[0014] The results disclosed herein are particularly surprising given that it is believed that it has never before been shown that Zscan4 expression can increase telomere length in human cells. The results disclosed herein are also unexpected. While Zscan4 expression has been previously shown to increase telomere length in mouse embryonic stem (ES) cells, the differences not only between human ZSCAN4 and mouse Zscan4, but also between the biology of human cells and mouse cells, as well as between ES cells and non-ES cells such as adult cells, would not lead one to expect that Zscan4 expression in human cells would also increase telomere length. This is particularly relevant given that it has been previously demonstrated that transcriptional regulatory elements in the human and mouse genomes differ dramatically. This is exceptionally striking when considering that even transcription factors with conserved function in both human and mouse exhibit a significant degree of species-specific binding event preferences (Odom *et al.*, *Nature Genetics* 6:39, 2007).

[0015] Advantageously, utilizing agents that increase Zscan4 expression, such as nucleic acid molecules encoding Zscan4, can be used to increase the success rate of *in vitro fertilization* (IVF) and successful pregnancies in older women by rejuvenating and/or correcting genomic and/or chromosomal abnormalities, such as aneuploidy, in oocyte cells, fertilized oocytes, or preimplantation embryos. Additionally, utilizing agents that increase Zscan4 expression, such as nucleic acid molecules encoding Zscan4, can be used to treat a patient suffering from a disease or condition associated with telomere shortening, such as Fanconi anemia, by increasing the length of telomeres in cells of the patient affected by the disease or condition. Furthermore, agents that increase Zscan4 expression, such as nucleic acid molecules encoding Zscan4, can be used to also rejuvenate cells in an individual, tissues in an individual, or organs in an individual; or to rejuvenate individuals by increasing the length of telomeres in aged cells, tissues, organs and individuals caused by telomere shortening.

[0016] Accordingly, certain ~~aspects~~ embodiments of the present disclosure relate to a method of increasing telomere length in one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the human cell, where increased expression of Zscan4 induces telomere lengthening in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0016a] In one aspect, there is provided an *in vitro* method of increasing telomere length in one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the human cell, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0016b] In one aspect, there is provided use of an agent that increases expression of Zscan4 in a human cell, in the manufacture of a medicament for increasing telomere length in one or more human cells, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

[0017] Other ~~aspects~~ embodiments of the present disclosure relate to a method of treating a subject in need of telomere lengthening, by contacting one or more human cells in the subject with an agent that

increases expression of Zscan4 in the one or more human cells, where increased expression of Zscan4 induces telomere lengthening in the one or more human cells.

[0017a] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for treating a subject in need of telomere lengthening, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells that are contacted with the agent.

[0018] Other aspects of the present disclosure relate to a method of treating a subject in need of telomere lengthening, ~~by~~comprising: i. isolating one or more human cells in need of telomere lengthening from the subject; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and iii. administering the contacted one or more human cells to the subject.

[0018a] In one aspect, there is provided use of one or more human cells in the manufacture of a medicament for treating a subject in need of telomere lengthening, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells.

[0019] Other ~~aspects~~ embodiments of the present disclosure relate to a method of treating a disease or condition associated with a telomere abnormality, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where increasing expression of Zscan4 induces telomere lengthening in the one or more human cells to treat the disease or condition associated with a telomere abnormality.

[0019a] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for treating a disease or condition associated with a telomere abnormality in the subject, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells to treat the disease or condition associated with a telomere abnormality.

[0020] Other aspects of the present disclosure relate to a method of treating a disease or condition associated with a telomere abnormality, ~~by~~comprising: i. isolating one or more human cells from a subject suffering from a disease or condition associated with a telomere abnormality; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a telomere abnormality.

[0020a] In one aspect, there is provided use of one or more human cells in the manufacture of a medicament for treating a disease or condition associated with a telomere abnormality in a subject suffering from the disease or condition associated with a telomere abnormality, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells.

