0 250 500
distance from Translation Stop Site (bp)

FIG. 10A

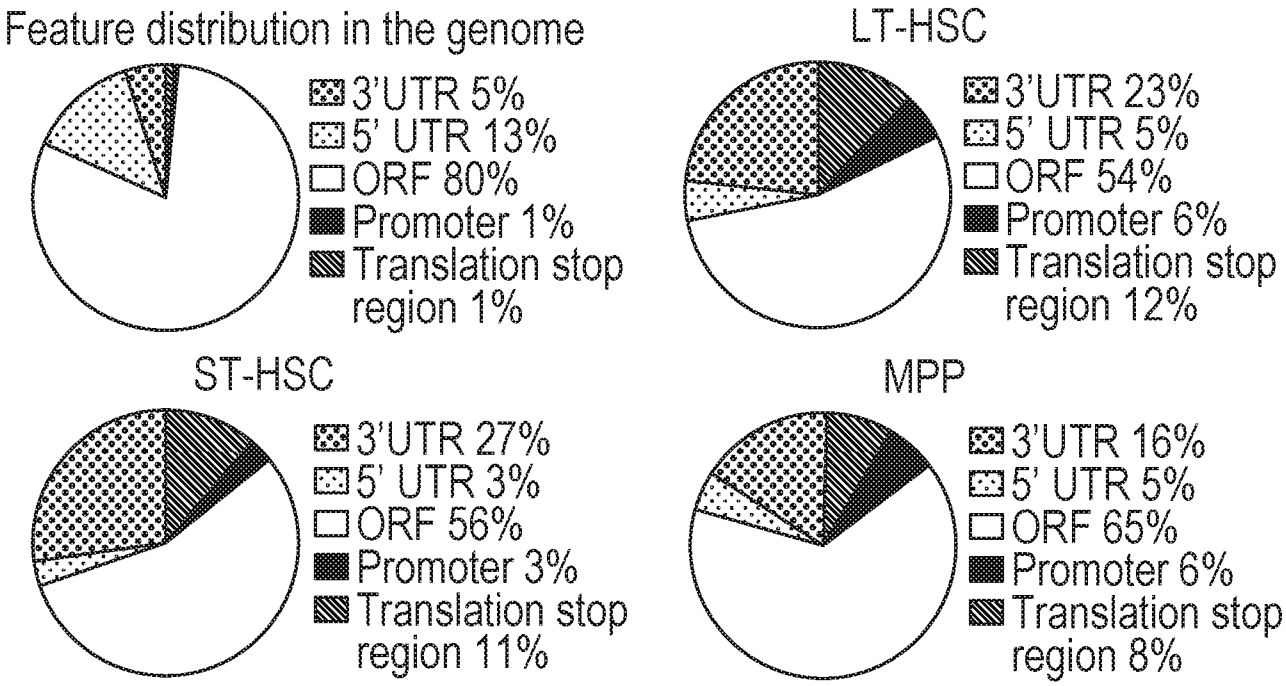


FIG. 10B

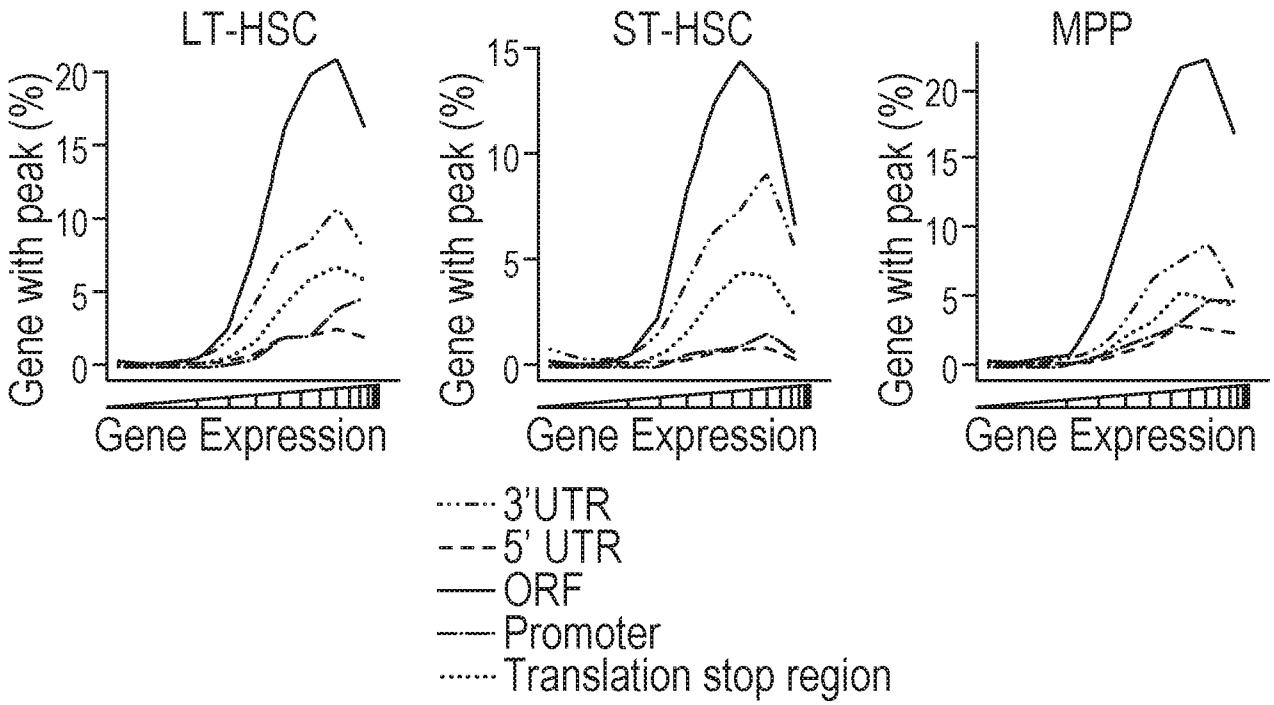


FIG. 10C

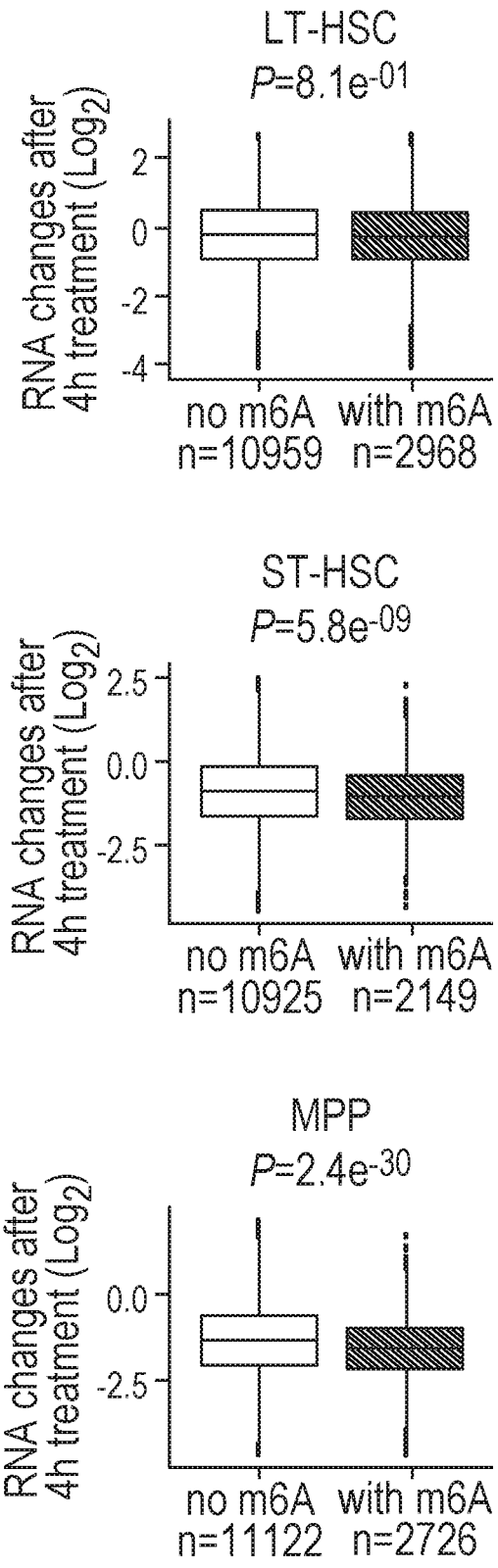

LT-HSC
P=8.1e-01
RNA changes after 4h treatment (Log2)
2
0
-2
-4
no m6A
n=10959
with m6A
n=2968
ST-HSC
P=5.8e-09
RNA changes after 4h treatment (Log2)
2.5
0.0
-2.5
no m6A
n=10925
with m6A
n=2149
MPP
P=2.4e-30
RNA changes after 4h treatment (Log2)
0.0
-2.5
no m6A
n=11122
with m6A
n=2726

FIG. 10D

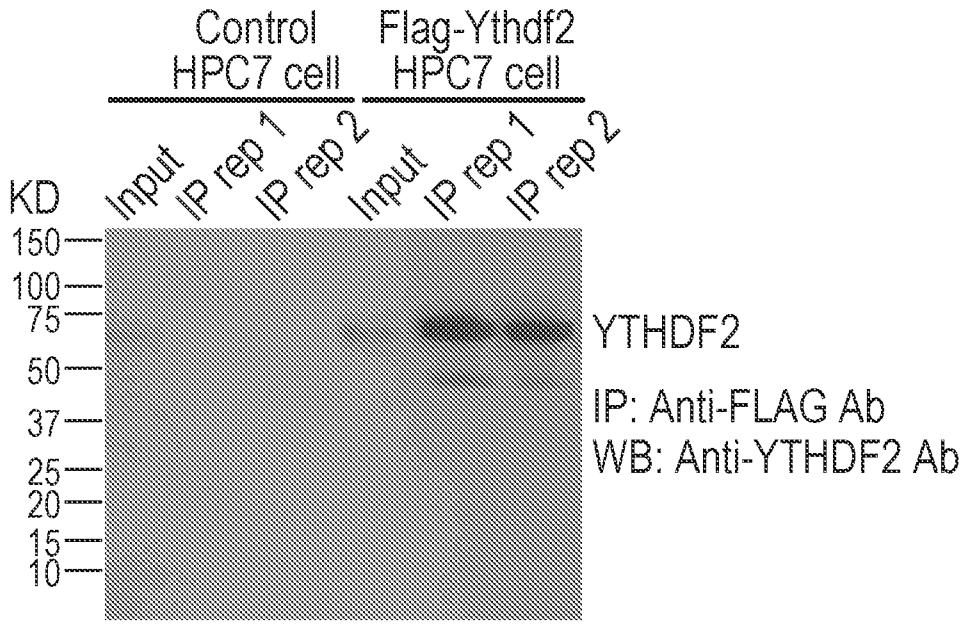


FIG. 11A

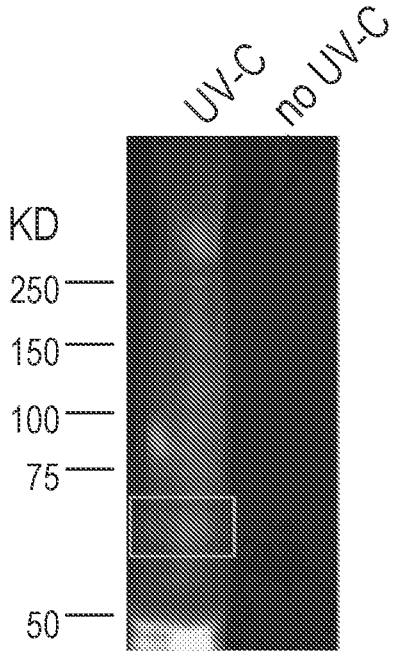


FIG. 11B

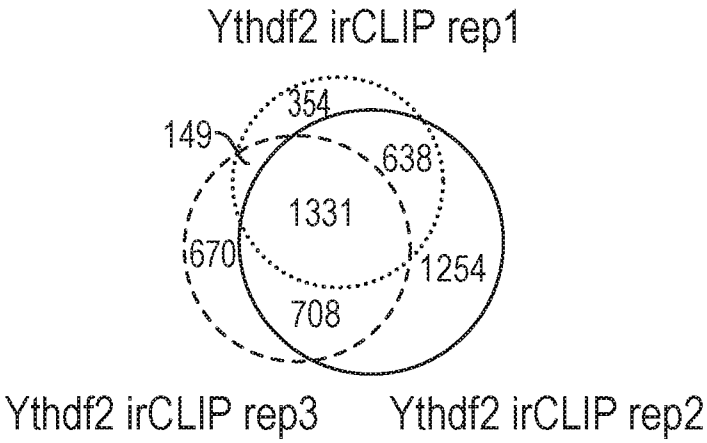


FIG. 11C

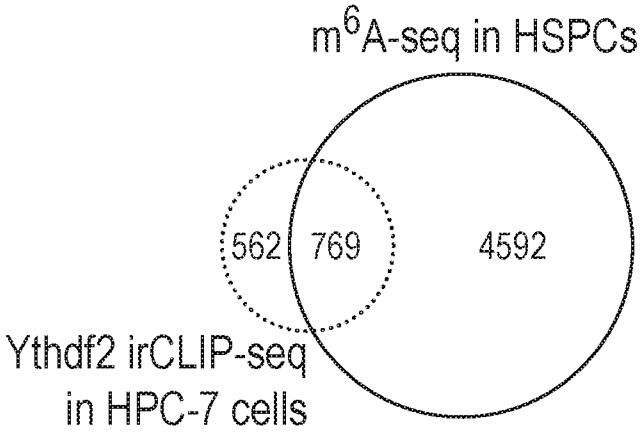


FIG. 11D

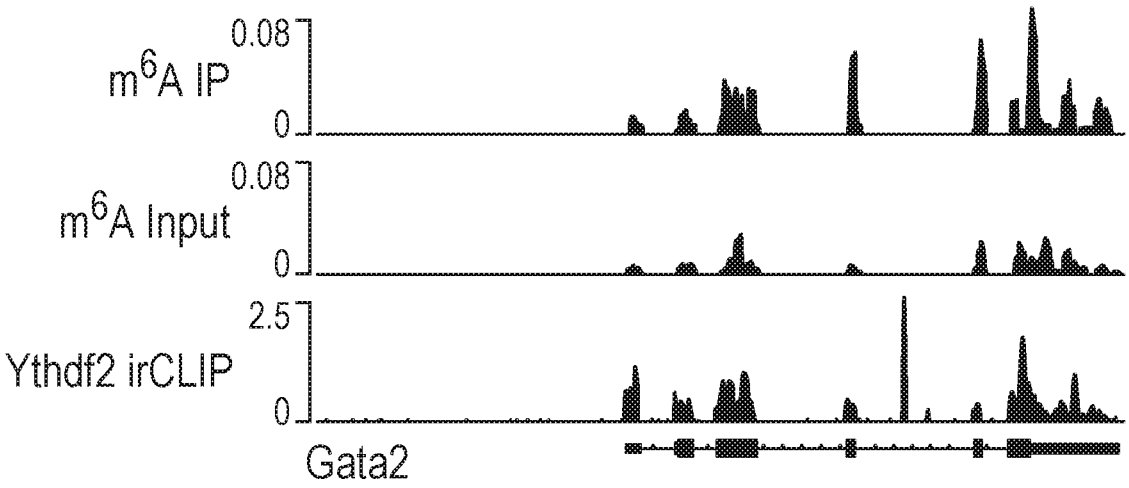


FIG. 11E

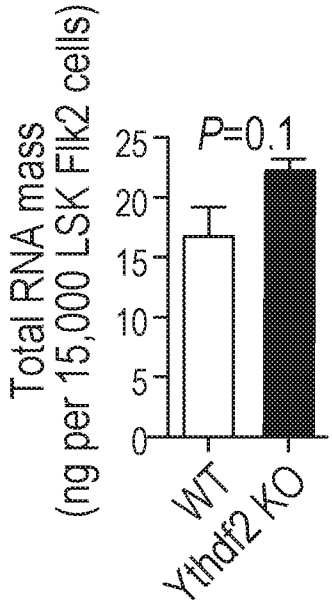


FIG. 12A

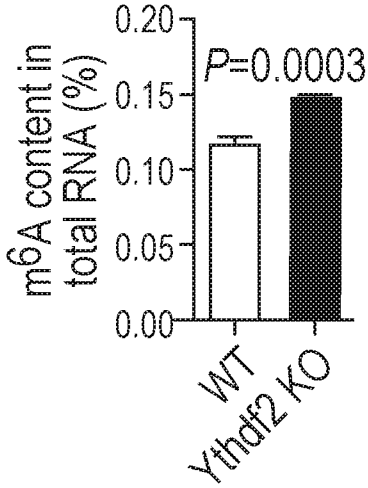


FIG. 12B

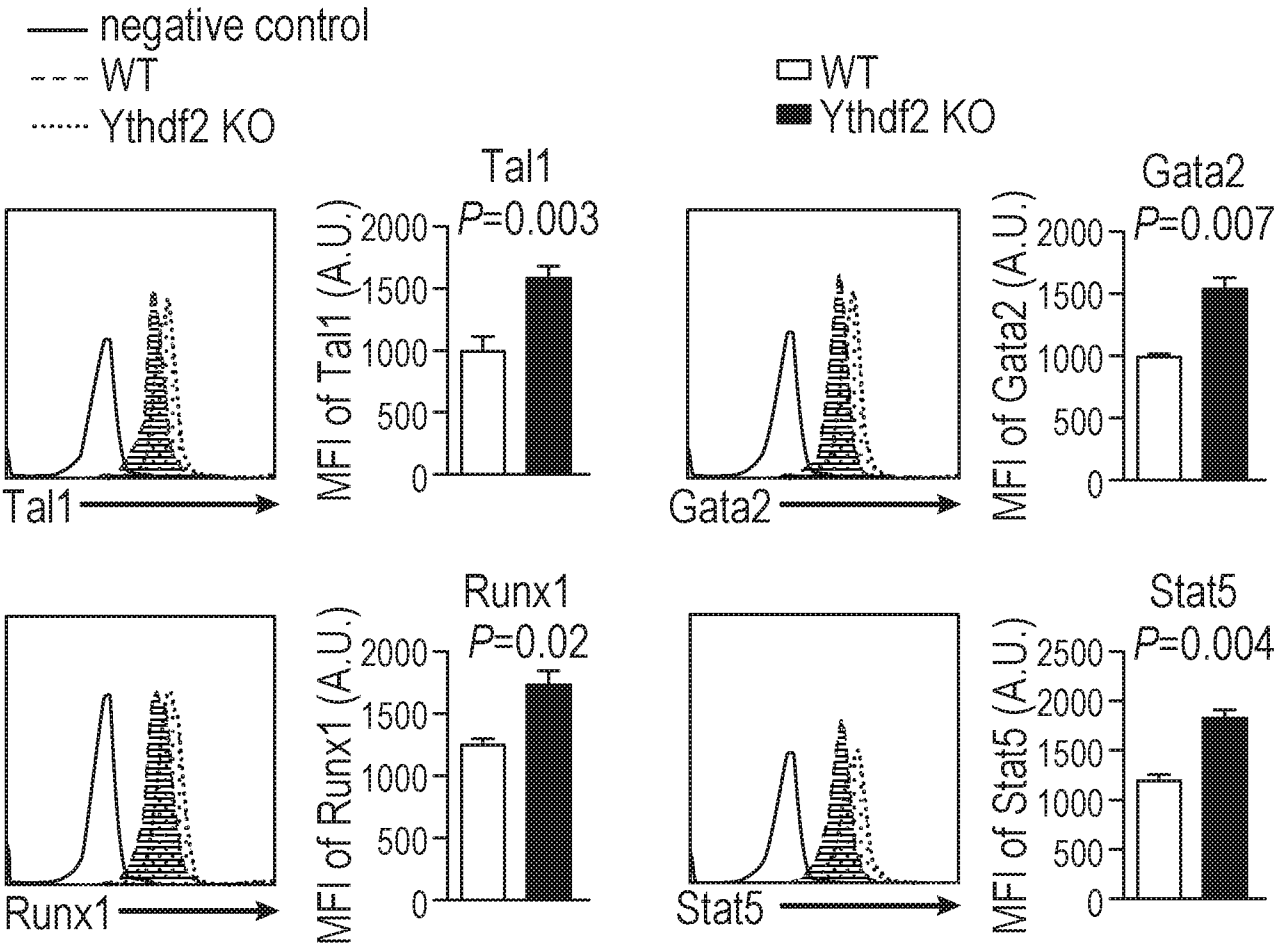


FIG. 12C

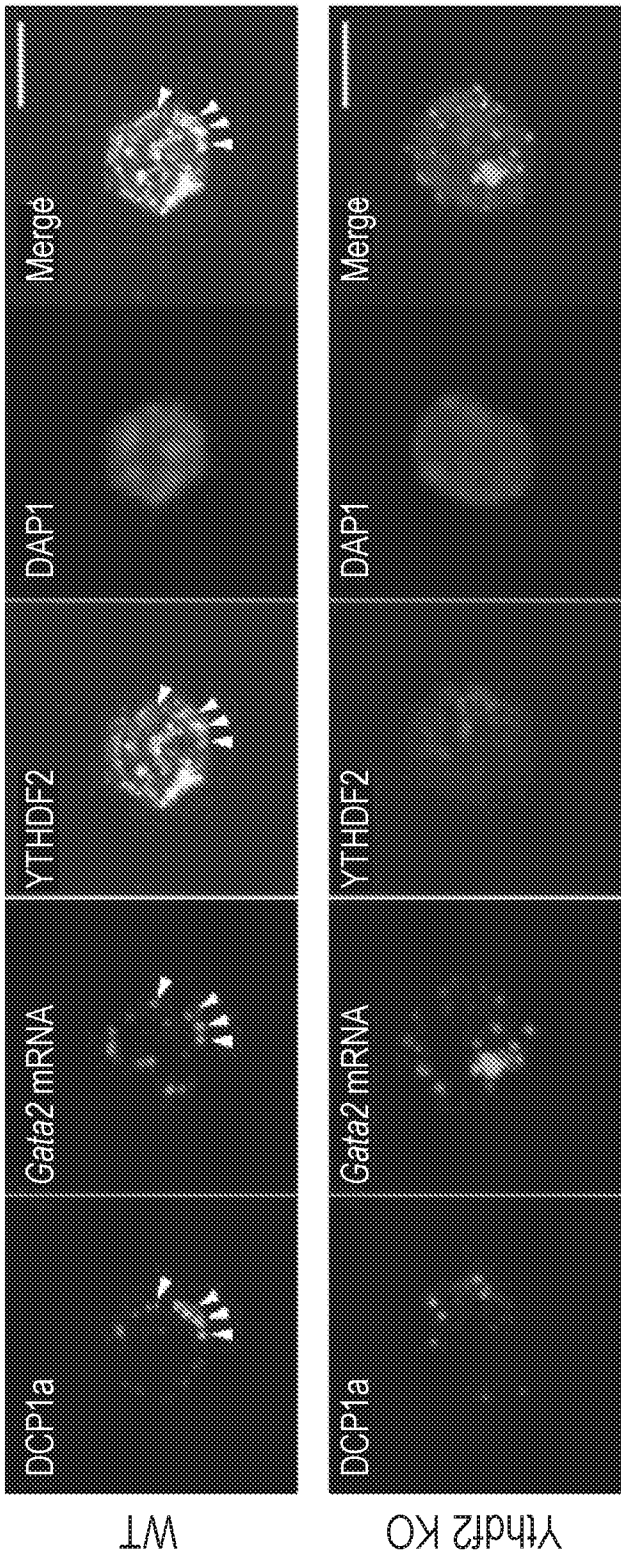


FIG. 12D

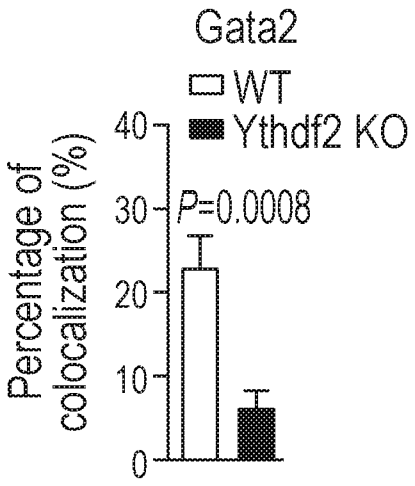


FIG. 12E

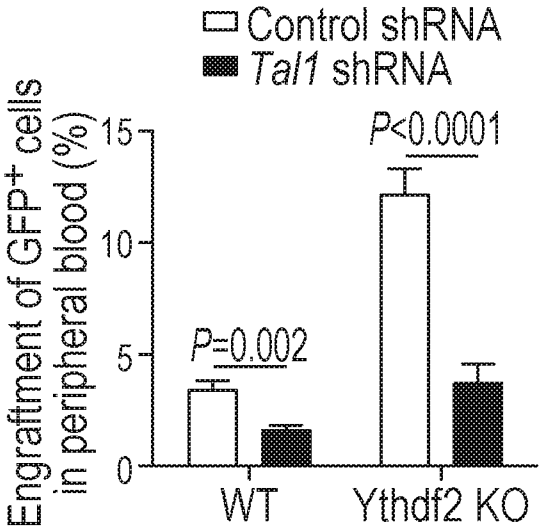


FIG. 12F

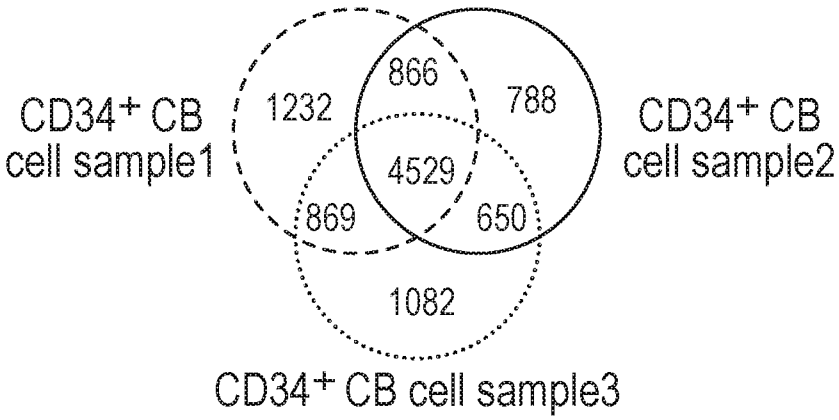


FIG. 13A

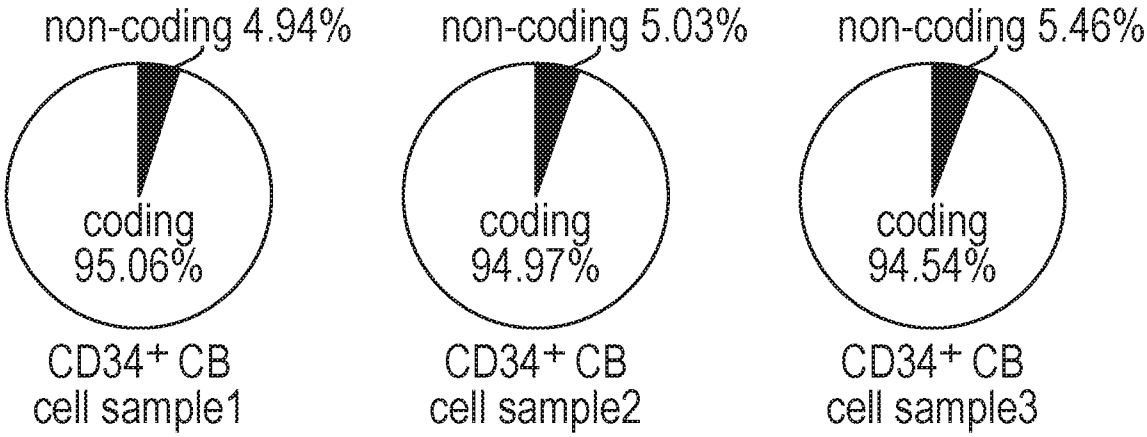


FIG. 13B

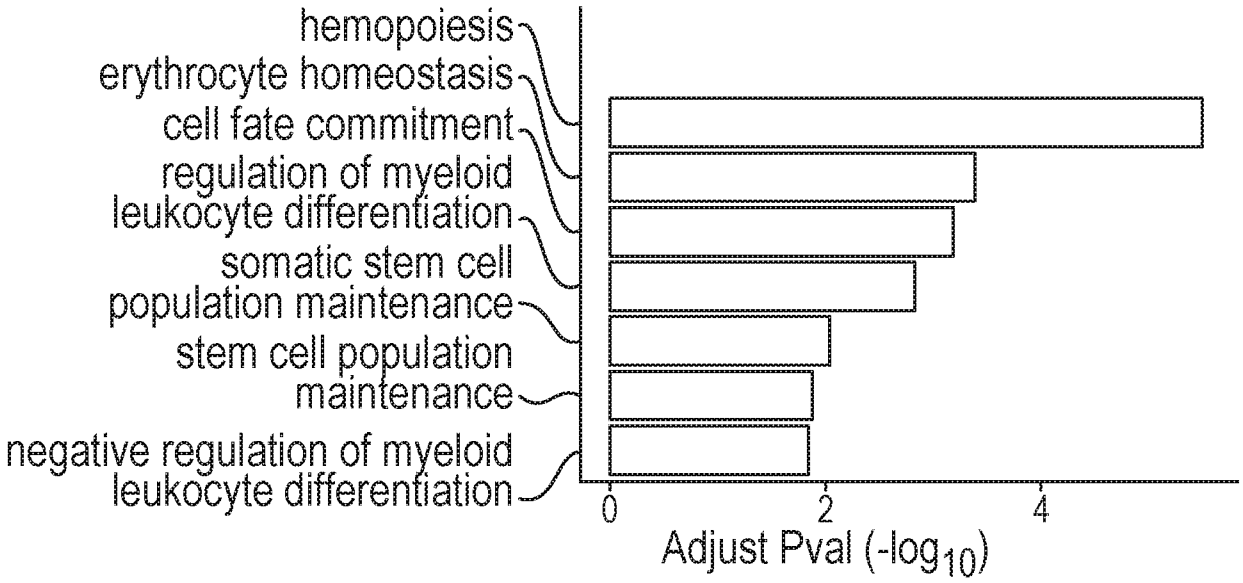

hemopoiesis
erythrocyte homeostasis
cell fate commitment
regulation of myeloid leukocyte differentiation
somatic stem cell population maintenance
stem cell population maintenance
negative regulation of myeloid leukocyte differentiation
0
2
4
Adjust Pval (-log10)

FIG. 13C

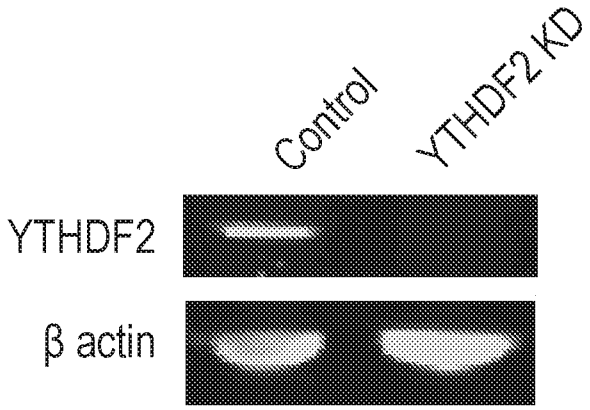


FIG. 13D

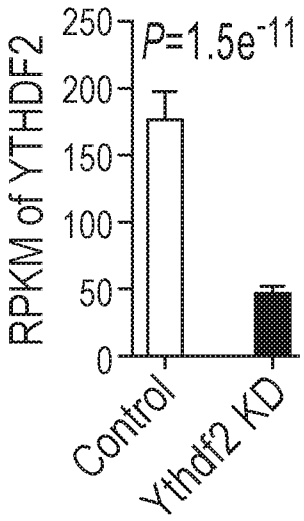


FIG. 13E

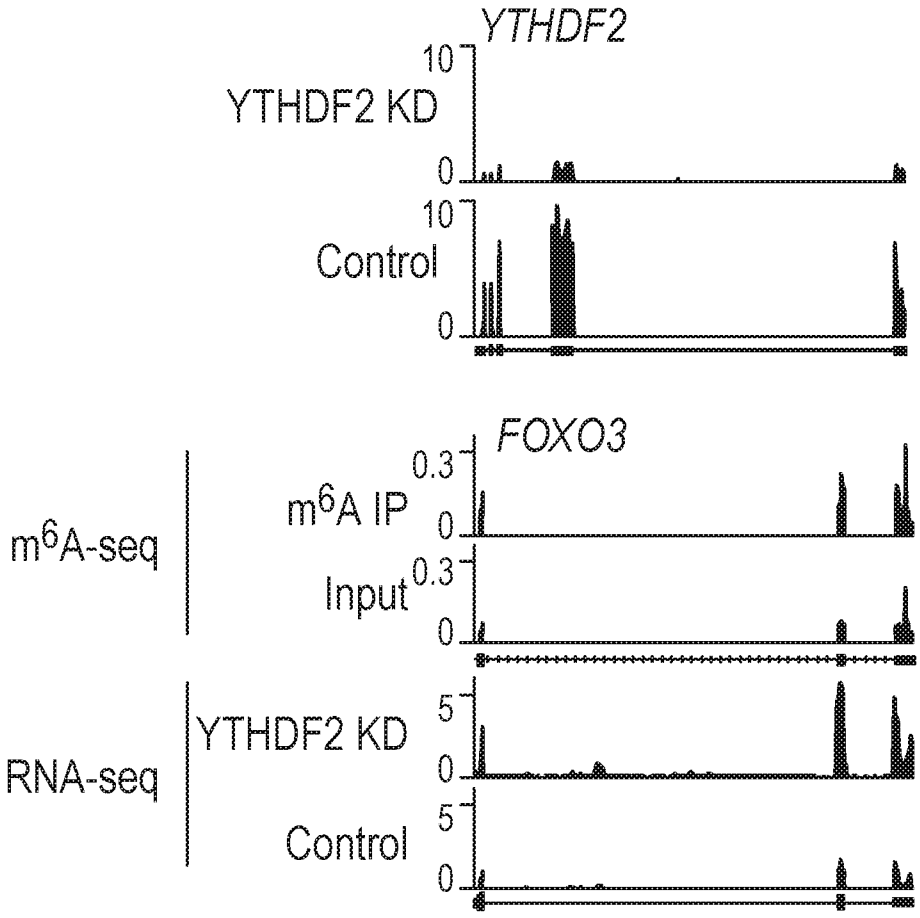


FIG. 13F

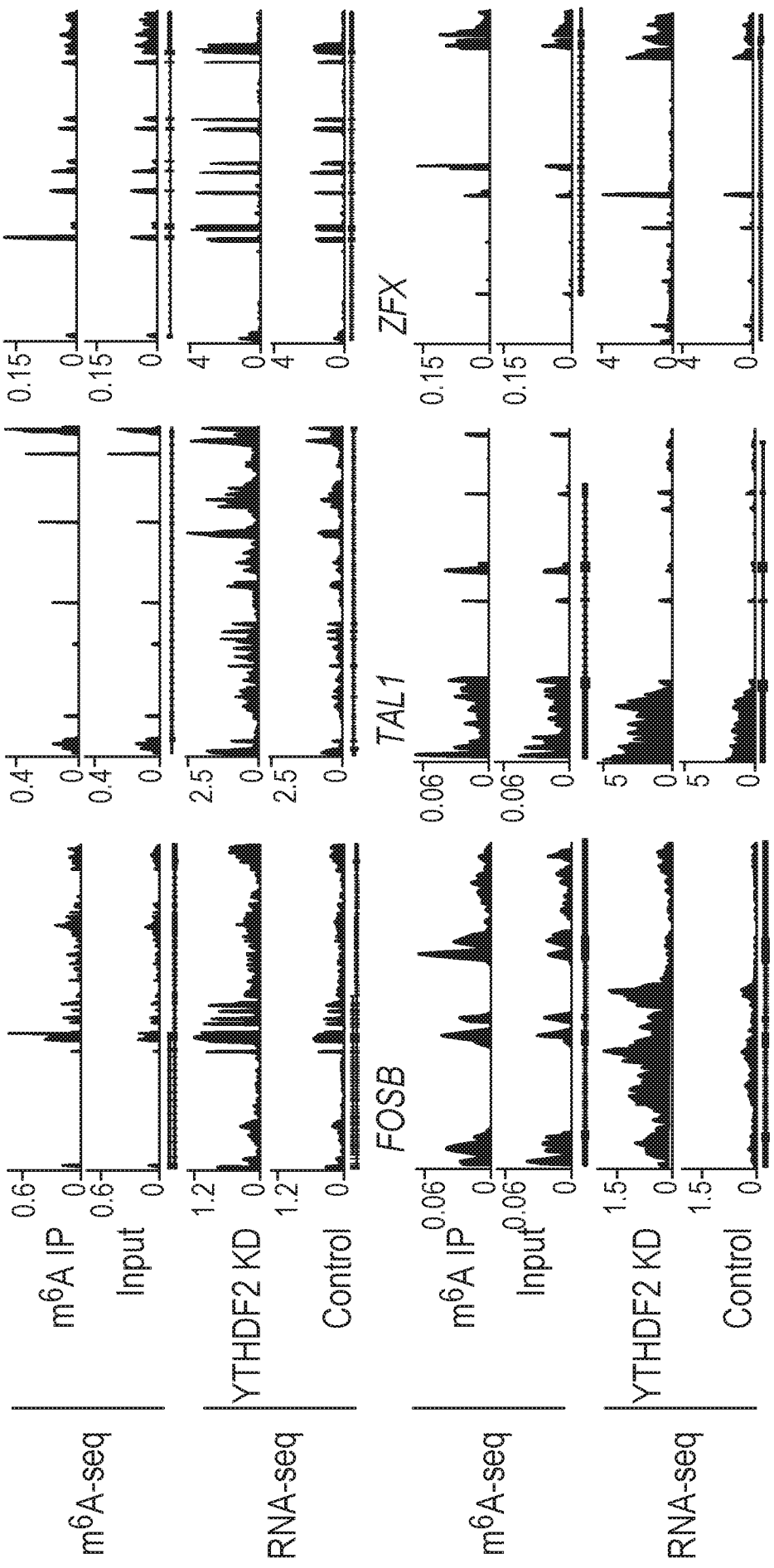

m6A-seq
RNA-seq
m6A-seq
RNA-seq
m6A IP
Input
YTHDF2 KD
Control
m6A IP
Input
YTHDF2 KD
Control
KMT2A
RUNX1
SMAD4
FOSB
TAL1
ZFX
0.6
0
0.4
2.5
0.15
0.06
1.2
1.5
5
4