[0021] Other ~~aspects~~ embodiments of the present disclosure relate to a method of treating a disease or condition associated with a chromosome abnormality, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells to treat the disease or condition associated with a chromosome abnormality.

[0021a] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for treating a disease or condition associated with a chromosome abnormality in the subject, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells to treat the disease or condition associated with a chromosome abnormality.

[0022] Other aspects of the present disclosure relate to a method of treating a disease or condition associated with a chromosome abnormality, ~~by~~comprising: i. isolating one or more human cells from a subject suffering from a disease or condition associated with a chromosome abnormality; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the

chromosome abnormality in the one or more human cells; and iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a chromosome abnormality.

[0022a] In one aspect, there is provided use of one or more human cells in the manufacture of a medicament for treating a disease or condition associated with a chromosome abnormality in a subject suffering from the disease or condition associated with a chromosome abnormality, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells.

[0023] Other ~~aspects~~ embodiments of the present disclosure relate to a method of treating a disease or condition associated with a karyotype abnormality, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells to treat the disease or condition associated with a karyotype abnormality.

[0023a] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for treating a disease or condition associated with a karyotype abnormality in the subject, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells to treat the disease or condition associated with a karyotype abnormality.

[0024] Other aspects of the present disclosure relate to a method of treating a disease or condition associated with a karyotype abnormality, ~~by~~comprising: i. isolating one or more human cells from a subject suffering from a disease or condition associated with a karyotype abnormality; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells; and iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a karyotype abnormality.

[0024a] In one aspect, there is provided use of one or more human cells in the manufacture of a medicament for treating a disease or condition associated with a karyotype abnormality in a subject suffering from the disease or condition associated with a karyotype abnormality, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells.

[0025] In some embodiments that may be combined with any of the preceding embodiments, the karyotype abnormality is selected from a chromosome nullisomy, a chromosome monosomy, a chromosome trisomy, a chromosome tetrasomy, and a chromosome pentasomy. In some embodiments that may be combined with any of the preceding embodiments, the karyotype abnormality is selected from trisomy 21, trisomy 16, trisomy 18, trisomy 13, monosomy X, XXX aneuploidy, XXY aneuploidy, XYY aneuploidy, and 1p36 duplication. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition associated with a karyotype abnormality is selected from dup(17)(p11.2p11.2) syndrome, Pelizaeus-Merzbacher disease, dup(22)(q11.2q11.2) syndrome, cat-eye syndrome, Cri-du-chat syndrome, Wolf-Hirschhorn, Williams-Beuren syndrome, Charcot-Marie-Tooth disease, Hereditary neuropathy with liability to pressure palsies, Smith-Magenis syndrome, Neurofibromatosis, Alagille syndrome, Velocardiofacial syndrome, DiGeorge syndrome, Steroid sulfatase deficiency, Kallmann syndrome, Microphthalmia with linear skin defects, Adrenal hypoplasia, Glycerol kinase deficiency, Pelizaeus-Merzbacher disease, Testis-determining factor on Y, Azoospermia (factor a), Azoospermia (factor b), Azoospermia (factor c), and 1p36 deletion. In some embodiments that may be combined with any of the preceding embodiments,