FIG. 13G

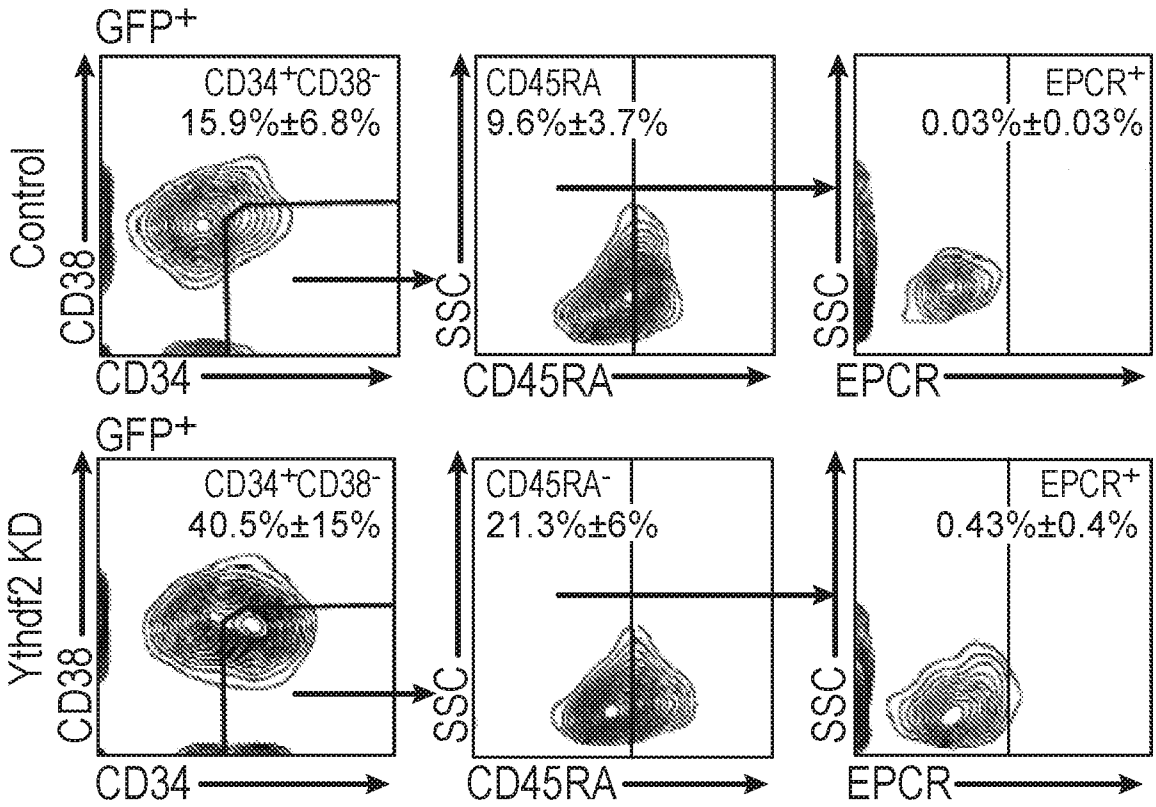


FIG. 14A

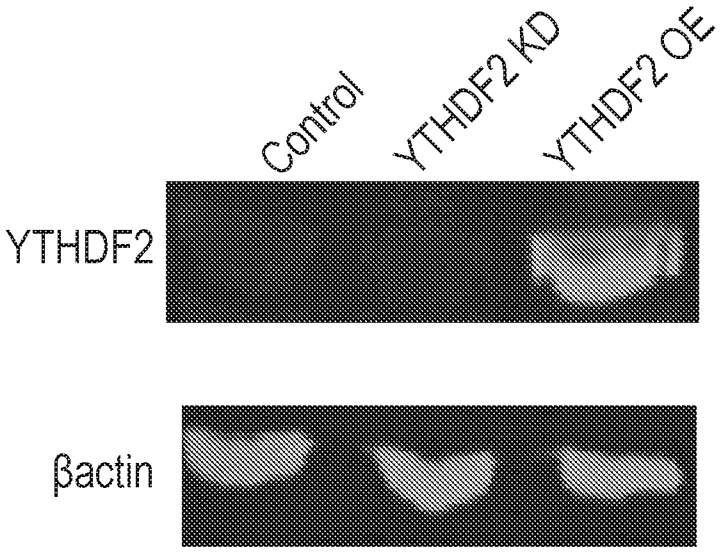


FIG. 14B

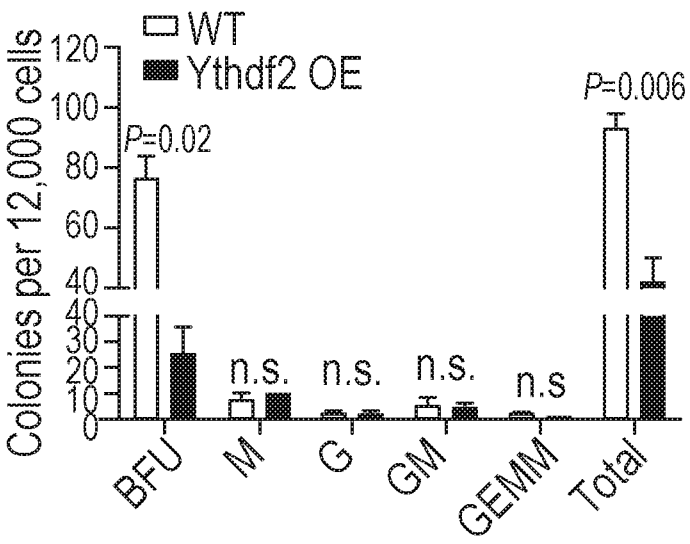


FIG. 14C

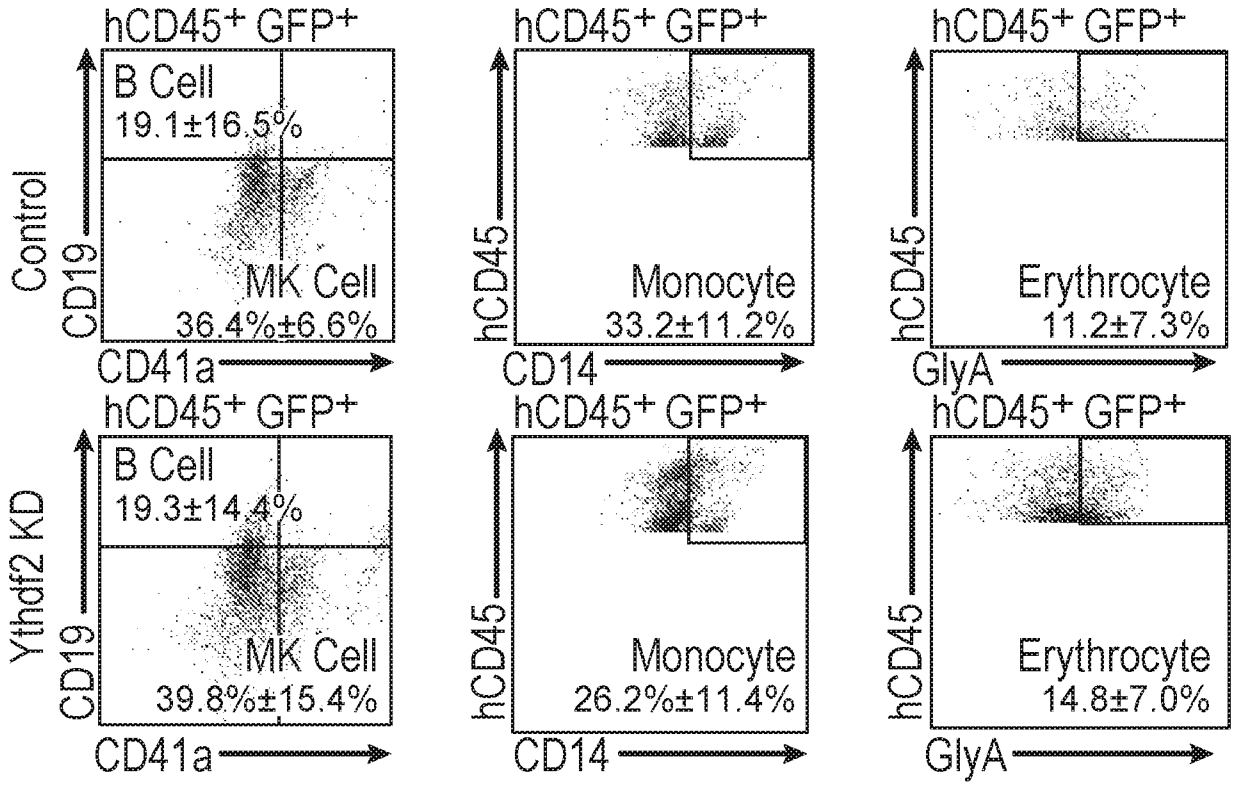


FIG. 15A

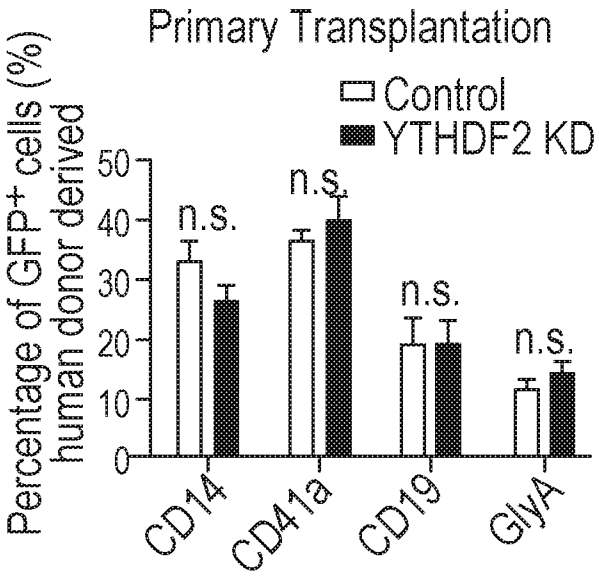


FIG. 15B

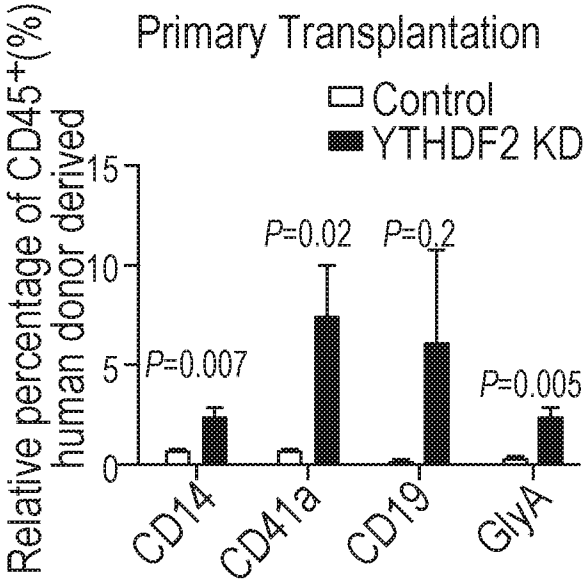


FIG. 15C

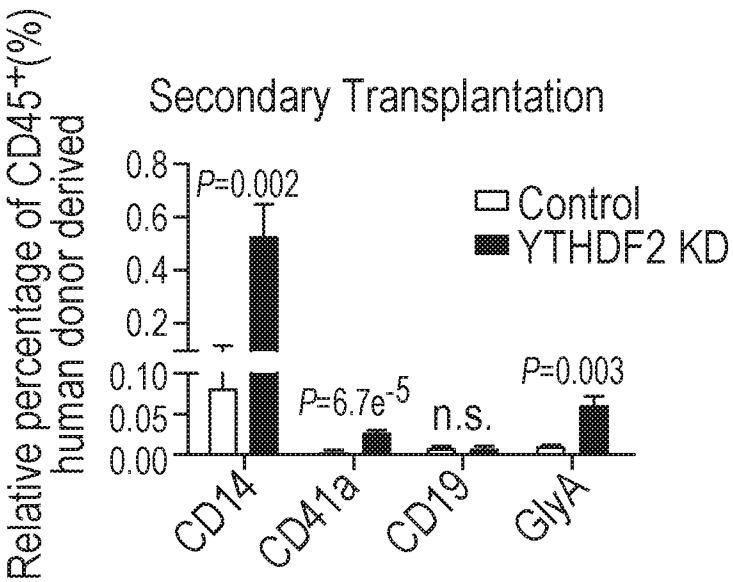


FIG. 15D

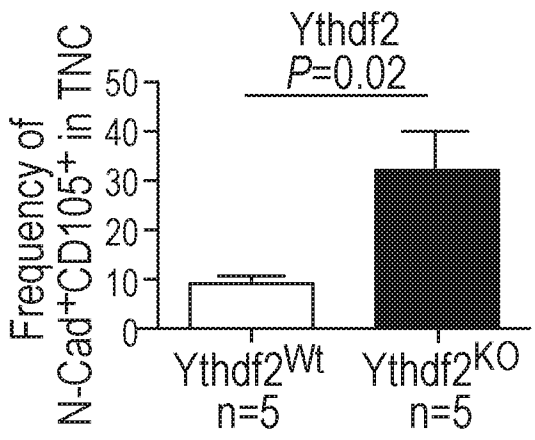


FIG. 16

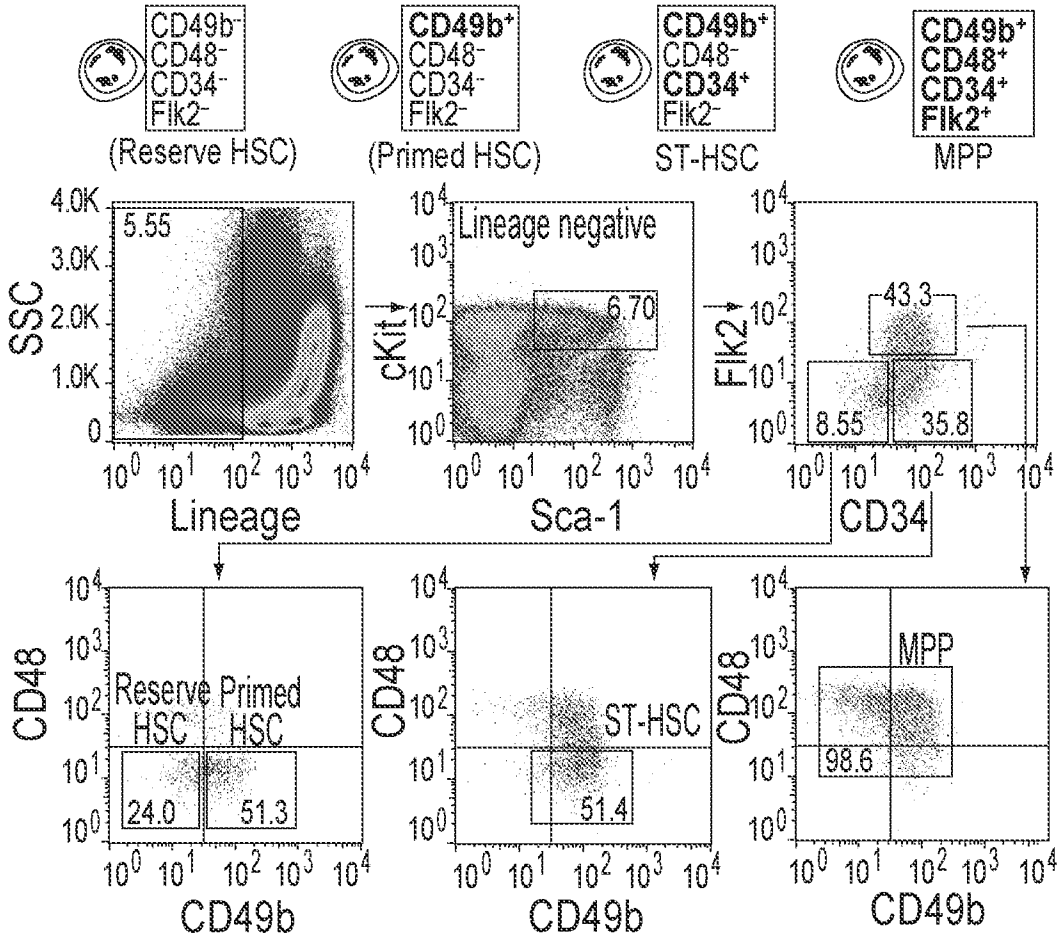


FIG. 17A

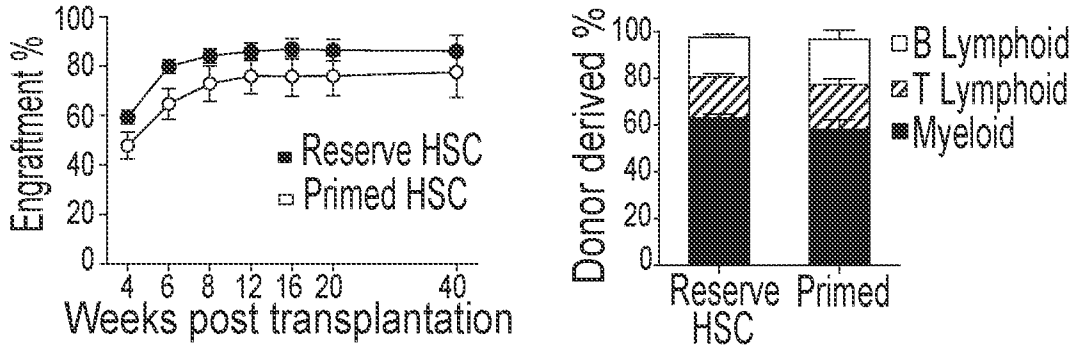


FIG. 17B

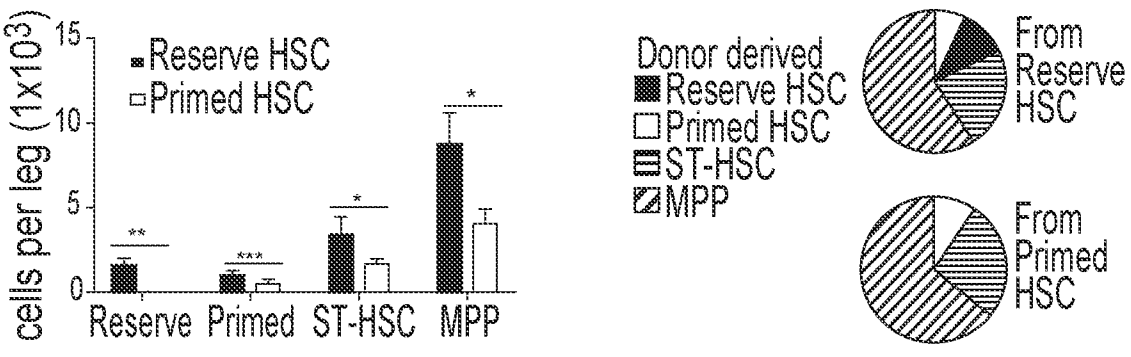


FIG. 17C

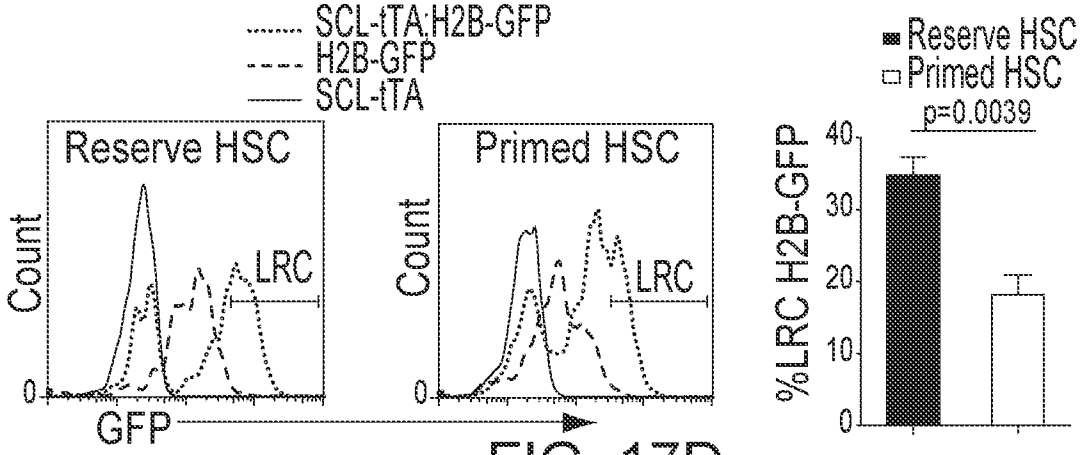


FIG. 17D

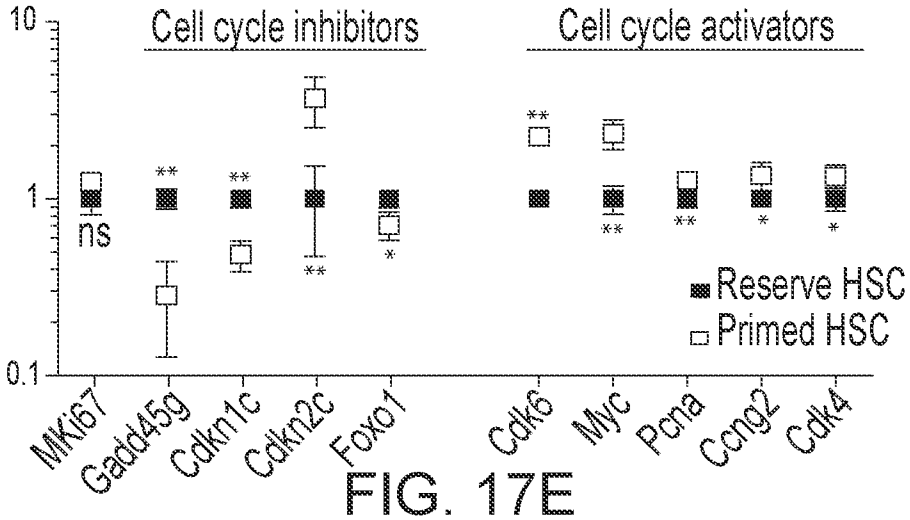


FIG. 17E

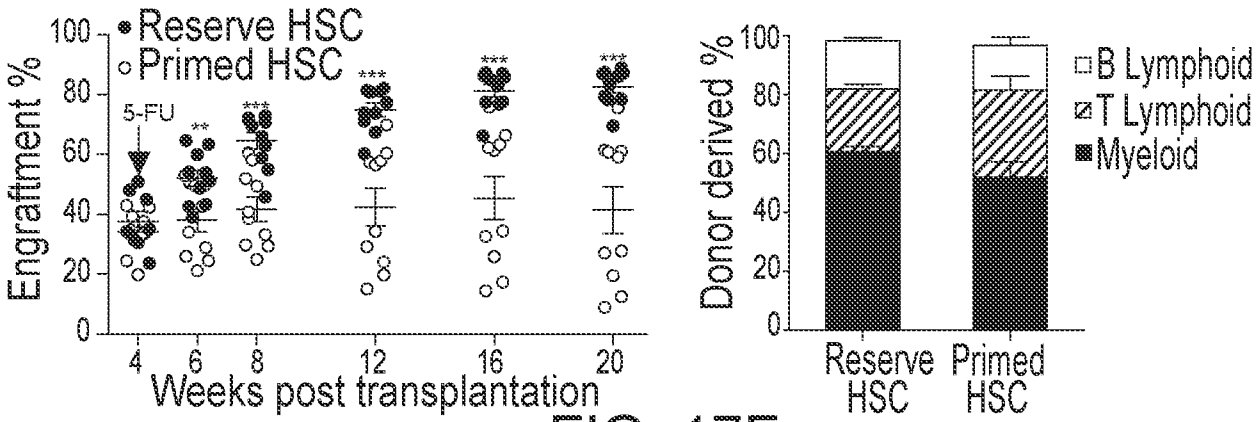


FIG. 17F

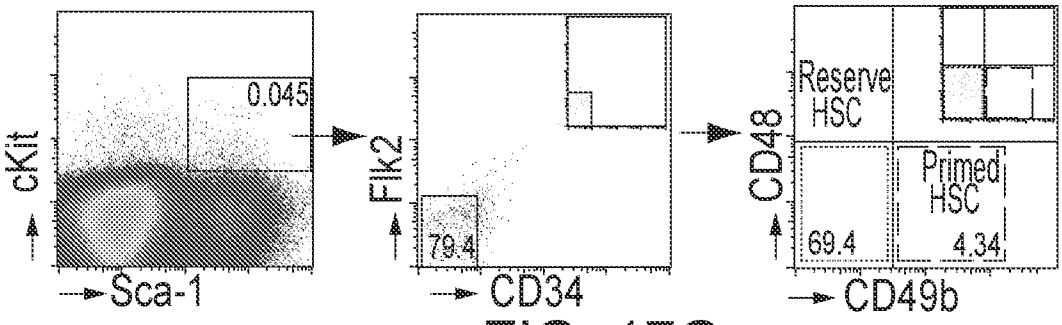


FIG. 17G

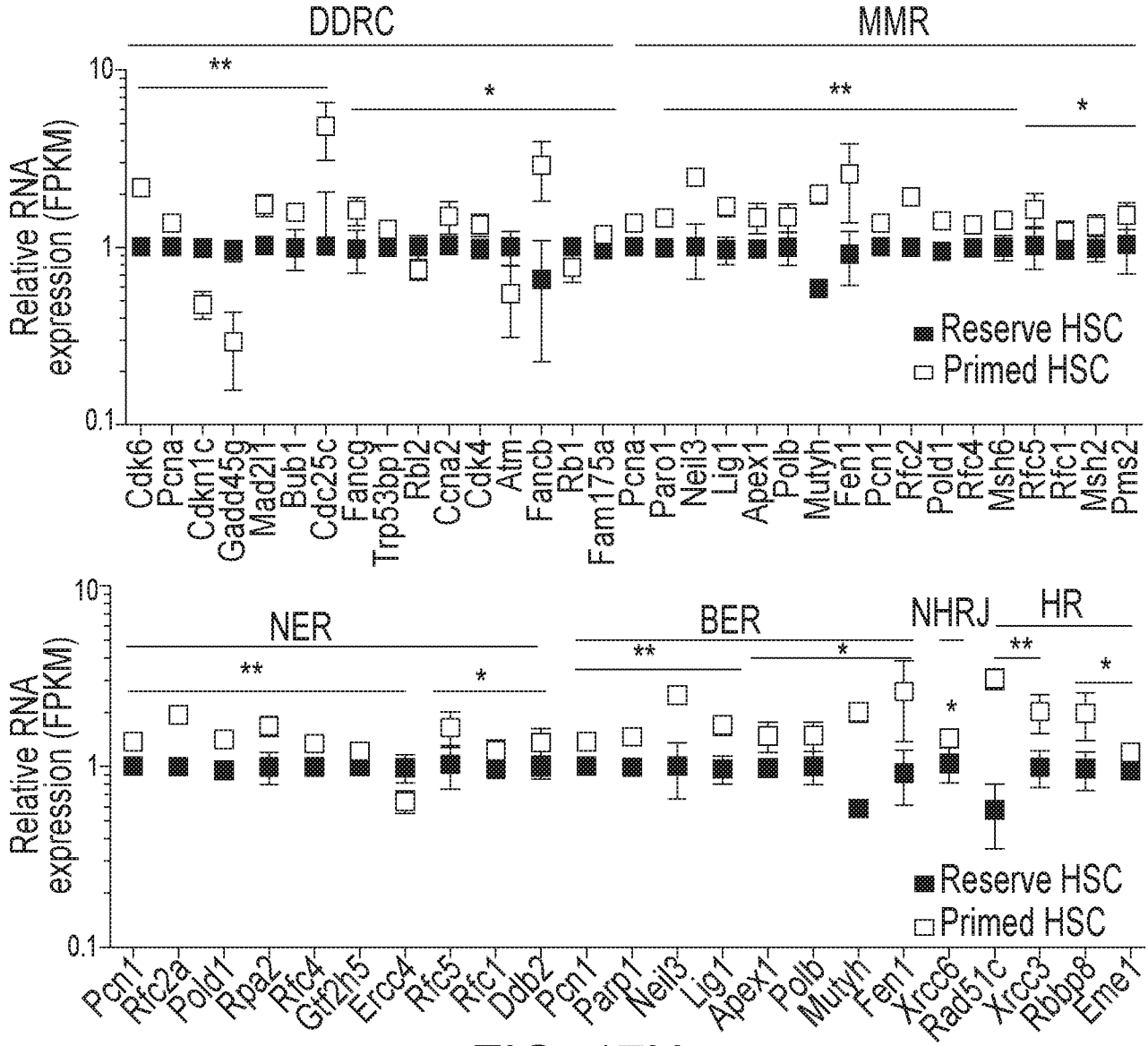


FIG. 17H

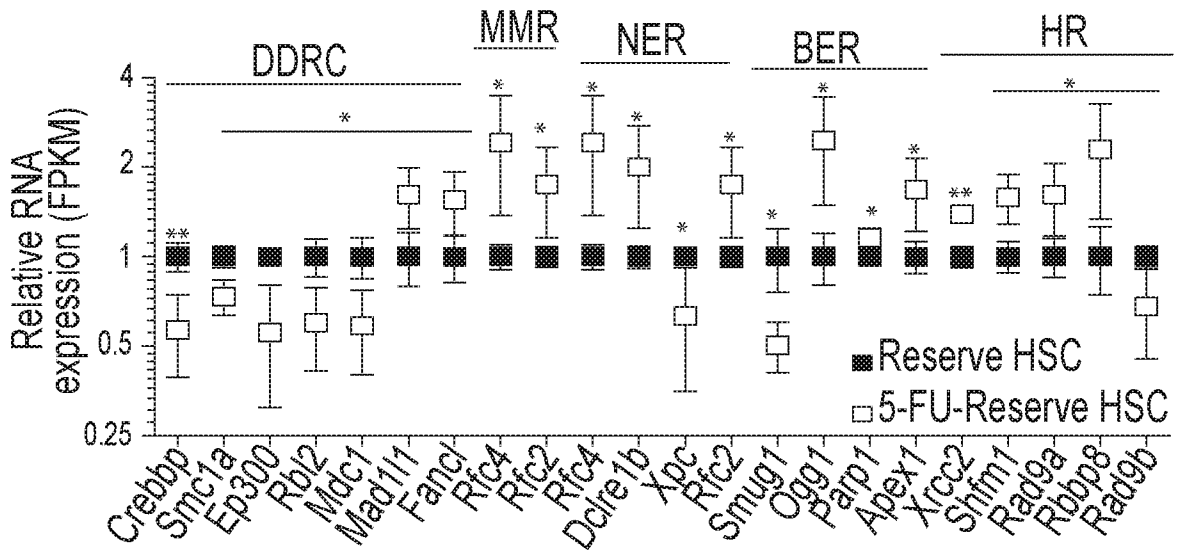


FIG. 17I

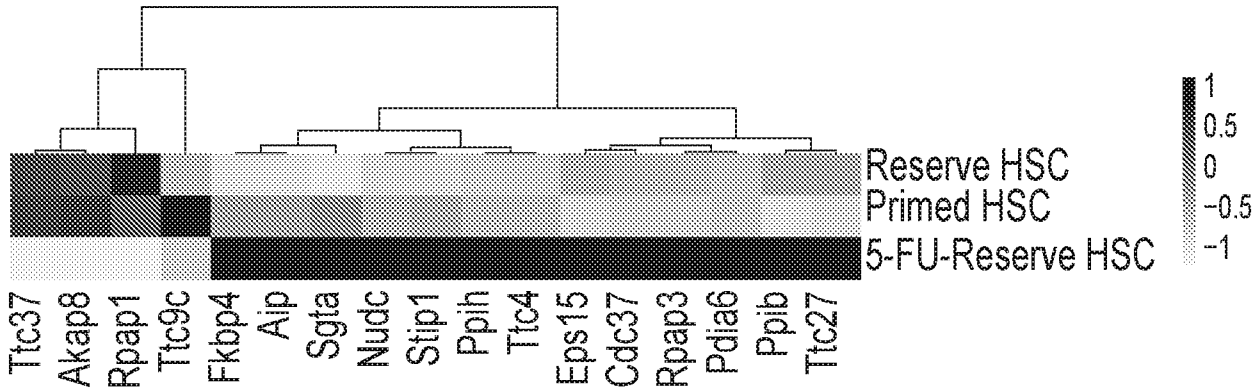

Reserve HSC
Primed HSC
5-FU-Reserve HSC
1
0.5
0
−0.5
−1
Ttc37
Akap8
Rpap1
Ttc9c
Fkbp4
Aip
Sgta
Nudc
Stip1
Ppih
Ttc4
Eps15
Cdc37
Rpap3
Pdia6
Ppib
Ttc27

FIG. 17J

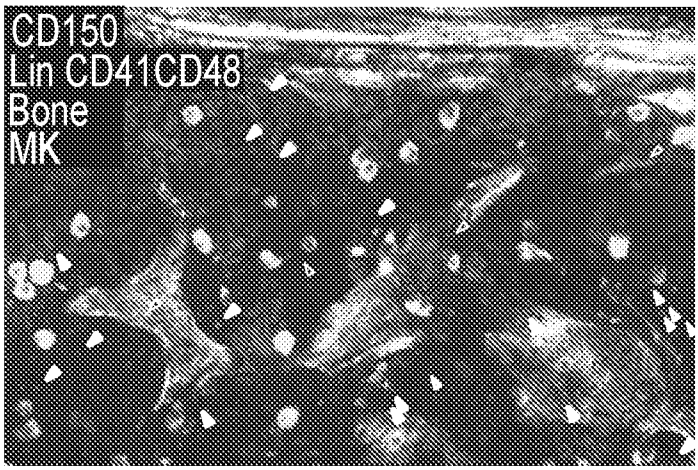


FIG. 18A

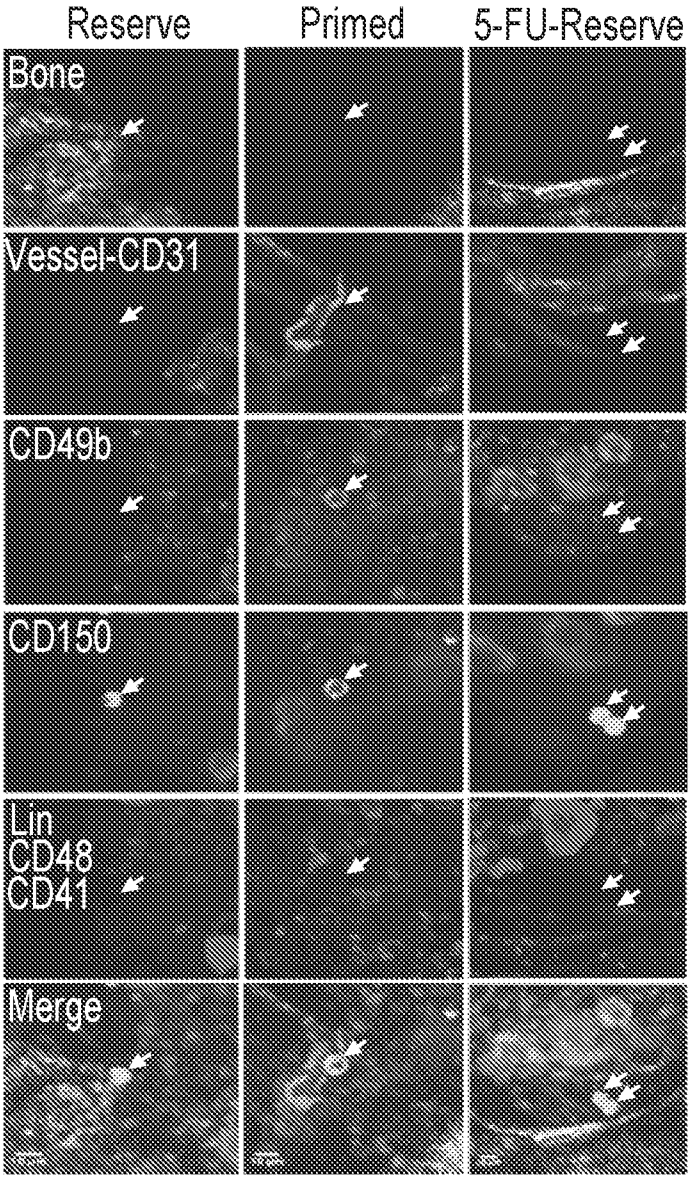


FIG. 18B

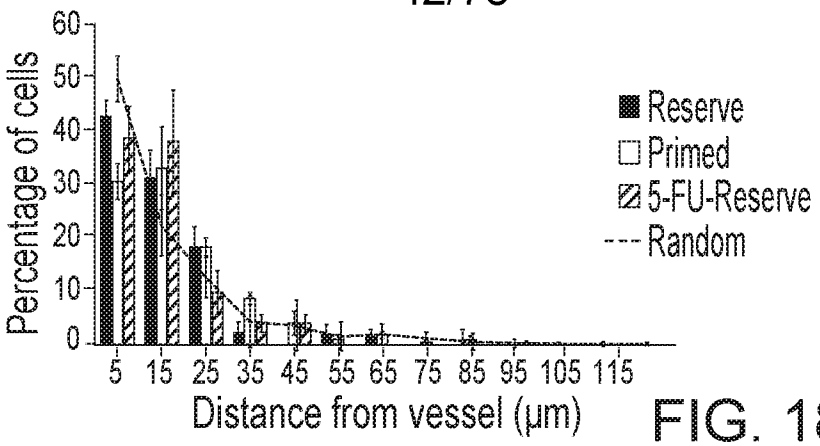


FIG. 18C

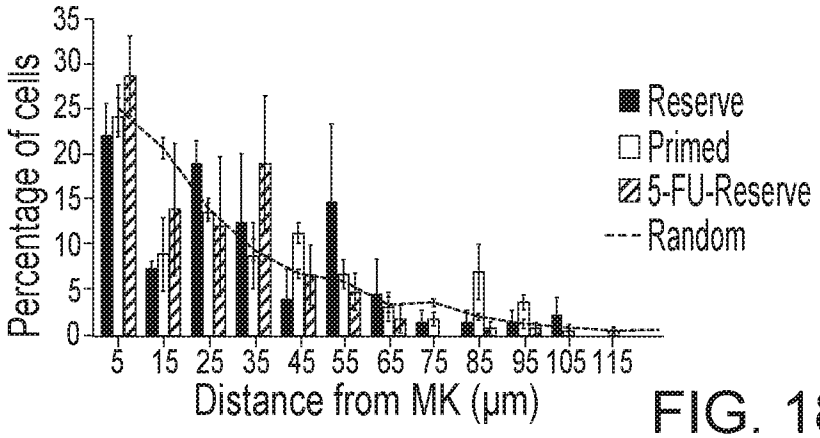


FIG. 18D

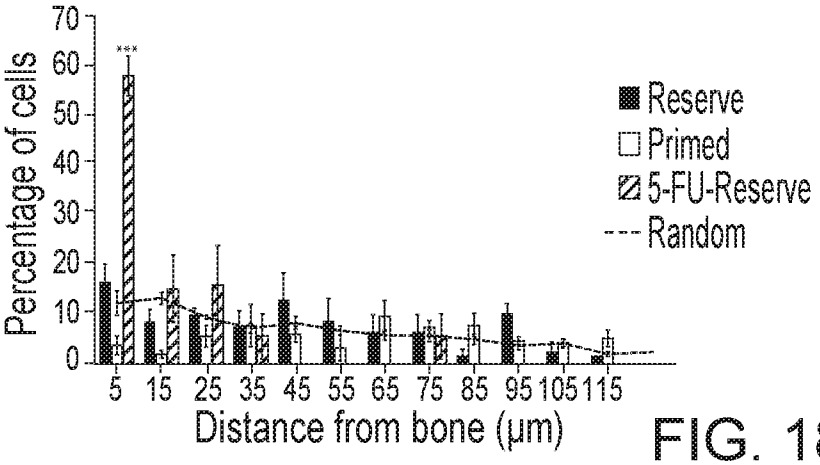


FIG. 18E

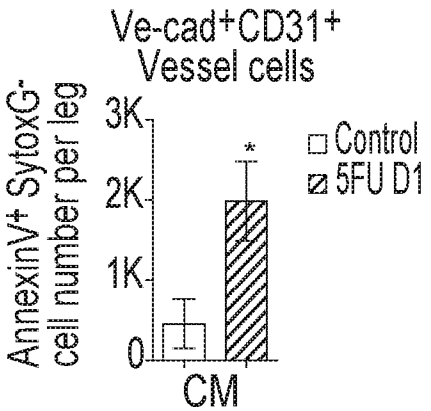


FIG. 18F

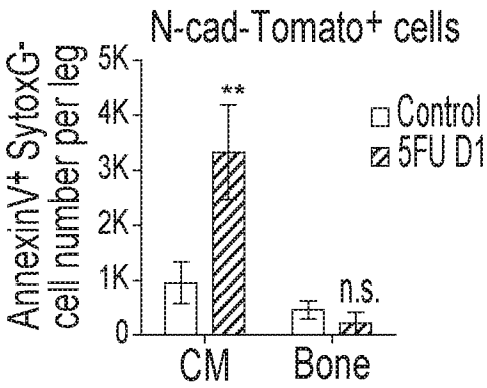


FIG. 18G

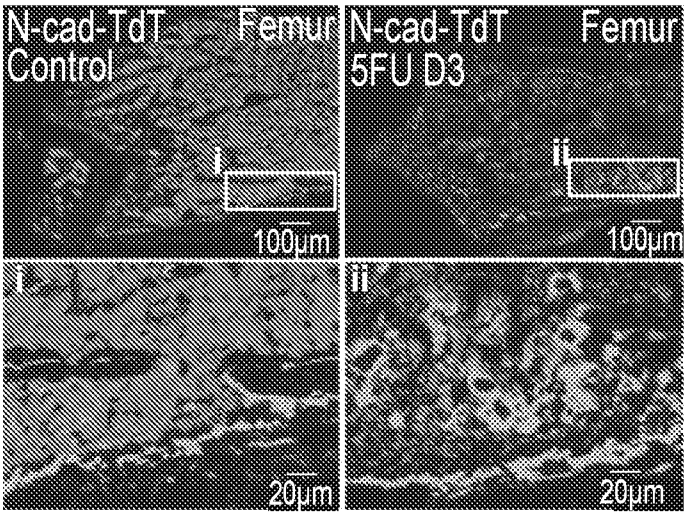


FIG. 18H

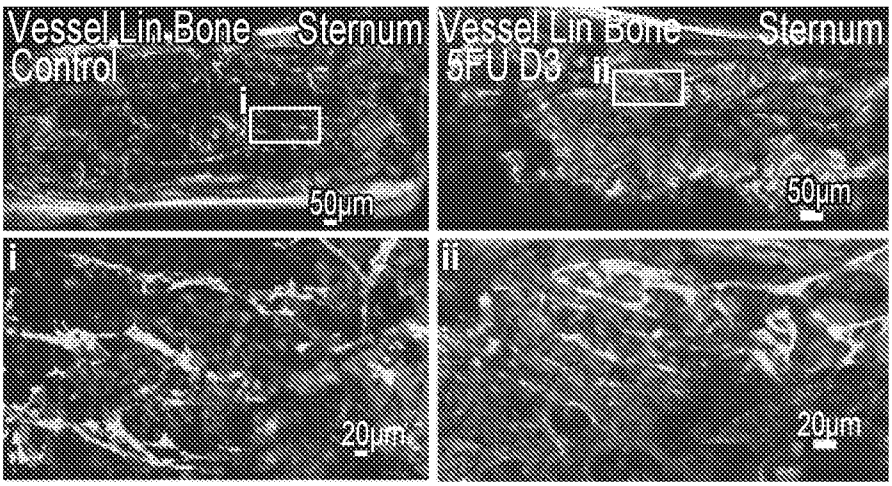


FIG. 18I

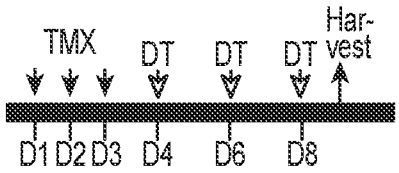


FIG. 19A

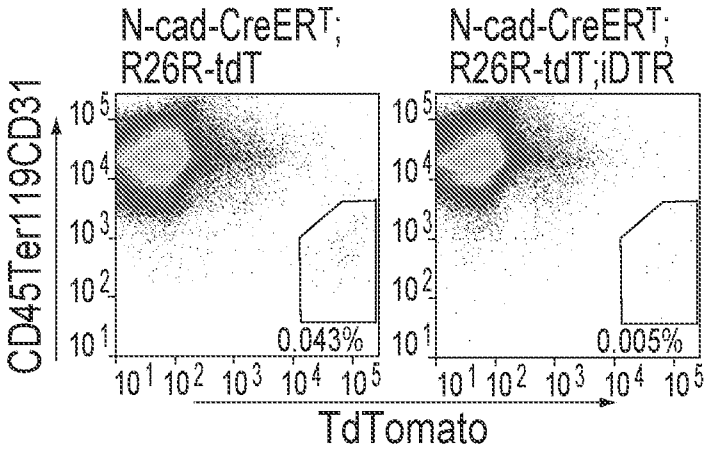


FIG. 19B

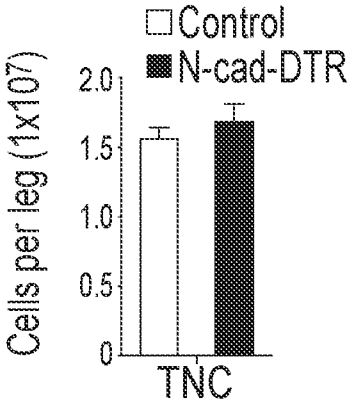


FIG. 19C

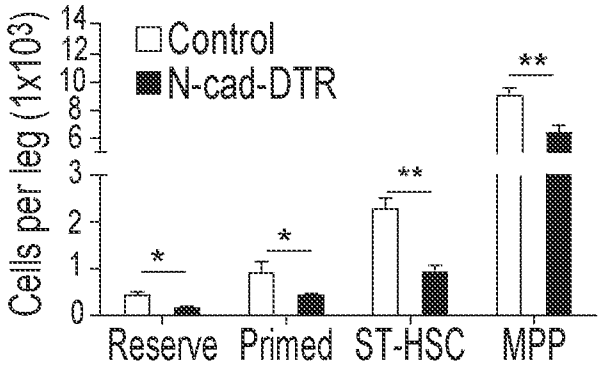


FIG. 19D

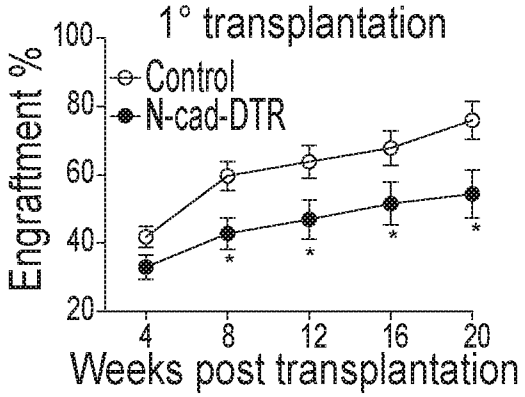


FIG. 19E

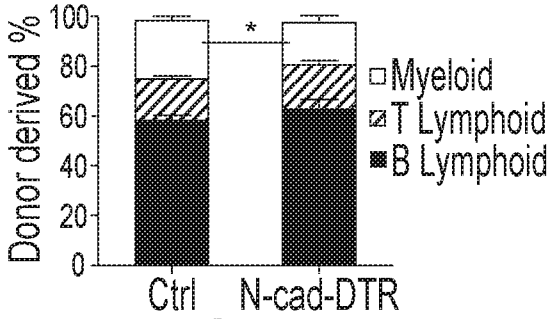


FIG. 19F

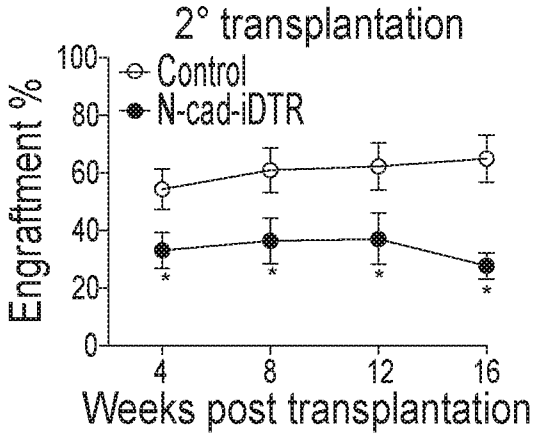


FIG. 19G

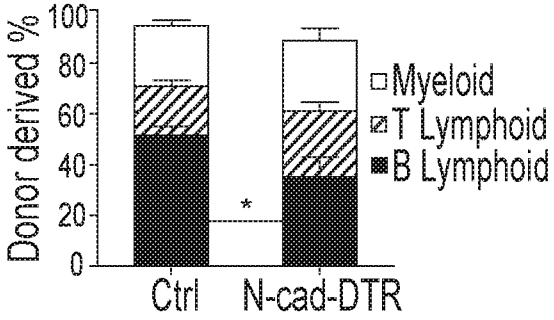


FIG. 19H

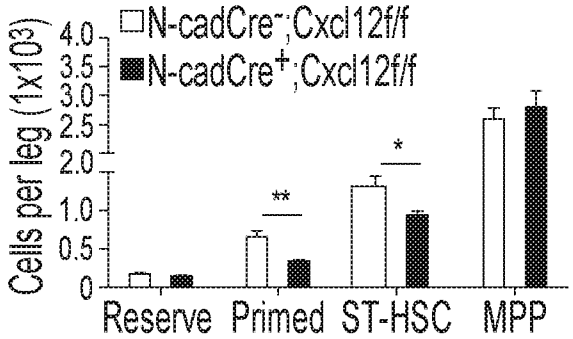


FIG. 19I

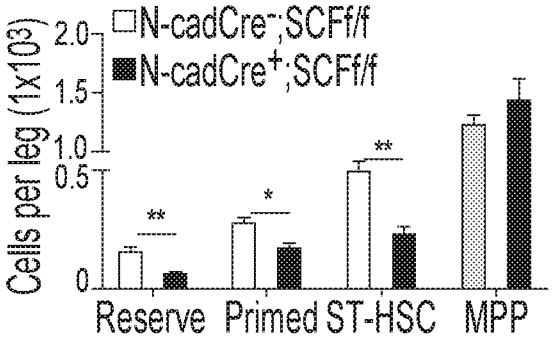


FIG. 19J

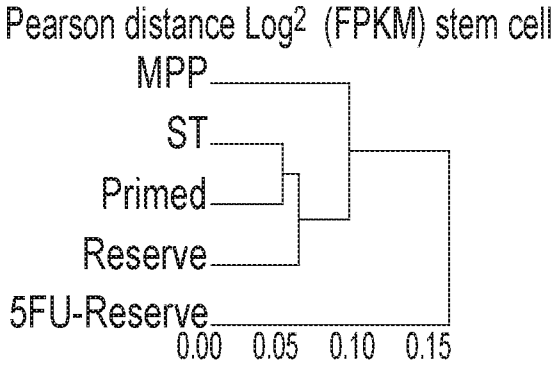


FIG. 20A

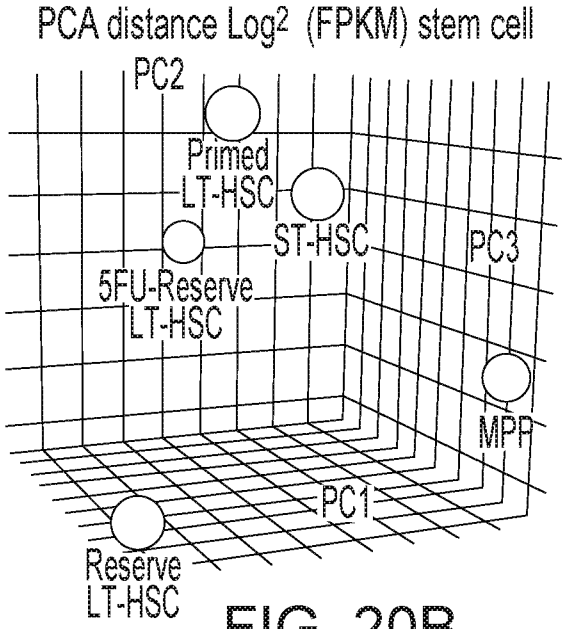


FIG. 20B

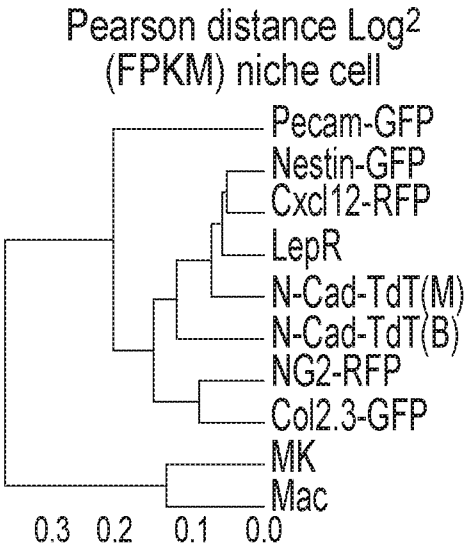


FIG. 20C

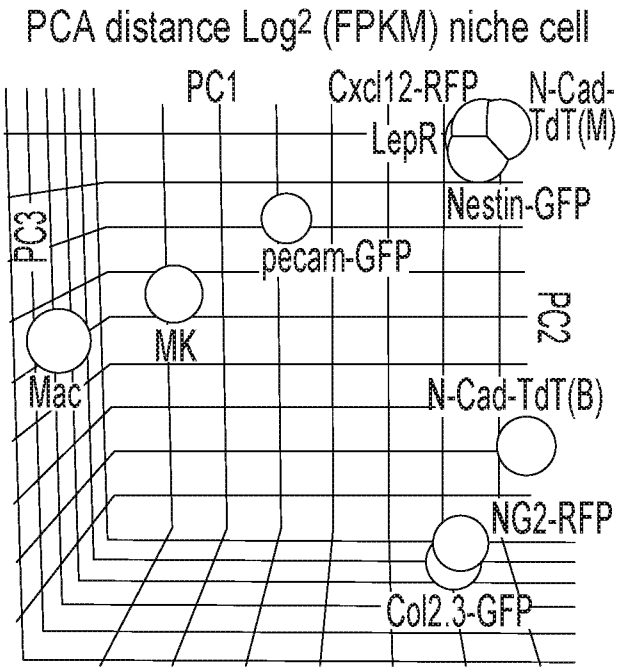


FIG. 20D

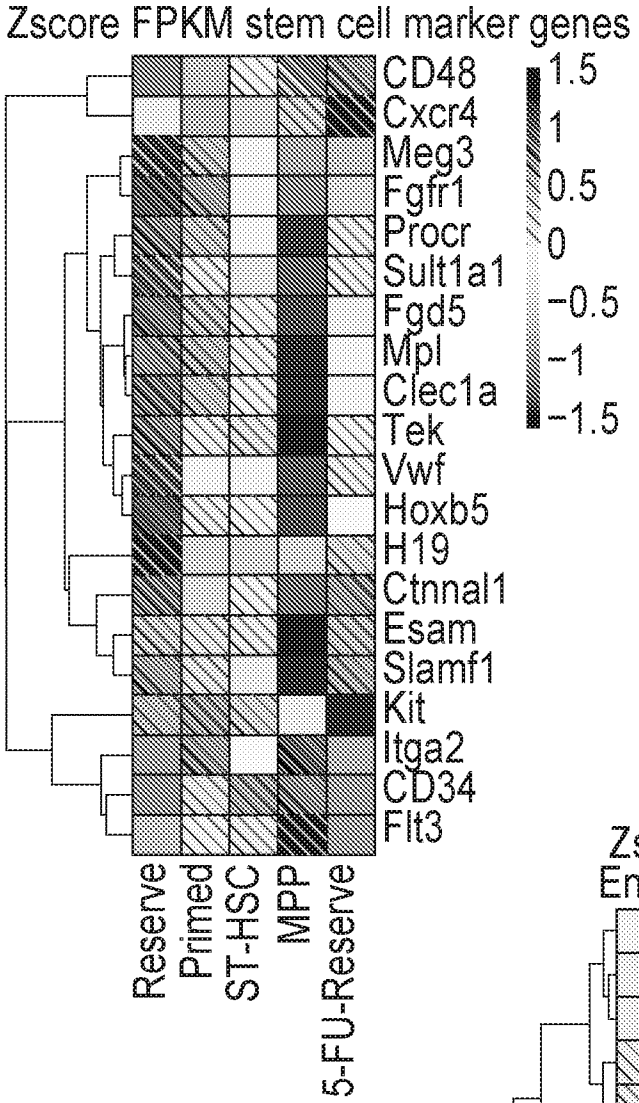


FIG. 20E

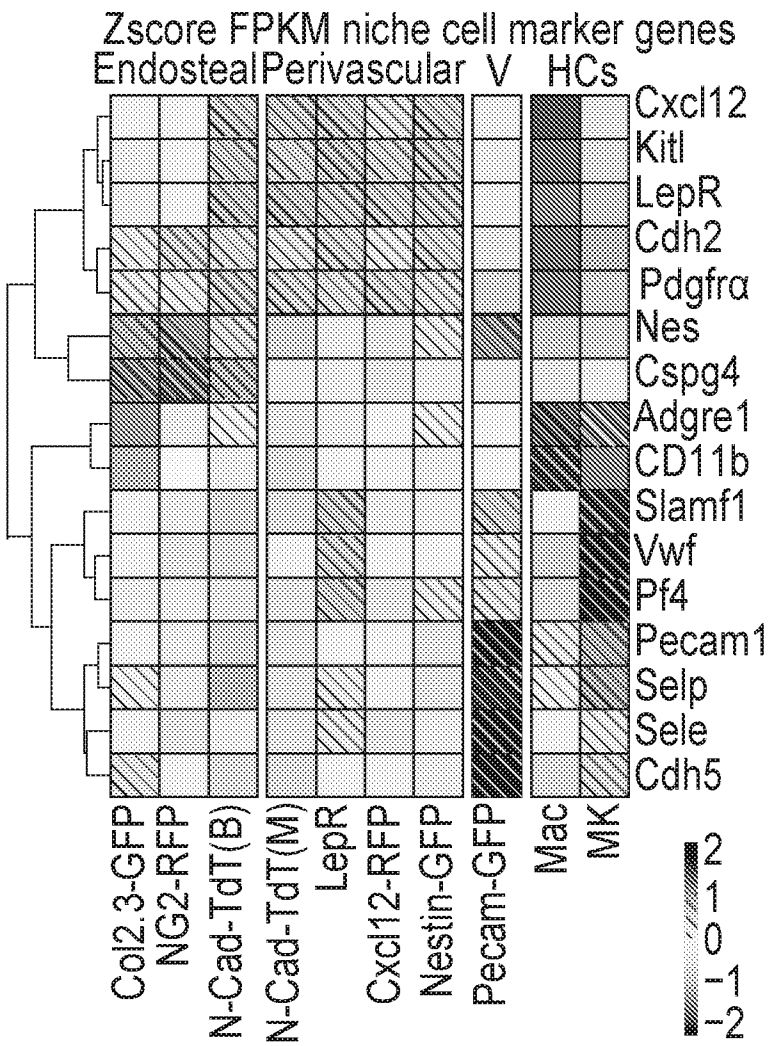


FIG. 20F

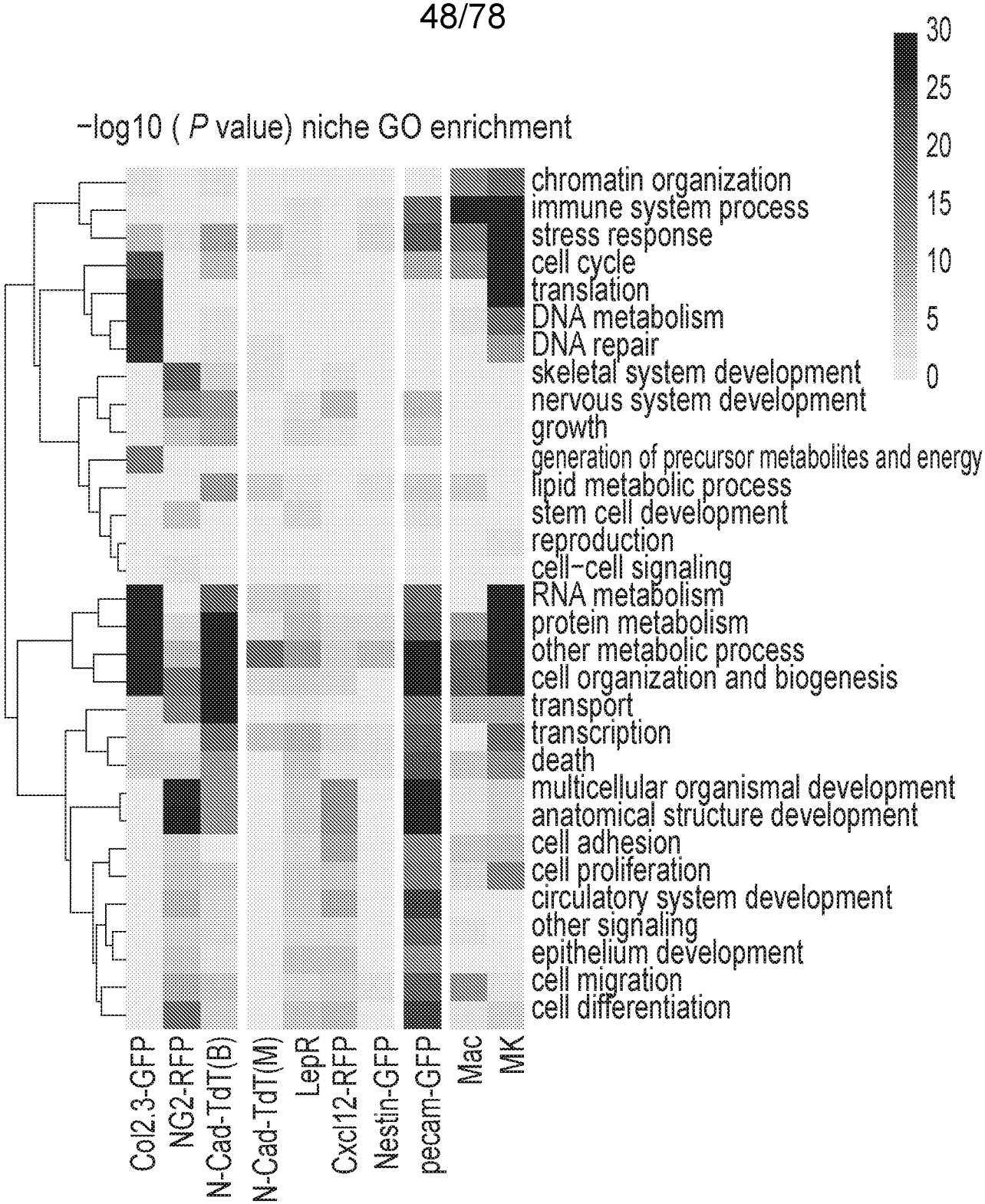

−log10 (P value) niche GO enrichment
30
25
20
15
10
5
0
chromatin organization
immune system process
stress response
cell cycle
translation
DNA metabolism
DNA repair
skeletal system development
nervous system development
growth
generation of precursor metabolites and energy
lipid metabolic process
stem cell development
reproduction
cell−cell signaling
RNA metabolism
protein metabolism
other metabolic process
cell organization and biogenesis
transport
transcription
death
multicellular organismal development
anatomical structure development
cell adhesion
cell proliferation
circulatory system development
other signaling
epithelium development
cell migration
cell differentiation
Col2.3-GFP
NG2-RFP
N-Cad-TdT(B)
N-Cad-TdT(M)
LepR
Cxcl12-RFP
Nestin-GFP
pecam-GFP
Mac
MK