inflammatory bowel disease, Crohn's disease, ulcerative colitis, autoimmune gastric atrophy, pemphigus vulgaris, psoriasis, vitiligo, type 1 diabetes, non-obese diabetes, myasthenia gravis, Grave's disease, Hashimoto' s thyroiditis, sclerosing cholangitis, sclerosing sialadenitis, systemic lupus erythematosis, autoimmune thrombocytopenia purpura, Addison' s disease, systemic sclerosis, polymyositis, dermatomyositis, autoimmune hemolytic anemia, and pernicious anemia. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is a neurodegenerative disease selected from adrenoleukodystrophy (ALD), alcoholism, Alexander's disease, Alper's disease, Alzheimer's disease, amyotrophic lateral sclerosis, Lou Gehrig's Disease, ataxia telangiectasia, Batten disease, Spielmeyer-Vogt-Sjogren-Batten disease, bovine spongiform encephalopathy (BSE), Canavan disease, cerebral palsy, Cockayne syndrome, Corticobasal degeneration, Creutzfeldt-Jakob disease, familial fatal insomnia, frontotemporal lobar degeneration, Huntington's disease, HIV-associated dementia, Kennedy's disease, Krabbe's disease, Lewy body dementia, neuroborreliosis, Machado- Joseph disease, Spinocerebellar ataxia type 3, Multiple System Atrophy, multiple sclerosis, narcolepsy, Niemann Pick disease, Parkinson's disease, Pelizaeus-Merzbacher Disease, Pick's disease, primary lateral sclerosis, prion diseases, progressive supranuclear palsy, Refsum's disease, Sandhoff disease, Schilder's disease, subacute combined degeneration of spinal cord secondary to Pernicious Anaemia, Spielmeyer-Vogt-Sjogren-Batten disease, Batten disease, spinocerebellar ataxia, spinal muscular atrophy, Steele- Richardson-Olszewski disease, Tabes dorsalis, and toxic encephalopathy.

[0026] Other ~~aspects~~ embodiments of the present disclosure relate to a method of treating a cancer, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more cancer cells in the subject, where increasing expression of Zscan4 represses growth of the one or more cancer cells, thereby treating the cancer. In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more cancer cells in a subject, in the manufacture of a medicament for treating a cancer in the subject, wherein increasing expression of Zscan4 represses growth of the one or more cancer cells, thereby treating the cancer. Other ~~aspects~~ embodiments of the present disclosure relate to a method of improving responsiveness to chemotherapy in a cancer patient, by administering to a subject in need thereof an agent that reduces expression of endogenous ZSCAN4 in one or more cancer stem cells in the subject, where reducing expression of endogenous ZSCAN4 reduces or eliminates resistance to one or more chemotherapeutic agents in the one or more cancer stem cells, thereby improving responsiveness to the one or more chemotherapeutic agents in the

subject. In one aspect, there is provided use of an agent that reduces expression of endogenous ZSCAN4 in one or more cancer stem cells in a cancer patient, in the manufacture of a medicament for improving responsiveness to chemotherapy in the cancer patient, wherein reducing expression of endogenous ZSCAN4 reduces or eliminates resistance to one or more chemotherapeutic agents in the one or more cancer stem cells, thereby improving responsiveness to the one or more chemotherapeutic agents in the cancer patient. In some embodiments, the agent that reduces expression of endogenous ZSCAN4 is an siRNA or shRNA specific for ZSCAN4. In some embodiments, the cancer selected from cancers of the heart (e.g. angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma, myxoma, rhabdomyoma, fibroma, lipoma and teratoma), lung cancers (e.g., bronchogenic carcinoma (squamous cell, undifferentiated small cell,

carcinoma, Kaposi's sarcoma, moles, dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis); and adrenal gland cancers (e.g., neuroblastoma).

[0027] Other embodimentsaspects of the present disclosure relate to a method of increasing genome stability of one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where increased expression of Zscan4 increases genome stability in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0027a] In one aspect, there is provided an *in vitro* method of increasing genome stability of one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases genome stability in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0027b] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for increasing genome stability of the one or more human cells, wherein increased expression of Zscan4 increases genome stability in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

[0028] Other embodimentsaspects of the present disclosure relate to a method of increasing DNA repair capacity of one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where increased expression of Zscan4 increases DNA repair capacity in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0028a] In one aspect, there is provided an *in vitro* method of increasing DNA repair capacity of one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases DNA repair capacity in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0028b] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for increasing DNA repair capacity of the one or more human cells, wherein increased expression of Zscan4 increases DNA repair capacity in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

[0029] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where increased expression of Zscan4 rejuvenates the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0029a] In one aspect, there is provided an *in vitro* method of rejuvenating one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 rejuvenates the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0029b] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for rejuvenating the one or more human cells, wherein increased expression of Zscan4 rejuvenates the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

[0030] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating skin, treating atopic dermatitis, and/or a skin lesion, by topically administering to the skin of a subject in need thereof an agent that increases expression of Zscan4. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture of a medicament for rejuvenating skin, treating atopic dermatitis, and/or a skin lesion, wherein the medicament is to be topically administered to a subject in need thereof.