FIG. 20G

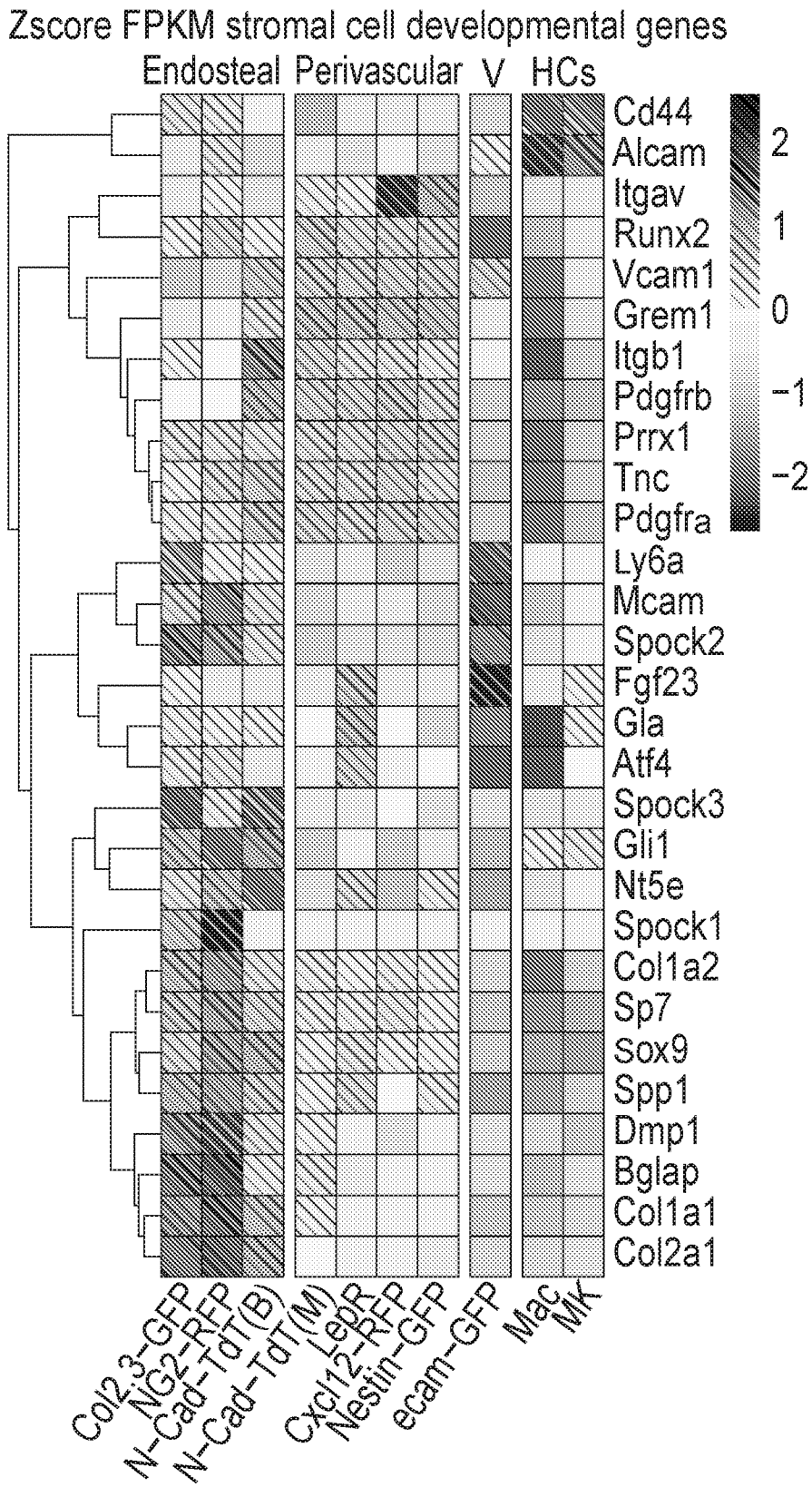

Zscore FPKM stromal cell developmental genes
Endosteal
Perivascular
V
HCs
Cd44
Alcam
Itgav
Runx2
Vcam1
Grem1
Itgb1
Pdgfrb
Prrx1
Tnc
Pdgfra
Ly6a
Mcam
Spock2
Fgf23
Gla
Atf4
Spock3
Gli1
Nt5e
Spock1
Col1a2
Sp7
Sox9
Spp1
Dmp1
Bglap
Col1a1
Col2a1
2
1
0
−1
−2
Col2.3−GFP
NG2−RFP
N−Cad−TdT(B)
N−Cad−TdT(M)
LepR
Cxcl12−RFP
Nestin−GFP
ecam−GFP
Mac
MK

FIG. 20H

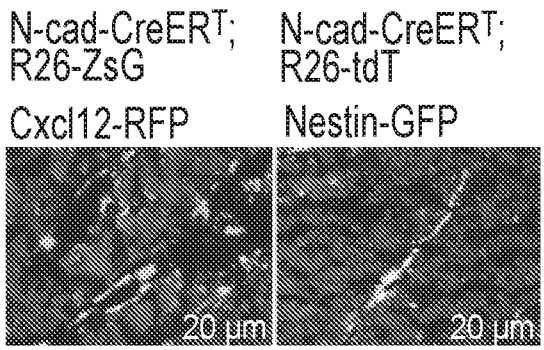

N-cad-CreER^T; R26-ZsG
Cxcl12-RFP
20 μm
N-cad-CreER^T; R26-tdT
Nestin-GFP
20 μm

FIG. 20I

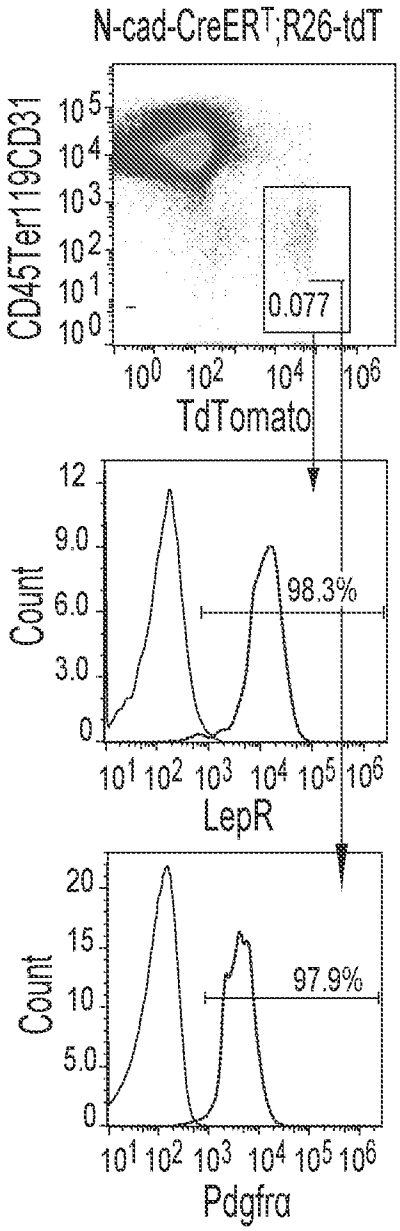


FIG. 20J

Stromal cell population	Cell dose	CFU-F colony per well	CFU-F frequency
N-cad-TdT(B)	1 5 10	4/32 12/32 12/16	1 in 8.79
LepR	1 5 10	1/8 17/40 25/40	1 in 9.7
NG2-RFP	1 5 10	1/2 4/5 4/7	1 in 6.72
Nestin-GFP	1 5 10	0/8 8/40 19/40	1 in 17.6
N-cad-CreER^T(B)	1 5 10	2/32 12/32 20/32	1 in 10.7
N-cad-CreER^T(M)	1 5 10	1/8 18/40 31/40	1 in 7.37

FIG. 20K

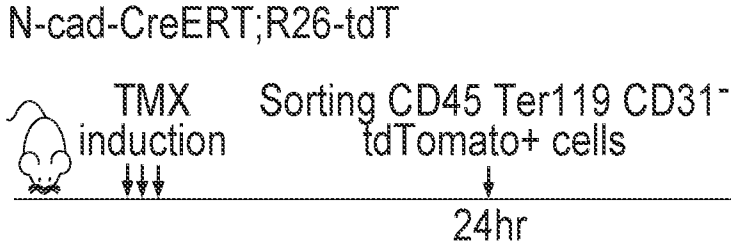


FIG. 21A

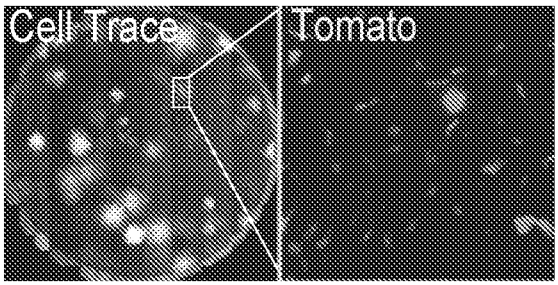


FIG. 21B

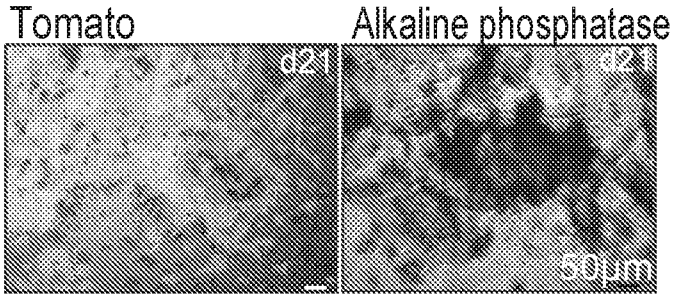


FIG. 21C

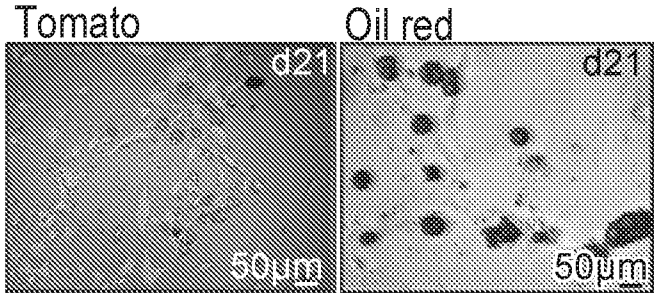


FIG. 21D

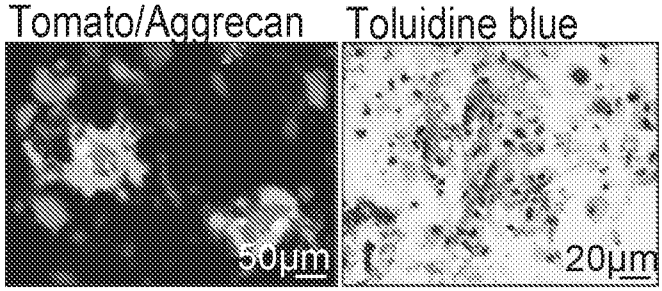


FIG. 21E

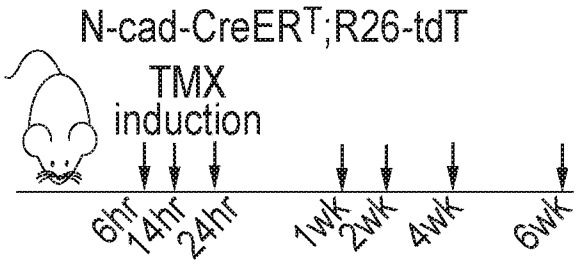


FIG. 21F

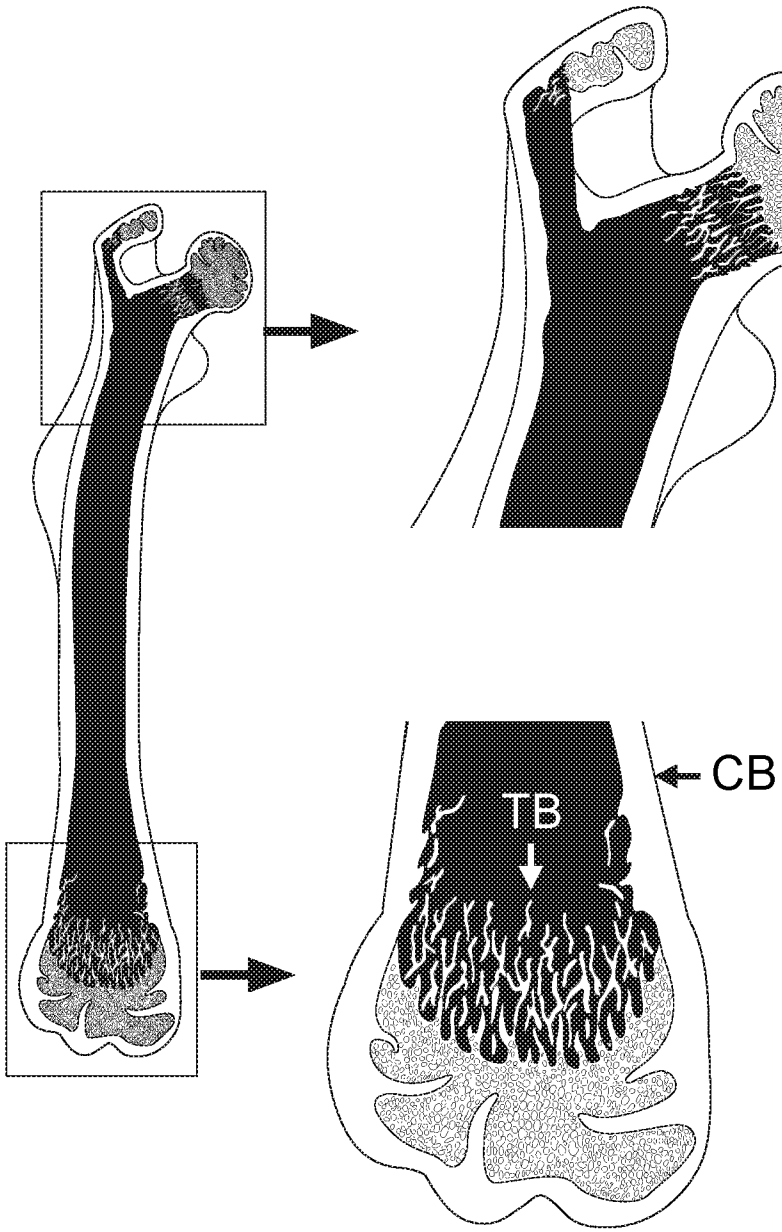


FIG. 21G

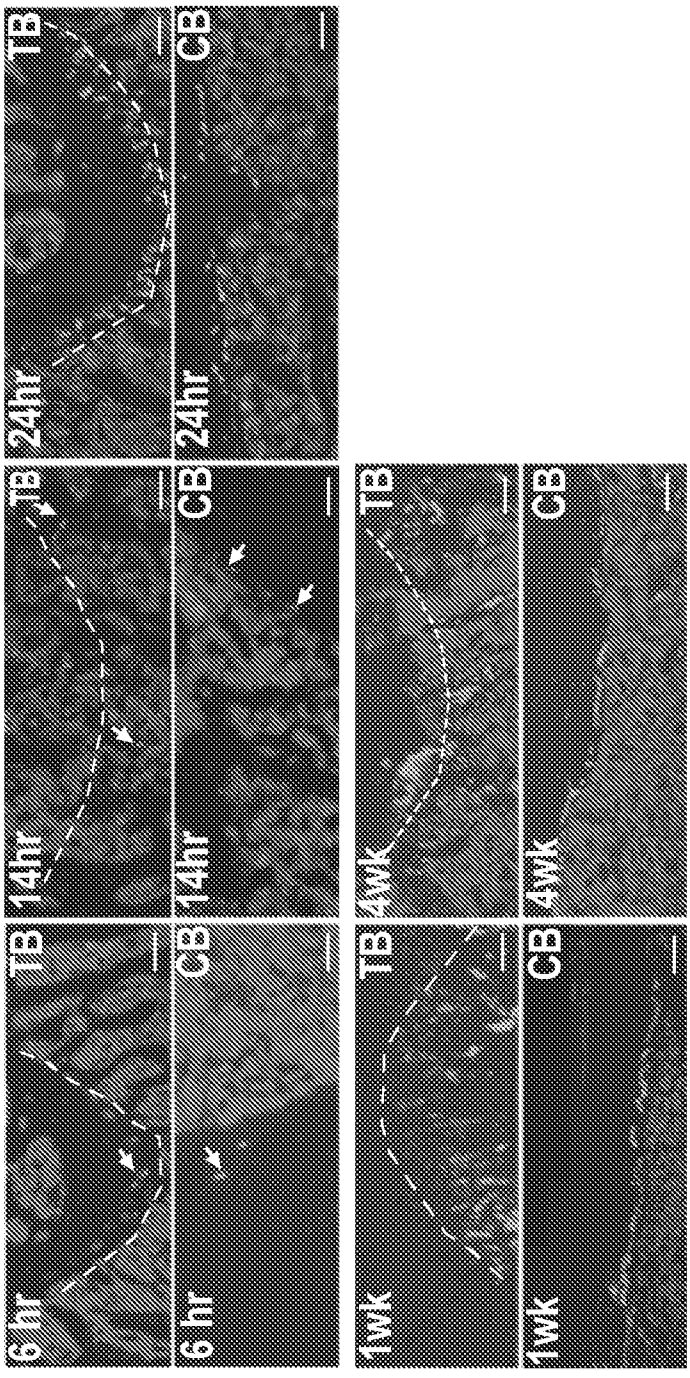


FIG. 21H

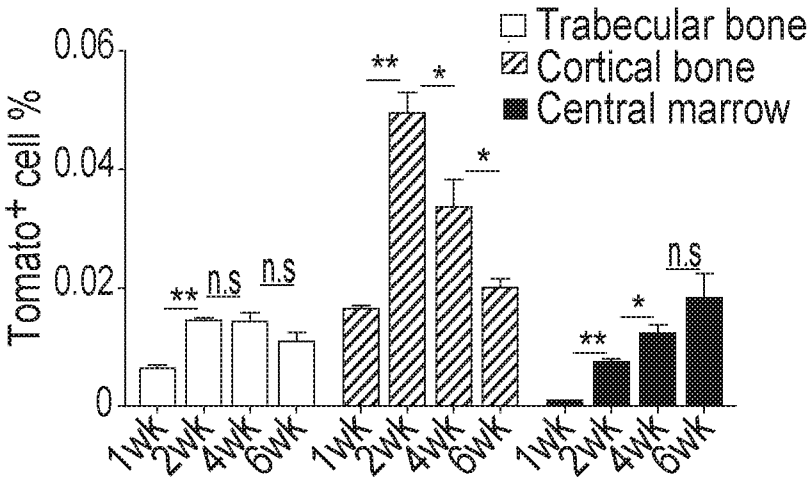

Trabecular bone
Cortical bone
Central marrow
Tomato+ cell %
0.06
0.04
0.02
0
**
n.s
n.s
**
*
*
**
*
n.s
1wk
2wk
4wk
6wk
1wk
2wk
4wk
6wk
1wk
2wk
4wk
6wk

FIG. 21I

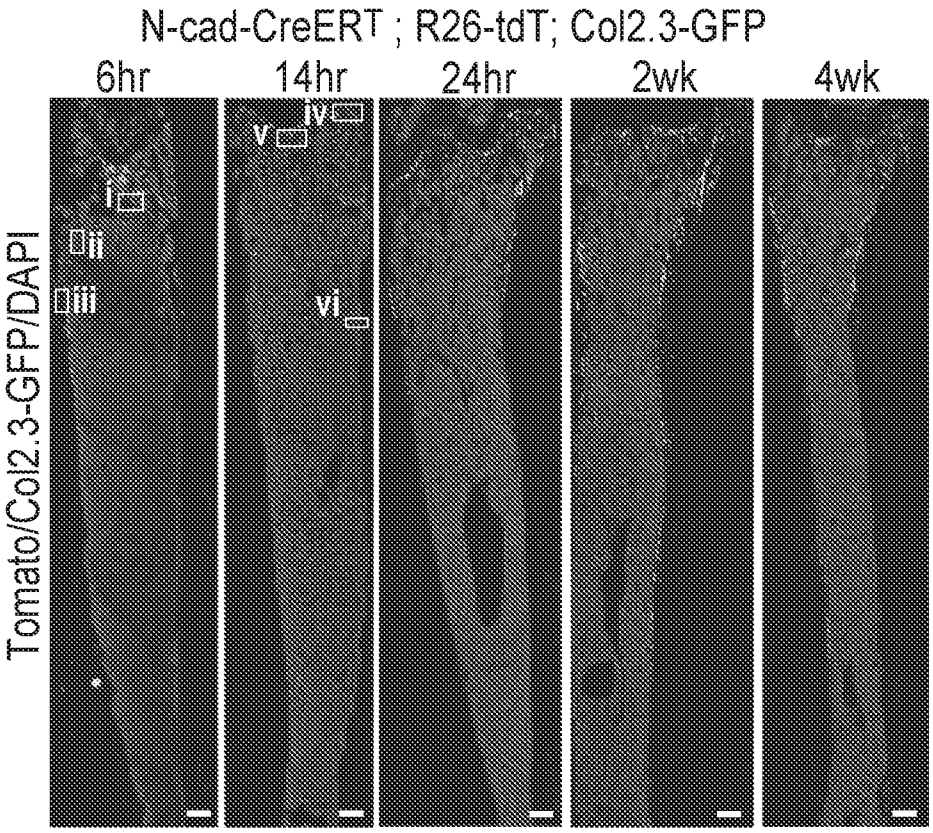


FIG. 22A

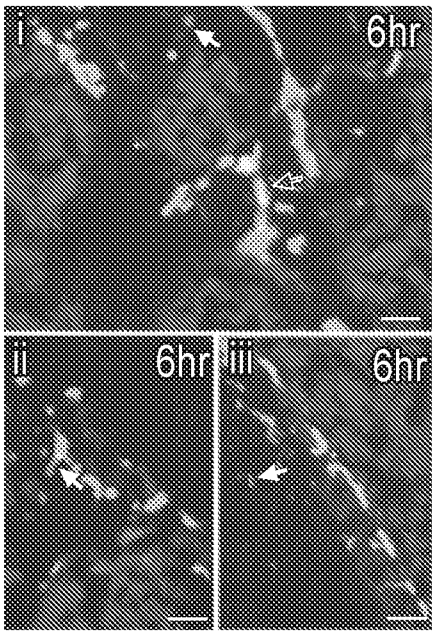


FIG. 22B

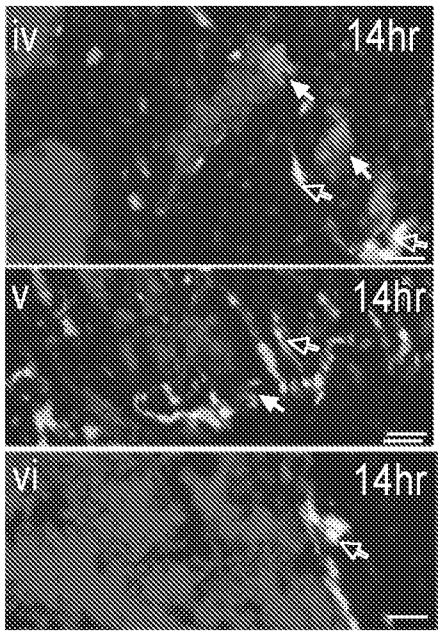


FIG. 22C

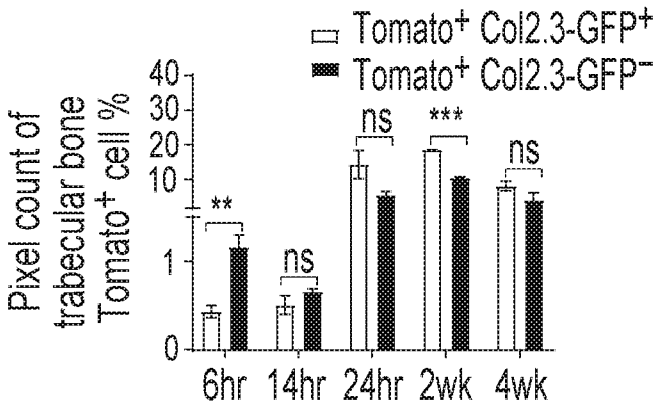


FIG. 22D

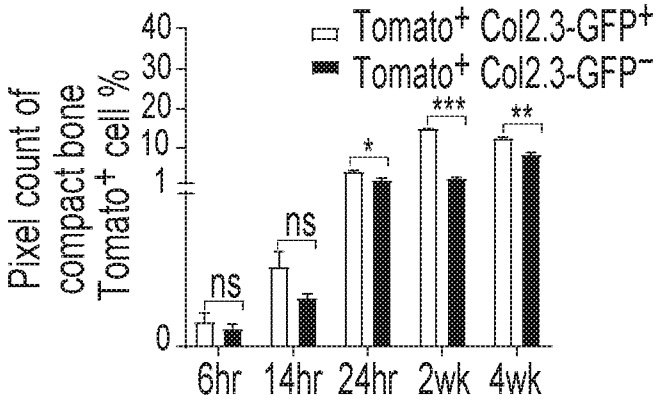


FIG. 22E

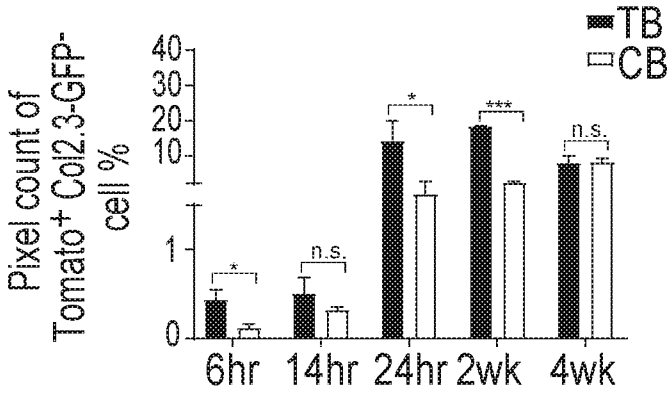


FIG. 22F

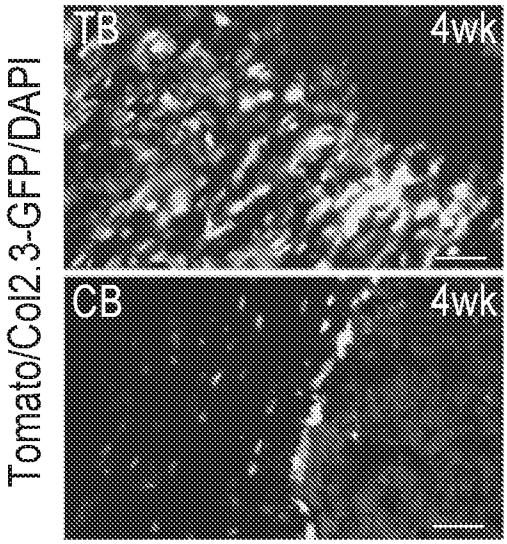


FIG. 22G

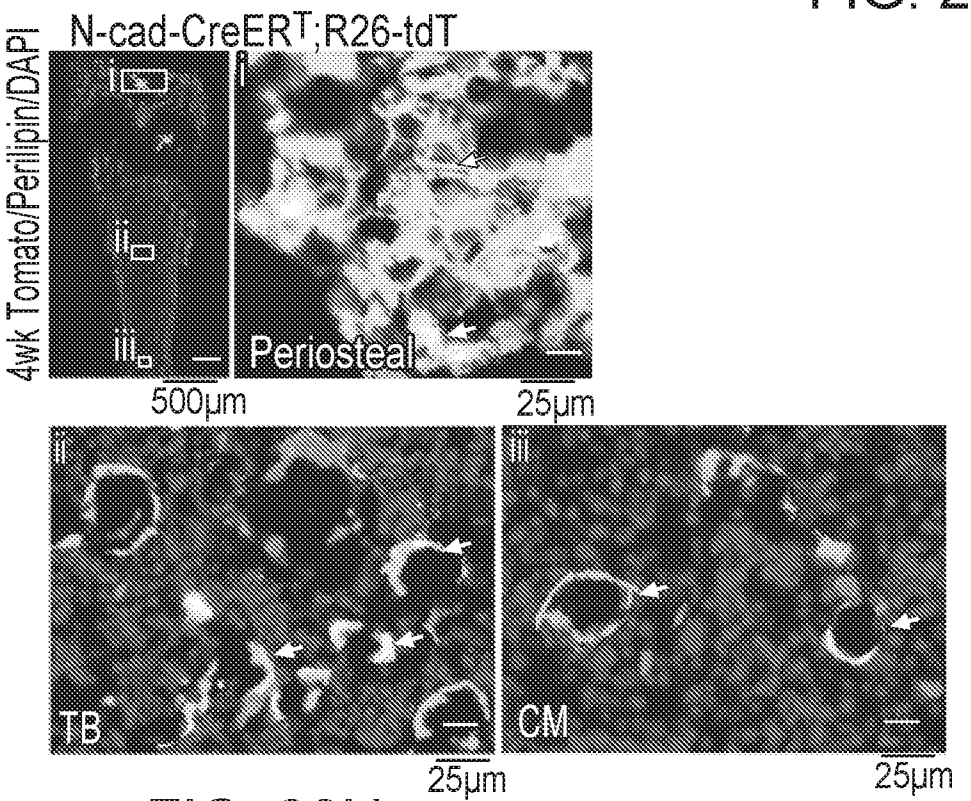


FIG. 22H

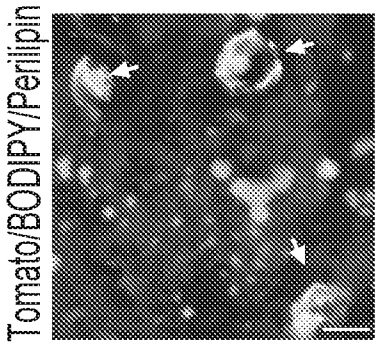


FIG. 22I

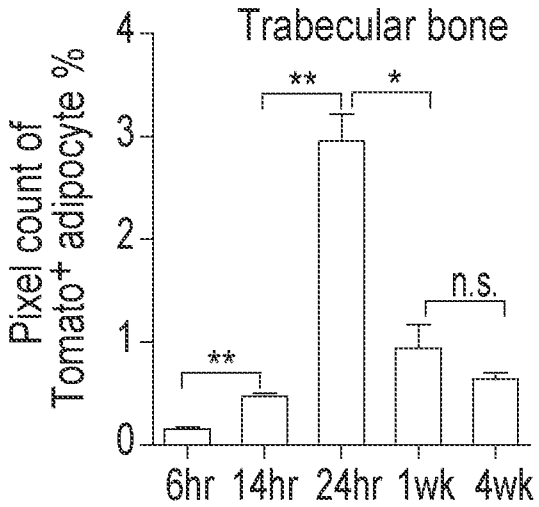


FIG. 22J

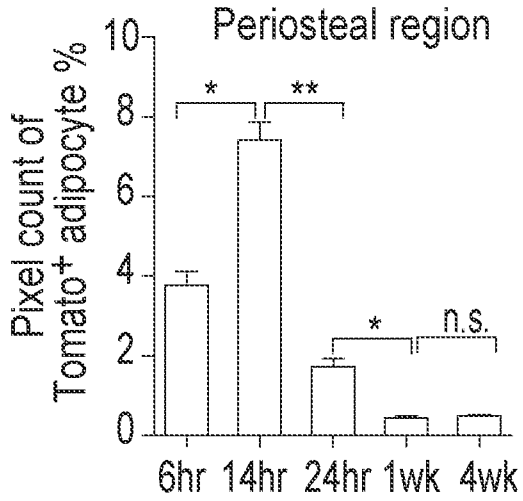


FIG. 22K

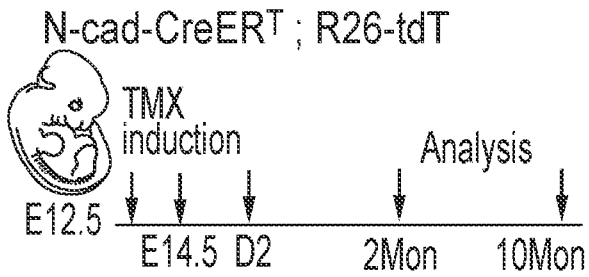


FIG. 23A

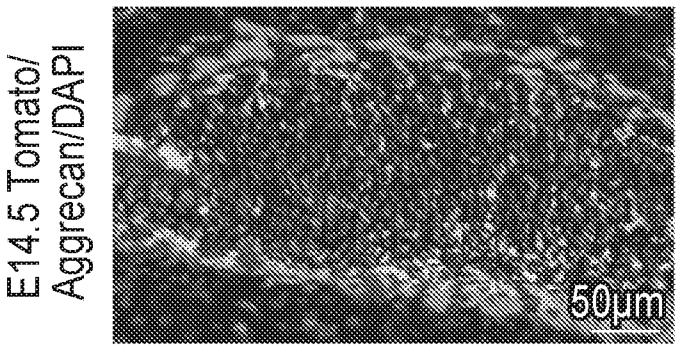


FIG. 23B

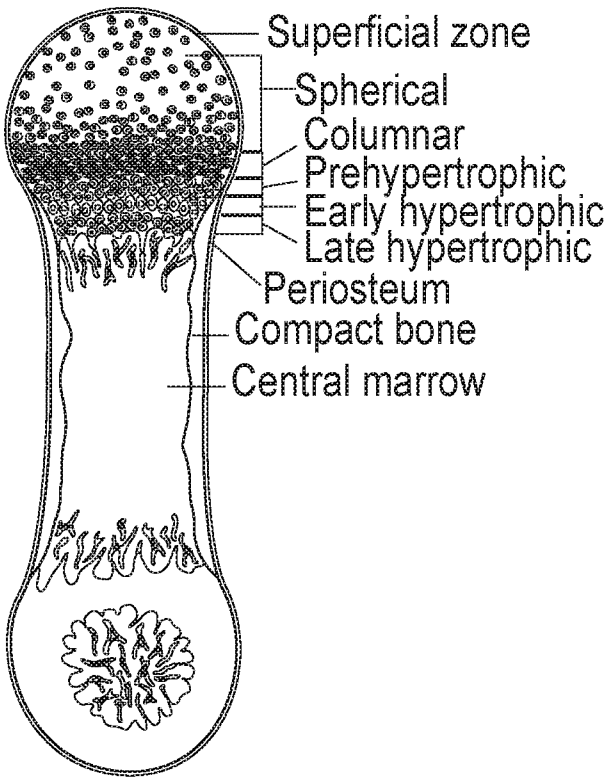


FIG. 23C

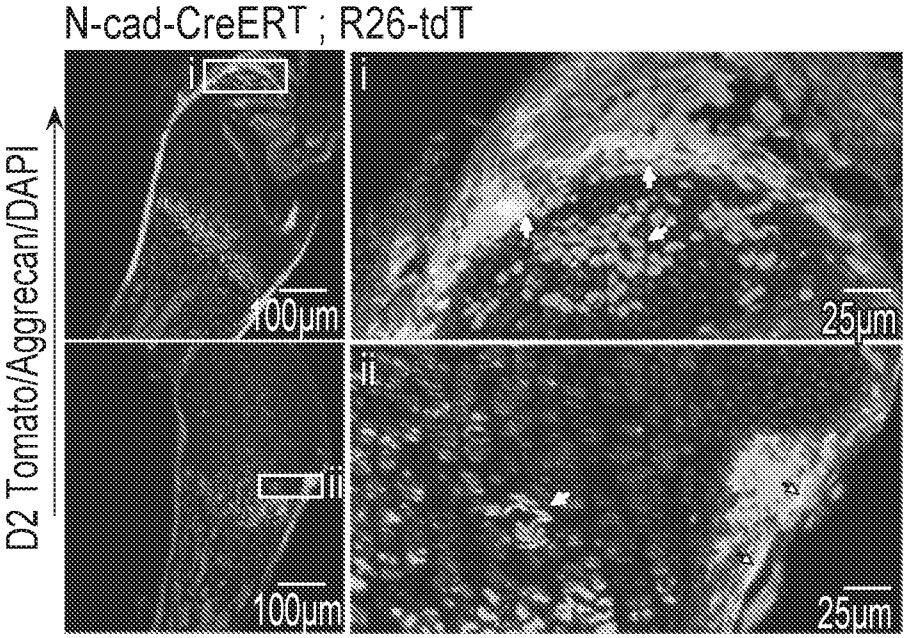


FIG. 23D

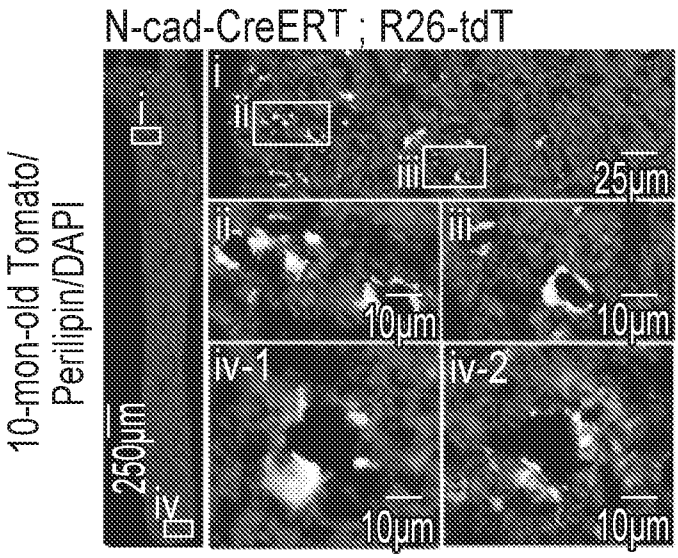


FIG. 23E

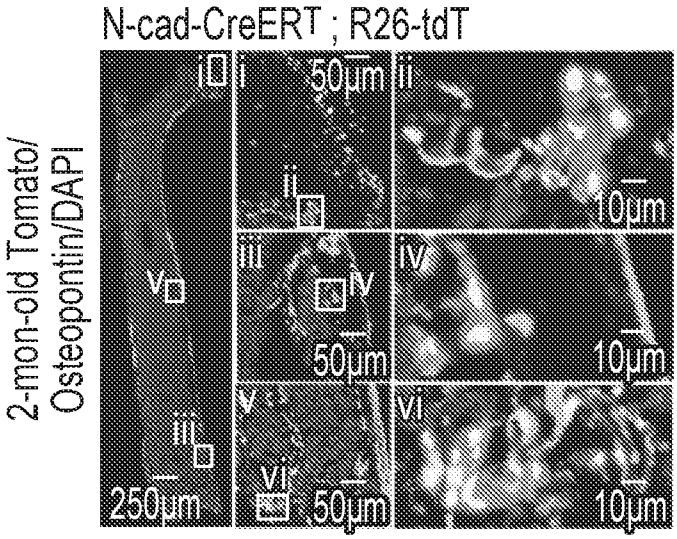


FIG. 23F

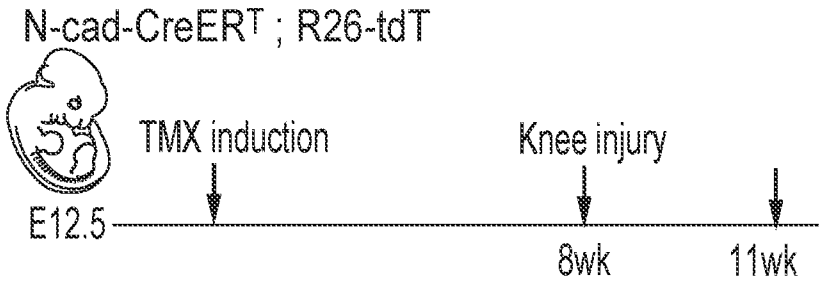


FIG. 23G

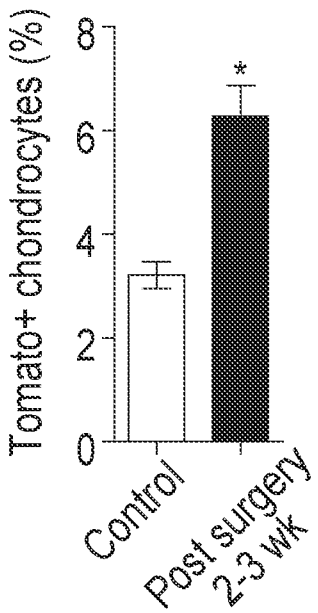


FIG. 23H

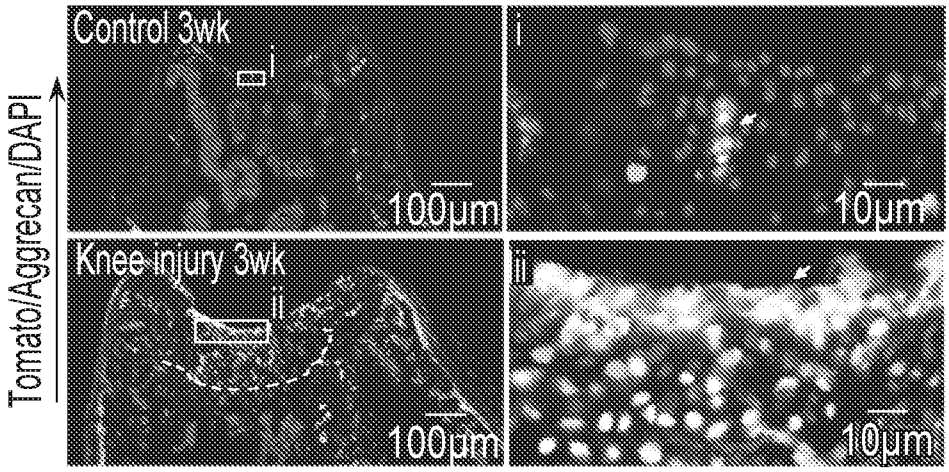


FIG. 23I

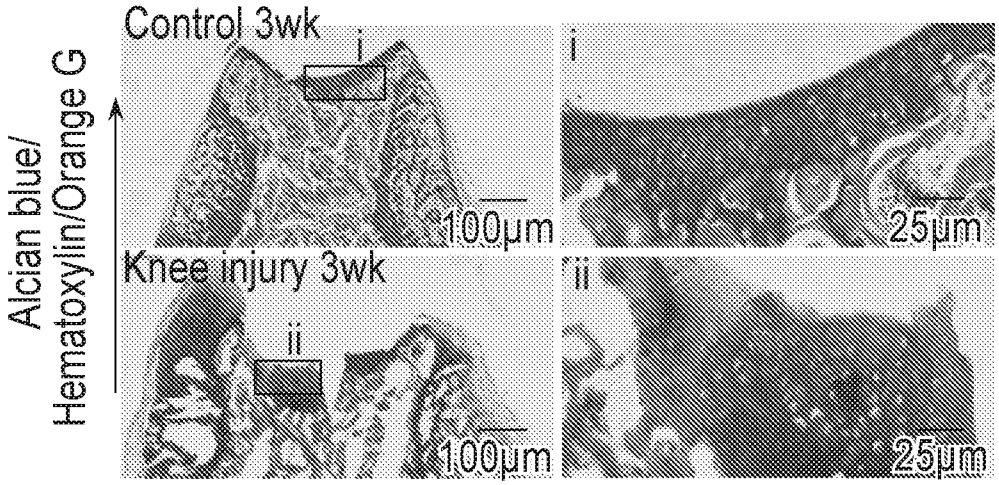


FIG. 23J

FIG. 24A

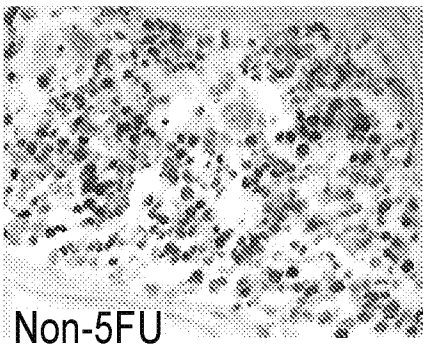


FIG. 24B

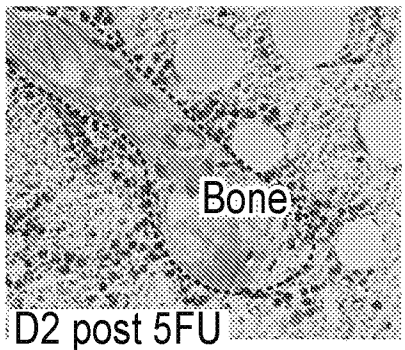
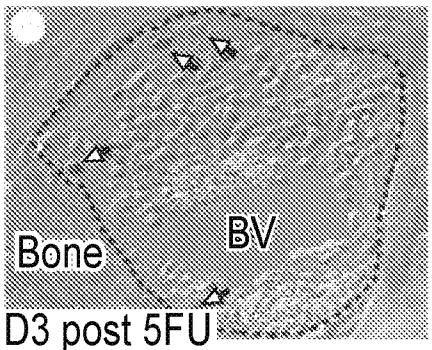


FIG. 24C



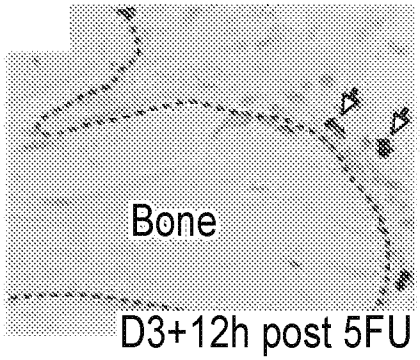


FIG. 24D

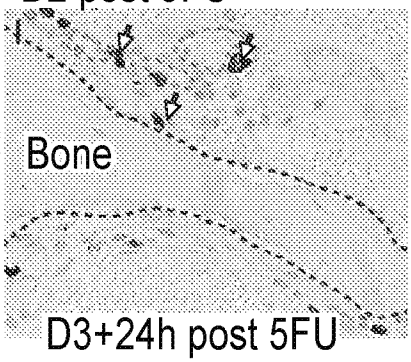


FIG. 24E

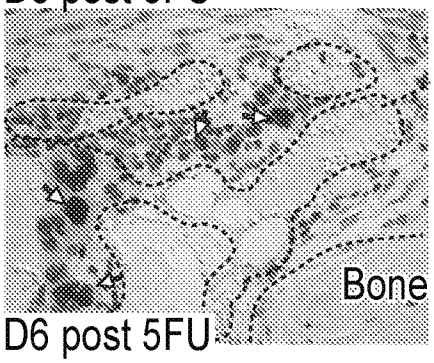


FIG. 24F

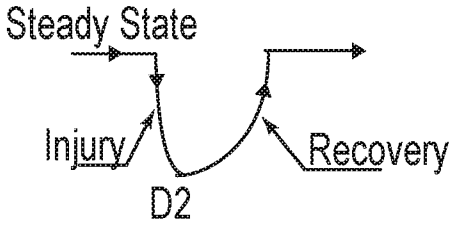


FIG. 24G

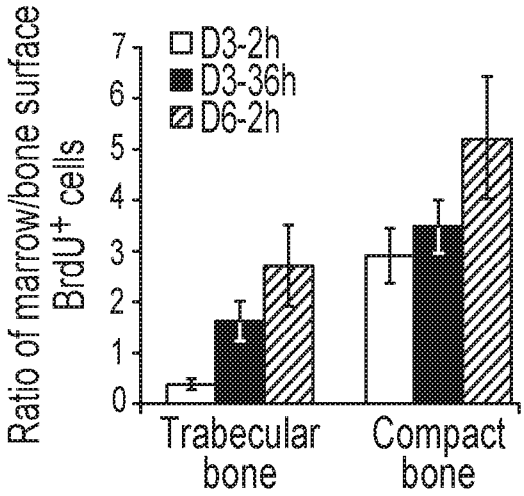


FIG. 24H

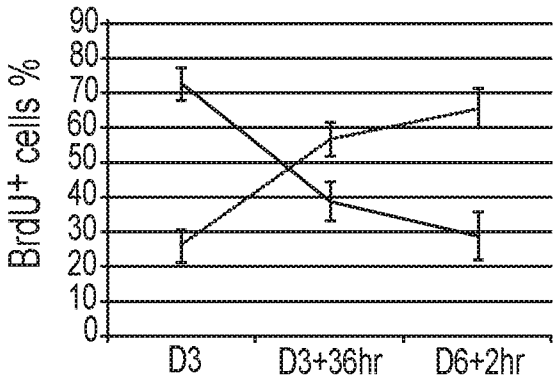


FIG. 24I

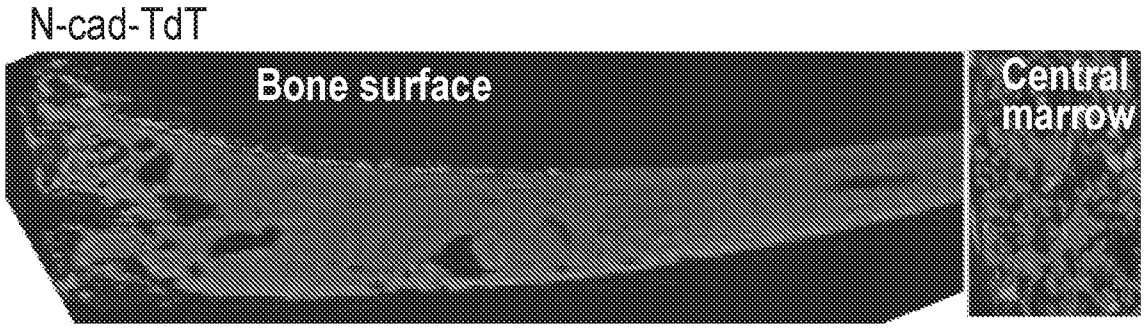


FIG. 24J

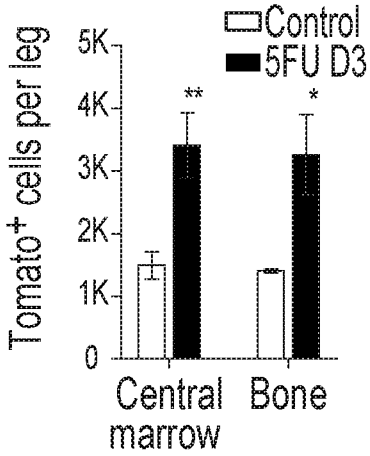


FIG. 24K

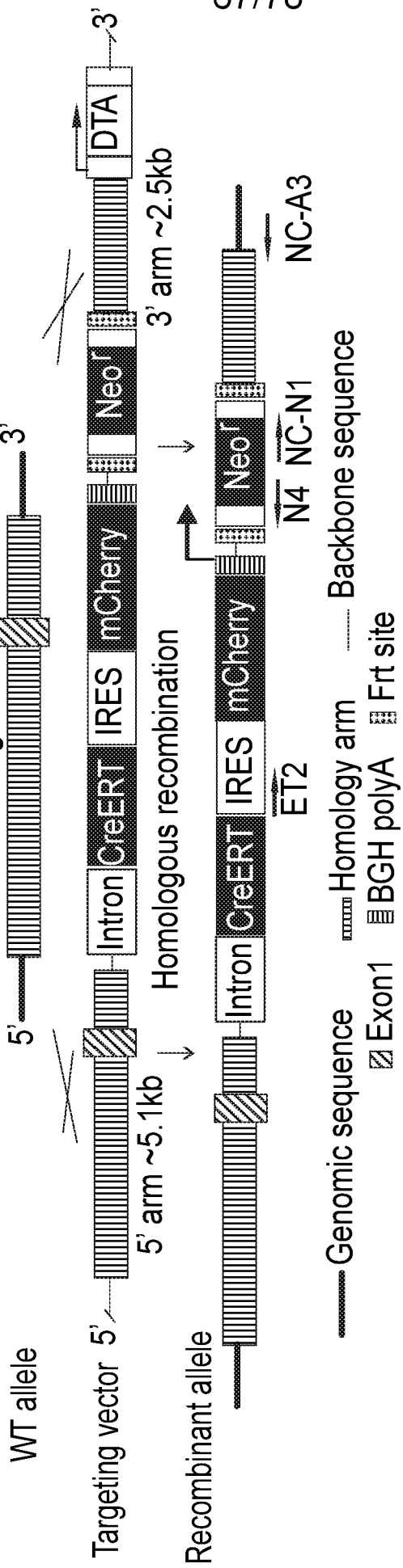

WT allele
5'
CDH2 gene
3'
Targeting vector
5'
5' arm ~5.1kb
Intron
CreERT
IRES
mCherry
Neo'
DTA
3'
3' arm ~2.5kb
Homologous recombination
Recombinant allele
Intron
CreERT
IRES
mCherry
Neo'
ET2
N4
NC-N1
NC-A3
Genomic sequence
Homology arm
Backbone sequence
Exon1
BGH polyA
Frt site

FIG. 25A

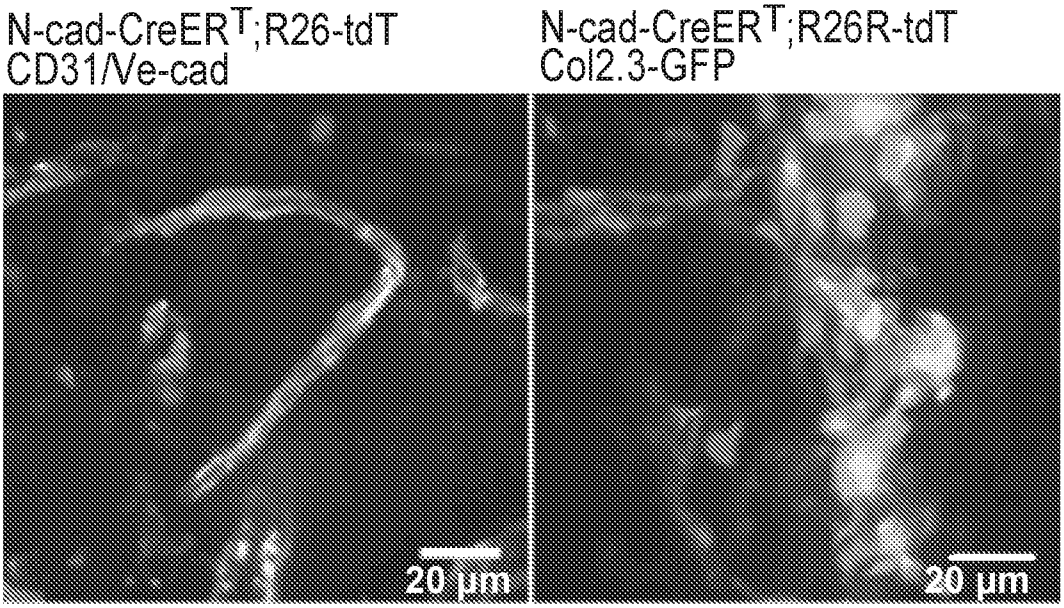

N-cad-CreER^T;R26-tdT
CD31/Ve-cad
20 μm
N-cad-CreER^T;R26R-tdT
Col2.3-GFP
20 μm

FIG. 25B

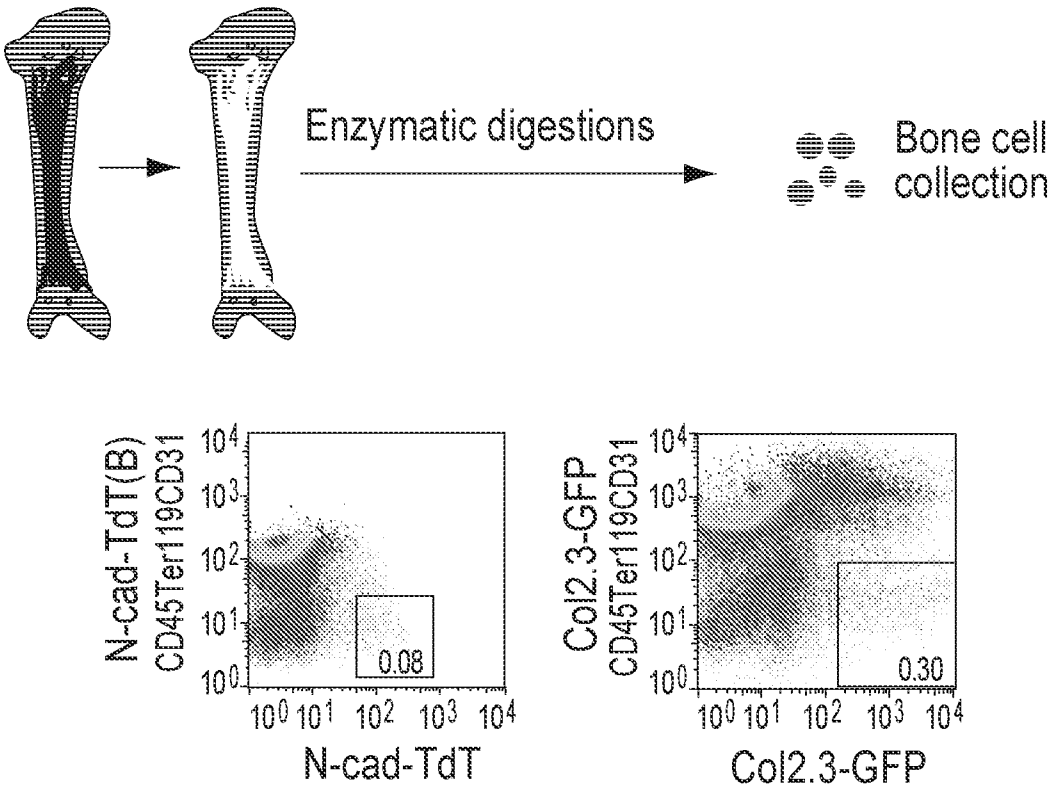

Enzymatic digestions
Bone cell collection
N-cad-TdT(B) CD45Ter119CD31
N-cad-TdT
0.08
Col2.3-GFP CD45Ter119CD31
Col2.3-GFP
0.30

Figure 26A

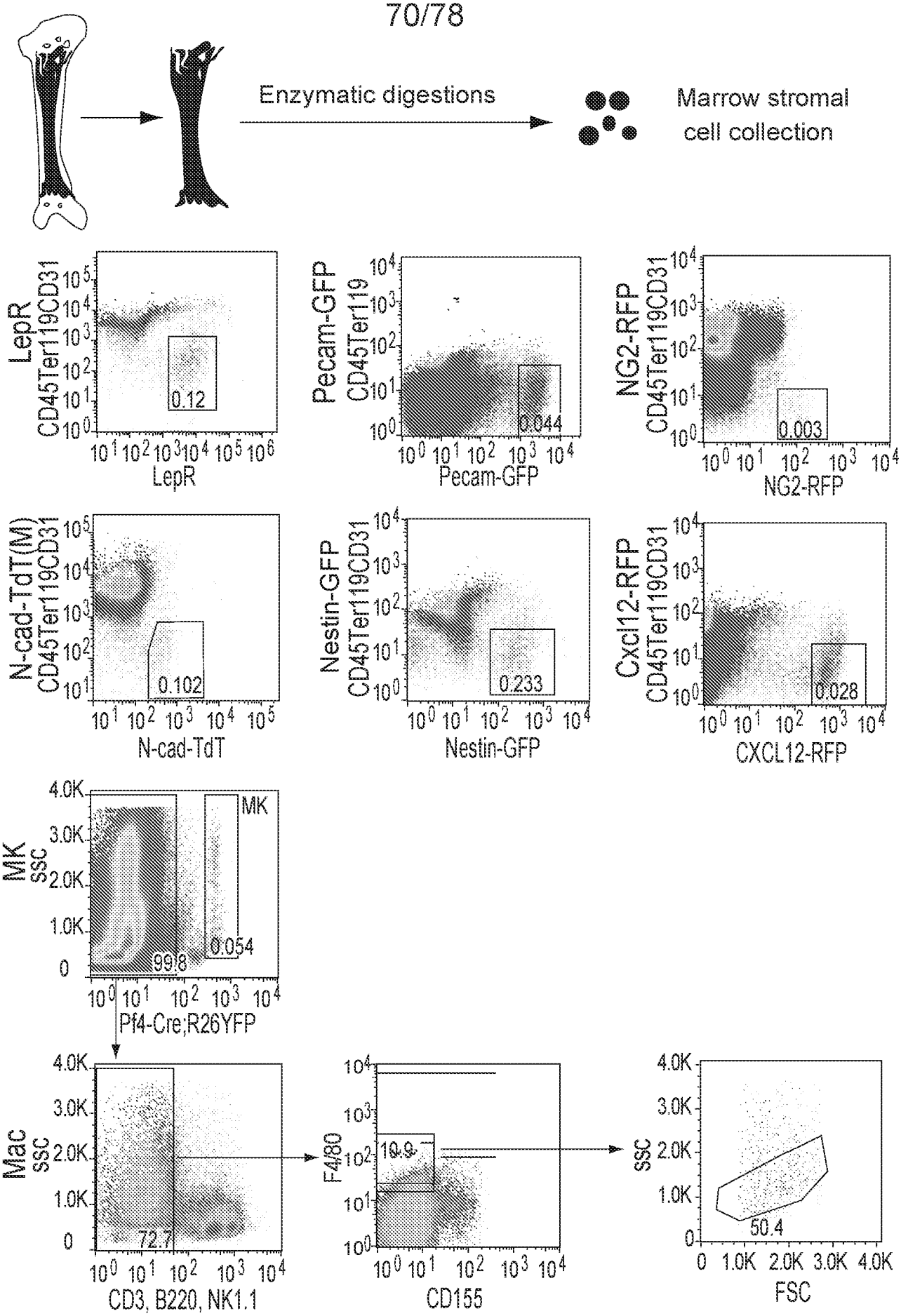

Enzymatic digestions
Marrow stromal cell collection
LepR
CD45Ter119CD31
0.12
LepR
Pecam-GFP
CD45Ter119
0.044
Pecam-GFP
NG2-RFP
CD45Ter119CD31
0.003
NG2-RFP
N-cad-TdT(M)
CD45Ter119CD31
0.102
N-cad-TdT
Nestin-GFP
CD45Ter119CD31
0.233
Nestin-GFP
Cxcl12-RFP
CD45Ter119CD31
0.028
CXCL12-RFP
MK
ssc
MK
0.054
99.8
Pf4-Cre;R26YFP
Mac
ssc
72.7
CD3, B220, NK1.1
F4/80
10.9
CD155
SSC
50.4
FSC

Figure 26B

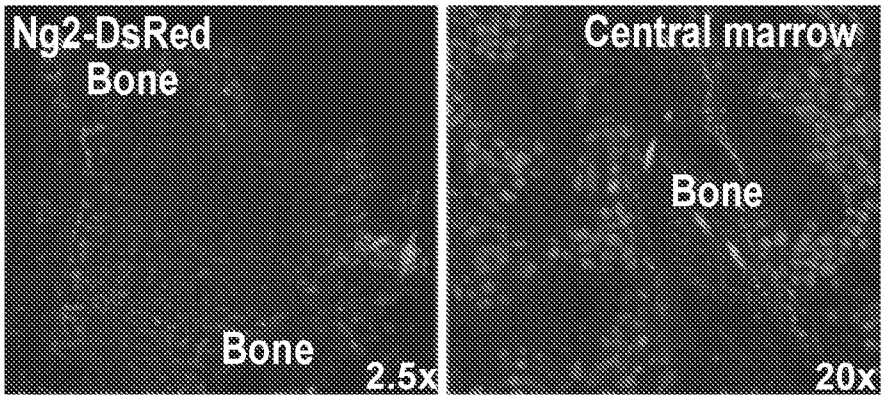


Figure 26C

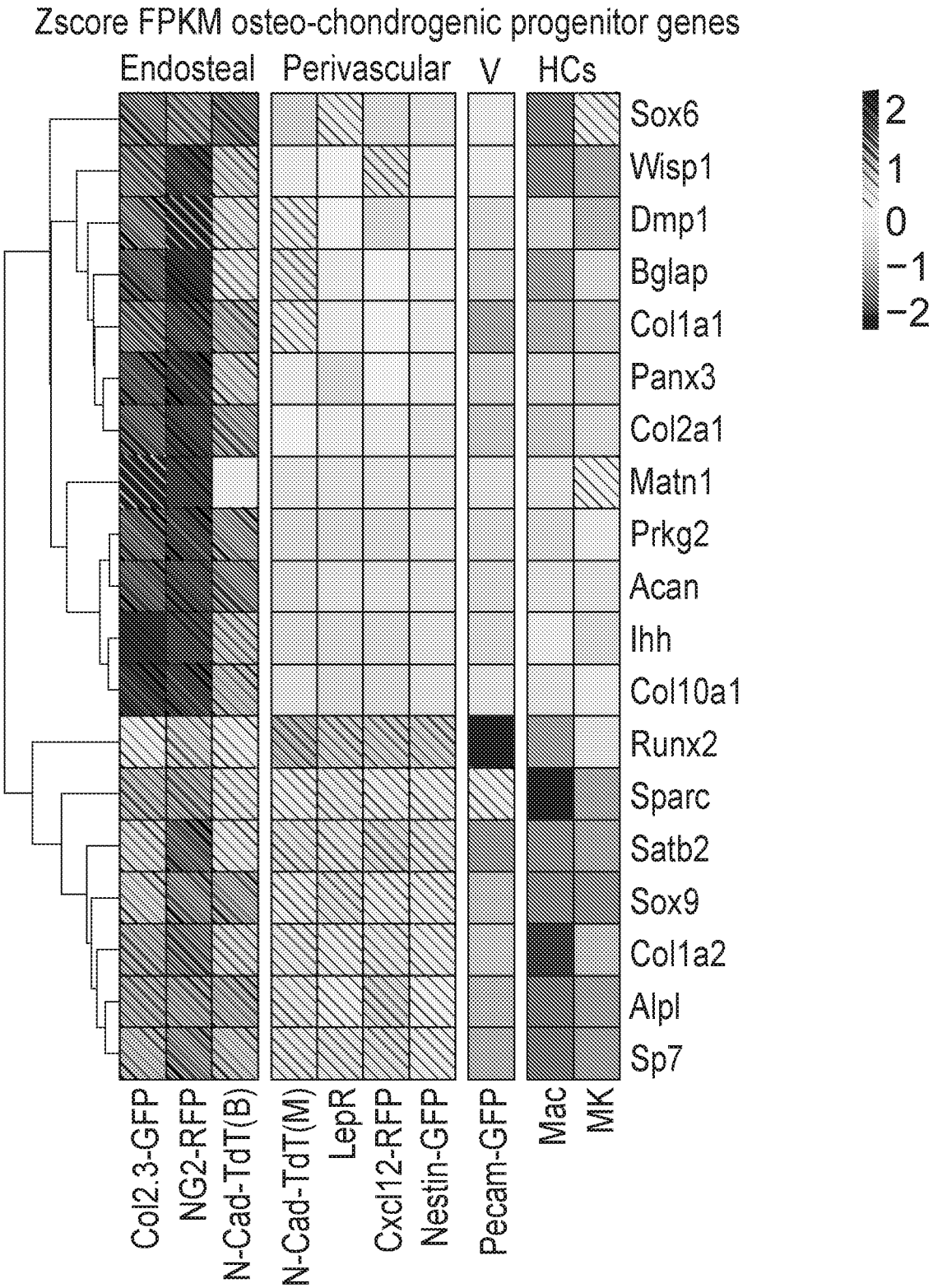

Zscore FPKM osteo-chondrogenic progenitor genes
Endosteal
Perivascular
V
HCs
Sox6
Wisp1
Dmp1
Bglap
Col1a1
Panx3
Col2a1
Matn1
Prkg2
Acan
Ihh
Col10a1
Runx2
Sparc
Satb2
Sox9
Col1a2
Alpl
Sp7
2
1
0
−1
−2
Col2.3-GFP
NG2-RFP
N-Cad-TdT(B)
N-Cad-TdT(M)
LepR
Cxcl12-RFP
Nestin-GFP
Pecam-GFP
Mac
MK

Figure 26D

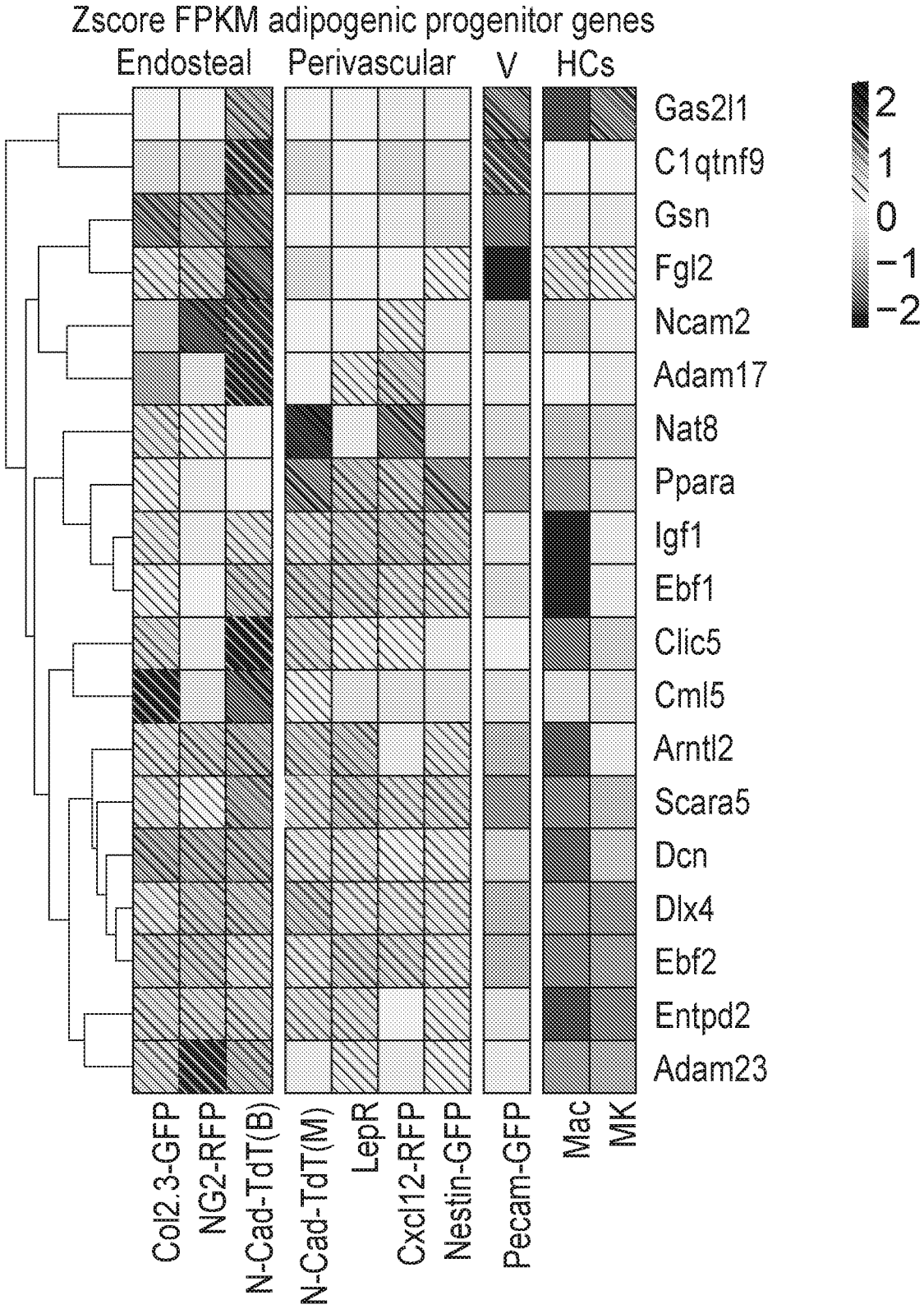

Zscore FPKM adipogenic progenitor genes
Endosteal
Perivascular
V
HCs
Gas2l1
C1qtnf9
Gsn
Fgl2
Ncam2
Adam17
Nat8
Ppara
Igf1
Ebf1
Clic5
Cml5
Arntl2
Scara5
Dcn
Dlx4
Ebf2
Entpd2
Adam23
2
1
0
−1
−2
Col2.3-GFP
NG2-RFP
N-Cad-TdT(B)
N-Cad-TdT(M)
LepR
Cxcl12-RFP
Nestin-GFP
Pecam-GFP
Mac
MK

Figure 26E

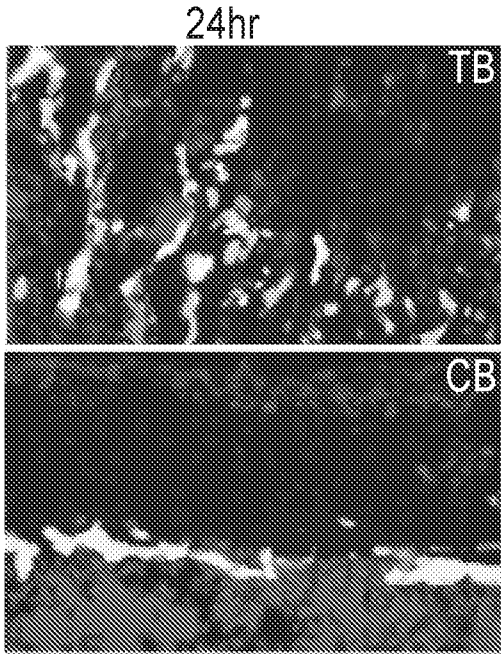


Figure 27A

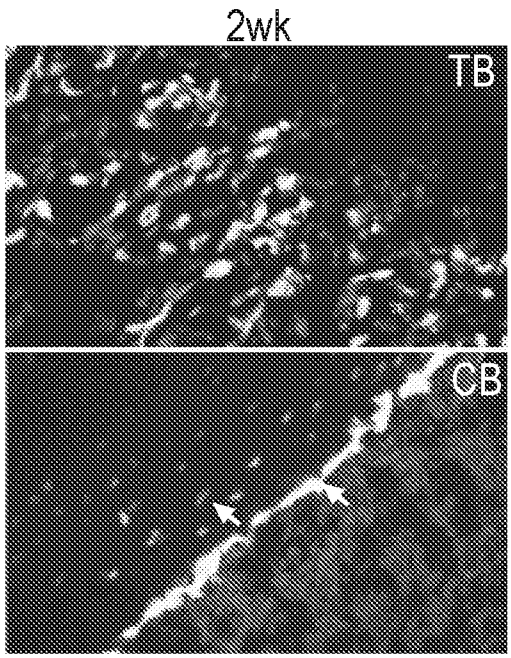


Figure 27B

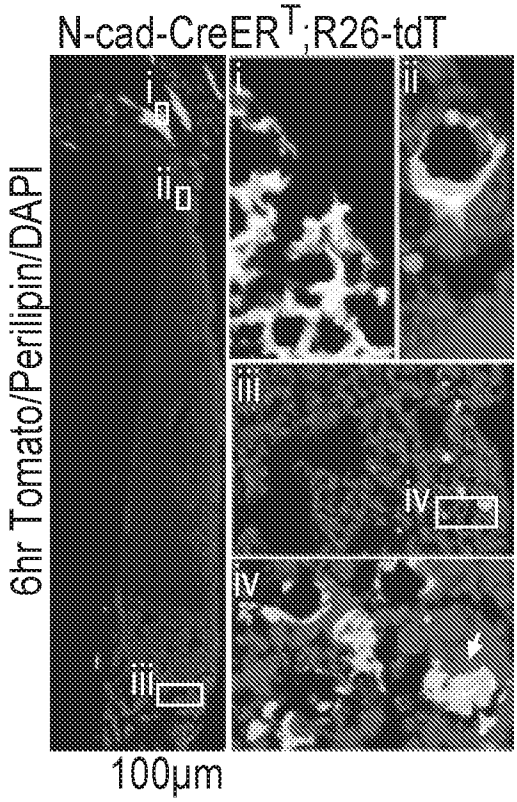


Figure 27C

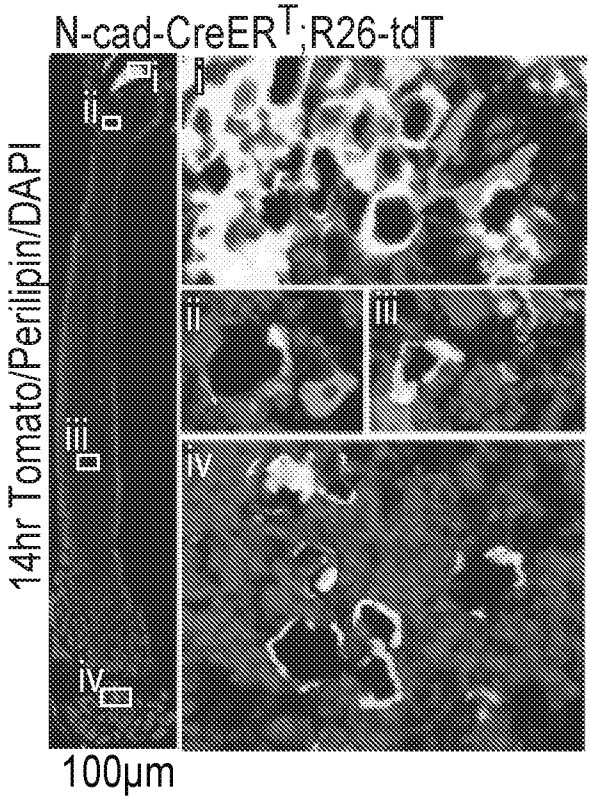


Figure 27D

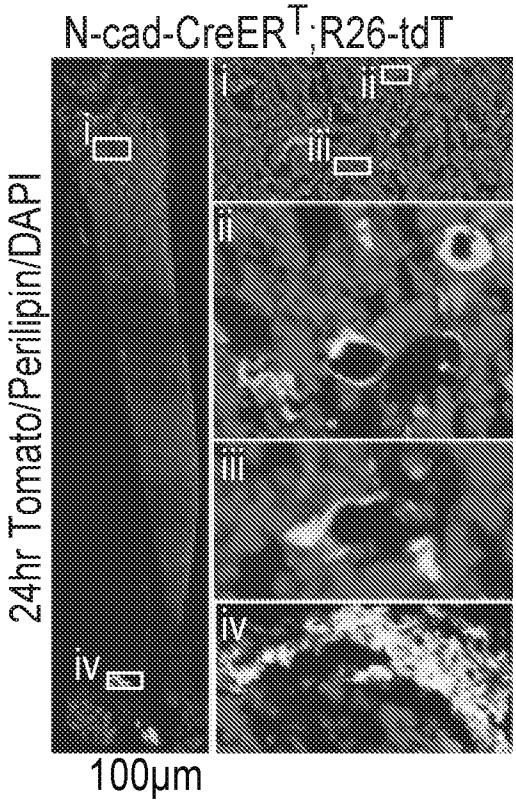


Figure 27E

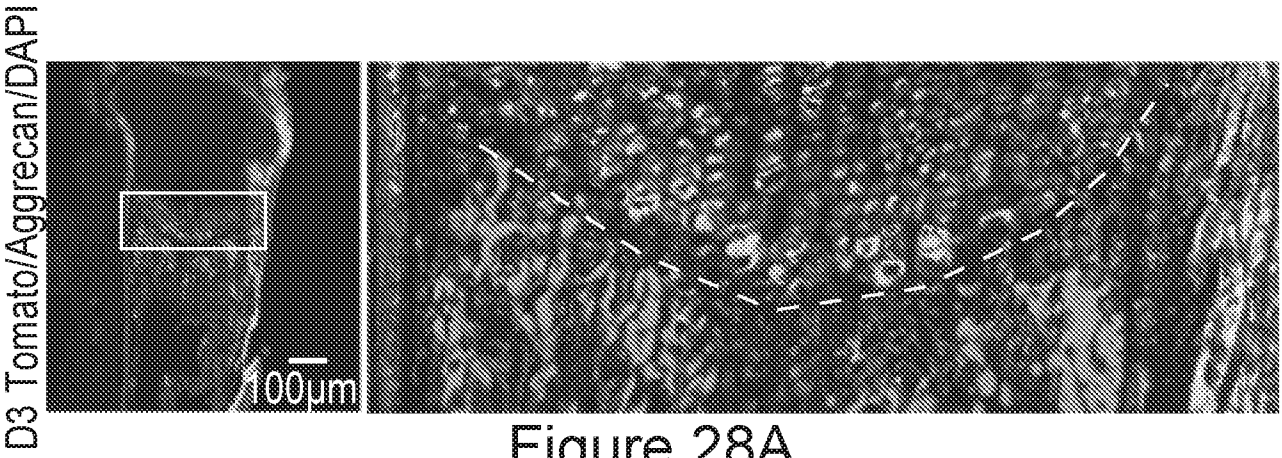


Figure 28A

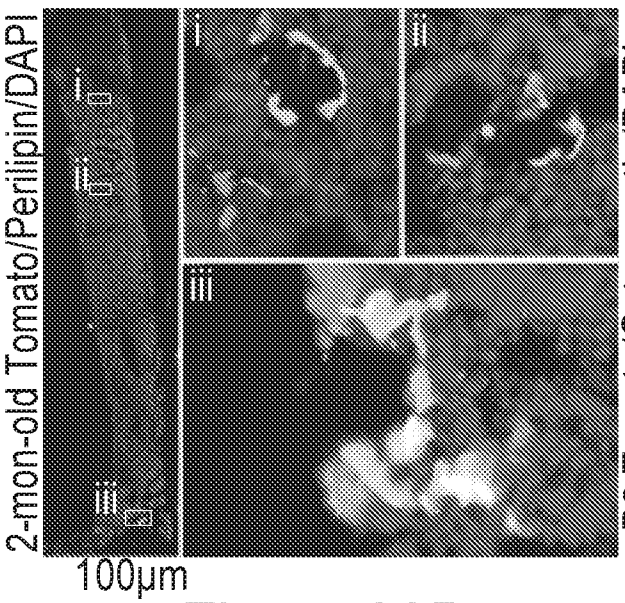


Figure 28B

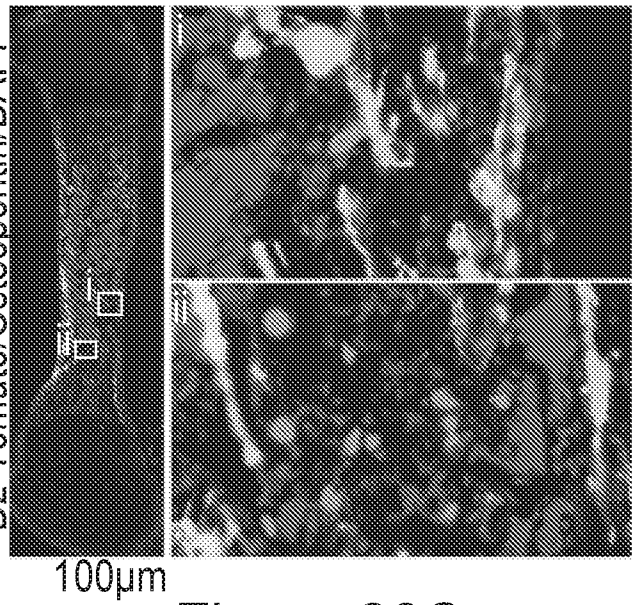


Figure 28C

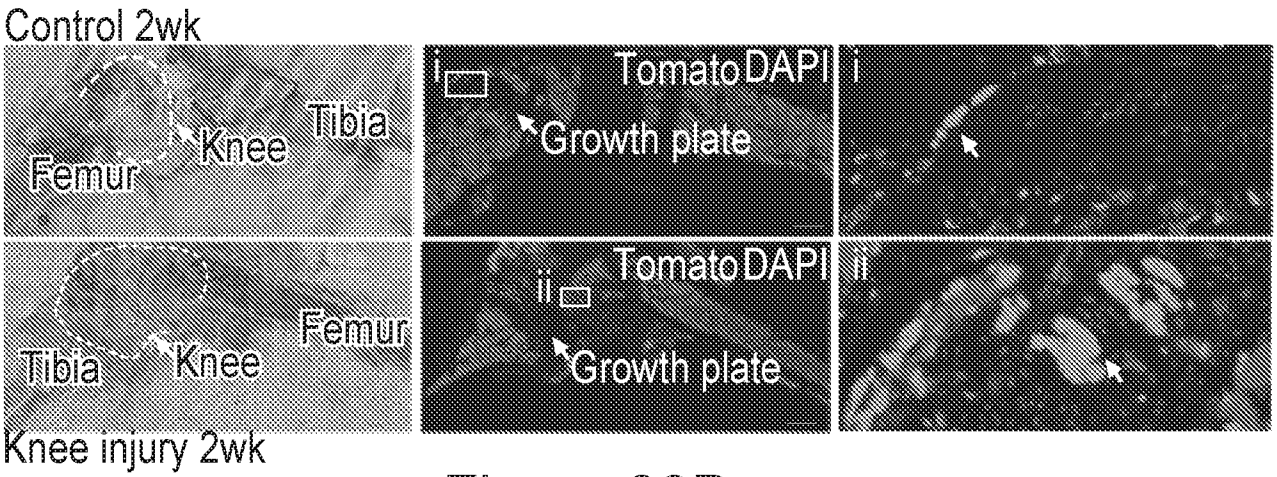


Figure 28D

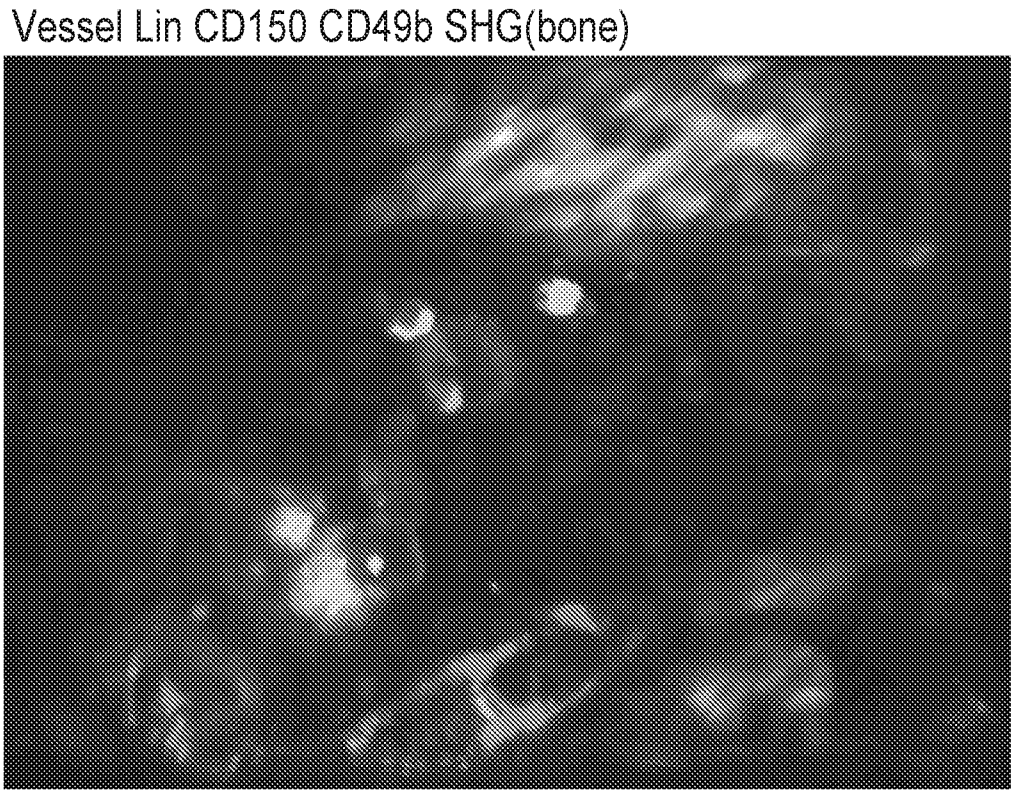


Figure 29

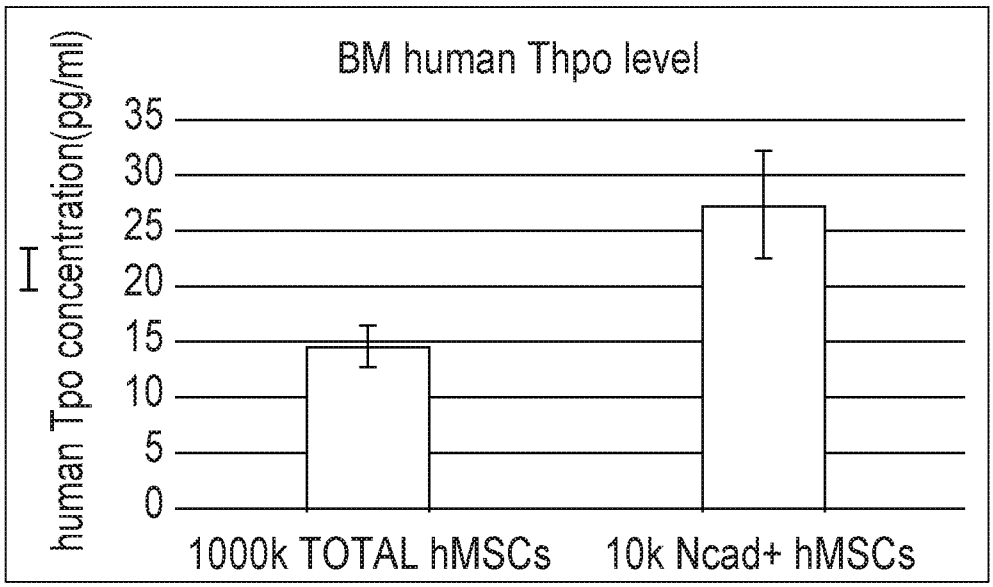

BM human Thpo level
human Tpo concentration(pg/ml)
35
30
25
20
15
10
5
0
1000k TOTAL hMSCs
10k Ncad+ hMSCs

Figure 30

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US18/55092

A. CLASSIFICATION OF SUBJECT MATTER
IPC - A61K 35/28; C12N 5/071, 15/09, 15/113 (2019.01)
CPC - A61K 35/28; C12N 5/0647, 15/09, 15/113

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2016/264934 A1 (THE GENERAL HOSPITAL CORPORATION, et al.) 15 September 2016; paragraphs [0007], [0014], [0023], [0033], [0037], [0044], [0095], [0121], [0136], [0158], [0194], [0201], [0271], [0277], [0288], [0306], [0433]; Figures 2F, 10H	1-3, 19-21, 24-25, 29, 30, 31/29, 32/31/29, 53 -- 4-6, 12, 15-16, 33/32/31/29, 34/33/32/31/29, 35/34/33/32/31/29, 41/31/29, 44-45, 61-63, 66-67, 74-75
X	WO 2012/027376 (THE RESEARCH FOUNDATION OF THE STATE UNIVERSITY OF NEW YORK, et al.) 1 March 2012; Figures 12, 27A; page 8, lines 21-29; page 11, lines 23-27; page 16, lines 1-4; page 23, lines 9-13; page 25, lines 4-8; page 26, lines 17-21; page 27, lines 7-11; page 28, lines 21-32; page 41, lines 3-5; page 54, line 13 – page 55, line 10; claims 1, 4-5, 10, 12	78-103
Y	(TIRUMURU, N et al.) N6-methyladenosine of HIV-1 RNA regulates viral infection and HIV-1 Gag protein expression. eLife – Microbiology And Infectious Disease. 2 July 2016, Vol. 5, No. e15528; page 14, 4th paragraph; Figure 3; DOI: 10.7554/eLife.15528	4-6, 15-16, 33/32/31/29, 34/33/32/31/29, 35/34/33/32/31/29, 44-45, 61-62, 66-67, 74-75
Y	(JOSEPH, C et al.) Deciphering Hematopoietic Stem Cells in Their Niches: A Critical Appraisal of Genetic Models, Lineage Tracing, and Imaging Strategies. Cell Stem Cell. 7 November 2013, Vol. 13, pages520-533; page 520, 2nd column, 3rd paragraph – page 521, 1st column, 2nd paragraph; Table 1; DOI: 10.1016/j.stem.2013.10.010	12, 41/31/29, 63

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
05 February 2019 (05.02.2019)	22 MAR 2019
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US18/55092

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

An invitation to Furnish Nucleotide and/or Amino Acid Sequence Listing and to Pay, Where Applicable, Late Furnishing Fee ("ISA/225") was mailed on 24 October 2018 (24.10.2018). No approved electronic sequence listing was received in response to the ISA/225. Therefore, the international search was carried out only to the extent possible.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US18/55092

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups I+, Claims 1-316, 371-407, a m6A modification reader YTHDF1 (m6A modification pathway molecule), MX1-Cre inactivation or deletion (modulation), and hematopoietic stem and progenitor cells (HSPCs) are directed toward methods and kits for expansion of a population of cells, administering cells to a subject, and reconstituting bone marrow with the cells.

-***-Continued on Supplemental Page-***-

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 2-6 (each in-part), 12 (in-part), 15, 16 (in-part), 19-23, 24 (in-part), 25 (in-part), 26, 27, 29, 30, 31-35 (each in-part), 41 (in-part), 44, 45 (in-part), 51 (in-part), 53, 54-56 (each in-part), 58 (in-part), 60 (in-part), 61-63, 66, 67, 74, 75, and 78-103; a m6A modification reader YTHDF1 (m6A modification pathway molecule), MX1-Cre inactivation or deletion (modulation), and hematopoietic stem and progenitor cells (HSPCs)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US18/55092

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 9,439,928 B2 (KASAHARA, N et al.) 13 September 2016; abstract; column 2, lines 15-17; column 4, lines 14-32; column 17, lines 19-21; claim 1	74-75

-***-Continued from Box No. III: Observations where unity of invention is lacking-***-

The methods and kits will be searched to the extent they encompass a m6A modification reader YTHDF1 (first exemplary m6A modification pathway molecule), MX1-Cre inactivation or deletion (first exemplary modulation method), and hematopoietic stem and progenitor cells (first exemplary cells). Applicant is invited to elect additional modification pathway molecule(s), and/or modulation method(s) (or specific inhibitor(s) used for modulation), and/or cell(s)(cell type(s)) to be searched. Additional modification pathway molecule(s), and/or modulation method(s) (or specific inhibitor(s) used for modulation), and/or cell(s) (cell type(s)) will be searched upon the payment of additional fees. It is believed that claims 1, 2-6 (each in-part), 12 (in-part), 15, 16 (in-part), 19-23, 24 (in-part), 25 (in-part), 26, 27, 29, 30, 31-35 (each in-part), 41 (in-part), 44, 45 (in-part), 48-51 (each in-part), 53, 54-56 (each in-part), 58 (in-part), 60 (in-part), 61-63, 66, 67, 74, 75, and 78-103 encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass YTHDF1 (m6A modification pathway molecule), MX1-Cre inactivation or deletion (modulation), and hematopoietic stem and progenitor cells (HSPCs). Applicants must specify the claims that encompass any additionally elected modification pathway molecule(s), and/or modulation method(s) (or specific inhibitor(s) used for modulation), and/or cell(s)(cell type(s)). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be a METTL3 m6A modification writer (m6A modification pathway molecule).

No technical features are shared between the modification pathway molecules and/or modulation methods or inhibitors and/or cells of Groups I+ and, accordingly, these groups lack unity a priori.

Additionally, even if Groups I+ were considered to share the technical features including: a methods for expanding, ex vivo, a population of cells, the method comprising modulating a N6-Methyladenosine (m6A) mRNA modification pathway in the population of cells, which is sufficient for subsequent transplantation into a subject in need thereof; an expanded cell population made by the method; a method for ex vivo expansion of cells by at least 2-fold, the expanded cells being competent to reconstitute a cell lineage upon transplantation into a mammal in need thereof, the method comprising introducing a mutation into the cells that results in deletion, replacement or reduced expression of a gene expressing a m6A mRNA modification reader and culturing the population of cells in a suitable culture medium; a kit for expanding a cell population for subsequent transplantation into a subject in need thereof, the kit comprising a system for introducing a mutation into the cell population that results in deletion, replacement or reduced expression of a gene expressing a m6A mRNA modification reader, and instructions for use thereof; an inhibitor of a m6A mRNA modification reader; a method for treating a subject in need of a transplant, comprising administering cells to a subject in need thereof, the method comprising: (a) introducing, into a sample containing a cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m6A mRNA modification reader, or an inhibitor of a m6A mRNA modification reader, (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of cells in the sample to a number sufficient to transplant into the subject; and (c), administering the cells to the subject; a method for reconstituting a cell lineage or bone marrow in a subject in need thereof, the method comprising: (a) obtaining from a mammal a tissue sample comprising a cell population; (b) expanding, in vitro, the cell population from the sample, wherein: (i) the cell population expands by at least 2-fold; and (ii) the expanded cell population has at least a 5-fold increase in total colony-forming units; and (c) transplanting the expanded cell population into a subject in need thereof; wherein the cells are stem cells; maintaining a multilineage differentiation potential in the stem cell population; stem cells obtained from a tissue selected from the group consisting of peripheral blood, cord blood and bone marrow; a method for treating cancer and/or a blood disorder in a subject in need thereof, comprising: culturing, in a suitable culture media, a sample containing a CAR T-cell population and administering to the subject a population of the CAR T-cells; these shared technical features are previously disclosed by US 2016/0264934 A1 to The General Hospital Corporation et al. (hereinafter 'General') in view of US 2014/0114070 A1 to Boitano et al. (hereinafter 'Boitano'), the article 'MicroRNA-145 Modulates N6-methyladenosine Levels by Targeting the 3'-Untranslated mRNA Region of the N6-Methyladenosine-binding TYH Domain Family 2 Protein' by Yang et al. (hereinafter 'Yang') and WO 2017/075147 A1 to Board of Regents, the University of Texas System (hereinafter 'Texas').

General discloses a method for expanding (a method for expanding: paragraphs [0012], [0138]), ex vivo (ex vivo; paragraphs [0012], [0138], [0158]), a population of cells (a population of cells; paragraphs [0012], [0138], [0158]), the method comprising modulating a N6-Methyladenosine (m6A) mRNA modification pathway in the population of cells (the method comprising inhibiting METTL3 (modulating a N6-Methyladenosine (m6A) mRNA modification pathway) in the population of cells; paragraphs [0012], [0138], [0158]), which is sufficient for subsequent transplantation into a subject in need thereof (which is sufficient for subsequent transplantation into a subject in need thereof; paragraphs [0044], [0271]); an expanded cell population made by the method (an expanded cell population made by the method; paragraphs [0012], [0037], [0044]); a method for ex vivo expansion of cells by at least 2-fold (a method for ex vivo expansion of cells by at least 2-fold; paragraphs [0012], [0080], [0138], [0158]), the method comprising introducing a mutation into the cells that results in deletion, replacement or reduced expression of a gene (the method comprising introducing a mutation into the cells that results in deletion, replacement or reduced expression of a gene; paragraph [0189]) expressing a m6A mRNA modification enzyme (expressing METTL3 (a m6A mRNA modification enzyme); paragraphs [0012], [0138], [0158]) and culturing the population of cells in a suitable culture medium (culturing the population of cells in a suitable culture medium; paragraph [0014]); a kit (a kit; paragraph [0007]), for expanding a cell population (for expanding a cell population; paragraphs [0007], [0012]) for subsequent transplantation into a subject in need thereof (for subsequent transplantation into a subject in need thereof; paragraphs [0044], [0271]), the kit comprising a system for introducing a mutation into the cell population that results in deletion, replacement or reduced expression of a gene expressing a m6A mRNA modification enzyme (the kit comprising a system for introducing a mutation into the cell population that results in deletion, replacement or reduced expression of a gene expressing a m6A mRNA modification enzyme; paragraphs [0007], [0189]), and instructions for use thereof (instructions for use thereof; paragraphs [0007], [0189] [0274]); wherein the cells are stem cells (wherein the cells are stem cells; paragraph [0014]); maintaining a multilineage differentiation potential in the stem cell population (maintaining pluripotency (a multilineage differentiation potential) in the stem cell population; paragraph [0014]); and stem cells obtained from a tissue selected from the group consisting of cord blood and bone marrow (stem cells obtained from a tissue selected from the group consisting of cord blood and bone marrow; paragraph [0306]). General further discloses wherein inhibiting or deleting METTL3 results in a decrease in m6A levels on target genes (wherein inhibiting or deleting METTL3 results in a decrease in m6A levels on target genes; paragraph [0012]).

-***-Continued Within the Next Supplemental Box-***-

-***-Continued from Previous Supplemental Box-***-

General does not disclose: the expanded cells being competent to reconstitute a cell lineage upon transplantation into a mammal in need thereof; expressing an m6A mRNA modification reader; an inhibitor of a m6A mRNA modification reader; a method for treating a subject in need of a transplant, comprising administering cells to a subject in need thereof, the method comprising: (a) introducing, into a sample containing a cell population, a mutation that results in deletion, replacement or reduced expression of a gene expressing a m6A mRNA modification reader, or an inhibitor of a m6A mRNA modification reader, (b) culturing the sample in a suitable culture media for a period of time sufficient to expand the number of cells in the sample to a number sufficient to transplant into the subject; and (c), administering the cells to the subject; a method for reconstituting a cell lineage or bone marrow in a subject in need thereof, the method comprising: (a) obtaining from a mammal a tissue sample comprising a cell population; (b) expanding, in vitro, the cell population from the sample, wherein: (i) the cell population expands by at least 2-fold; and (ii) the expanded cell population has at least a 5-fold increase in total colony-forming units; and (c) transplanting the expanded cell population into a subject in need thereof; and a method for treating cancer and/or a blood disorder in a subject in need thereof, comprising: culturing, in a suitable culture media, a sample containing a CAR T-cell population and administering to the subject a population of the CAR T-cells.

Boitano discloses expanded cells being competent to reconstitute a cell lineage upon transplantation into a mammal in need thereof (expanded cells being competent to reconstitute a cell lineage upon transplantation into a mammal in need thereof; abstract); a method for treating a subject in need of a transplant, comprising administering cells to a subject in need thereof (a method for treating a subject in need of a transplant, comprising administering cells to a subject in need thereof; paragraph [0078]); culturing the sample in a suitable culture media for a period of time sufficient to expand the number of cells in the sample to a number sufficient to transplant into the subject (culturing the sample in a suitable culture media for a period of time sufficient to expand the number of cells in the sample to a number sufficient to transplant into the subject; paragraphs [0078], [0092]); and administering the cells to the subject (administering the cells to the subject; paragraph [0078]); a method for reconstituting a cell lineage or bone marrow in a subject in need thereof (a method for reconstituting a cell lineage or bone marrow in a subject in need thereof; abstract, paragraph [0122]), the method comprising: (a) obtaining from a mammal a tissue sample comprising a cell population (the method comprising: (a) obtaining from a mammal a tissue sample comprising a cell population; paragraph [0024]); (b) expanding, in vitro, the cell population from the sample (expanding, in vitro, the cell population from the sample; paragraphs [0024], [0116]), wherein: (i) the cell population expands by at least 2-fold (wherein: (i) the cell population expands by at least 2-fold; paragraph [0116]); and (ii) the expanded cell population has at least a 5-fold increase in total colony-forming units (expanded cell population has at least a 5-fold increase in total colony-forming units; paragraph [0280]); and (c) transplanting the expanded cell population into a subject in need thereof (transplanting the expanded cell population into a subject in need thereof; abstract, paragraphs [0122]).

Yang discloses expressing an m6A mRNA modification reader (expressing YTHDF2 (an m6A modification reader); abstract); and an inhibitor of an m6A mRNA modification reader (miR-145 (an inhibitor of a m6A mRNA modification reader); abstract).

Texas discloses a method for treating cancer and/or a blood disorder in a subject in need thereof (a method for treating cancer and/or a blood disorder in a subject in need thereof; paragraphs [0055], [0059]), comprising: culturing, in a suitable culture media, a sample containing a CAR T-cell population (comprising: culturing, in a suitable culture media, a sample containing a CAR T-cell population; paragraph [0059]) and administering to the subject a population of the CAR T-cells (administering to the subject a population of the CAR T-cells; paragraph [0059]).

It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to have modified the disclosure of General to have expanded cells to an appropriate extent, as disclosed by Boitano, by culturing the cells in a suitable medium, for reconstituting a cell lineage or bone marrow in a subject in need thereof, using cells expanded by modification of the m6A system in the cells, as disclosed by General. It further would have been obvious to a person of ordinary skill in the art at the time of the invention was made to have modified the disclosure of General to have included the deletion or suppression of additional or alternative m6A enzymes, including an m6A reader, as disclosed by Yang, using an inhibitor, as disclosed by Yang, or deletion of the gene for the enzyme, as disclosed by General, in order to modulate or affect the m6A pathway in the cells accordingly. It also would have been obvious to a person of ordinary skill in the art at the time of the invention was made to have modified the disclosure of General to have used cells, such as CAR T-cells, as disclosed by Texas, comprising a modified m6A pathway, as disclosed by General, for the treatment of cancer, as disclosed by Texas, in order to provide an appropriate amount of expanded or proliferating CAR-T cells for effective treatment.

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by a combination of the General, Boitano, Yang, and Texas references, unity of invention is lacking.