[0031] Other embodimentsaspects of the present disclosure relate to a method of treating hair loss, by topically administering to the scalp of a subject in need thereof an agent that increases expression of Zscan4. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating hair loss, wherein the medicament is to be topically administered to the scalp of a subject in need thereof.

[0032] Other embodimentsaspects of the present disclosure relate to a method of preventing hair graying, treating hair graying, or both, by administering to one or more hair follicles of a subject in need thereof an agent that increases expression of Zscan4. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture of a medicament for preventing hair graying, treating hair graying, or both, wherein the medicament is to be administered to one or more hair follicles of a subject in need thereof.

[0033] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating a cornea, by administering to a cornea of a subject in need thereof an agent that increases expression of Zscan4. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture of a medicament for rejuvenating a cornea in a subject in need thereof.

[0034] Other embodimentsaspects of the present disclosure relate to a method of treating dry eye, by administering to a cornea of a subject in need thereof an agent that increases expression of Zscan4. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating dry eye in a subject in need thereof.

[0035] Other embodimentsaspects of the present disclosure relate to a method of treating idiopathic pulmonary fibrosis, by administering to a lung of a subject in need thereof an agent that increases expression of Zscan4. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating idiopathic pulmonary fibrosis, wherein the medicament is to be administered to a lung of a subject in need thereof.

[0036] Other embodimentsaspects of the present disclosure relate to a method of treating atherosclerosis, a coronary heart disease, or both, by administering to the bloodstream of a subject in need thereof an agent that increases expression of Zscan4. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating atherosclerosis, a coronary heart disease, or both, wherein the medicament is to be administered to the bloodstream of a subject in need thereof.

[0037] Other embodimentsaspects of the present disclosure relate to a method of providing resistance to one or more genotoxic agents in one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where increased expression of Zscan4 increases resistance to one or more genotoxic agents in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent. In some embodiments, the genotoxic agent is mitomycin C or cisplatin.

[0037a] In one aspect, there is provided an *in vitro* method of providing resistance to one or more genotoxic agents in one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases resistance to one or more genotoxic agents in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0037b] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for providing resistance to one or more genotoxic agents in the one or more human cells, wherein increased expression of Zscan4 increases resistance to one or more genotoxic agents in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

[0038] In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are human adult cells. In some embodiments, the one or more human cells are adult stem cells, tissue stem cells, progenitor cells, or induced pluripotent stem cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are one or more adult stem cells, tissue stem cells, or progenitor cells selected from hematopoietic stem cells, mesenchymal stem cells, adipose stem cells, neuronal stem cells, and germ stem cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are somatic cells, mature cells, or differentiated cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are somatic cells, mature cells, or differentiated cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are one or more somatic cells, mature cells, or differentiated cells selected from epidermal cells, fibroblasts, lymphocytes, hepatocytes, epithelial cells, myocytes, chondrocytes, osteocytes, adipocytes, cardiomyocytes, pancreatic β cells, keratinocytes, erythrocytes, peripheral blood cells, neurocytes, astrocytes, germ cells, sperm cells, and oocytes.

[0039] Other embodimentsaspects of the present disclosure relate to a method for inducing a human embryonic stem cell-like DNA methylation pattern in one or more human induced pluripotent stem (iPS) cells, by contacting the one or more human iPS cells with an agent that increases expression of Zscan4 in the one or more human iPS cells, where increased expression of Zscan4 induces a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells as compared to one or more corresponding human iPS cells that are not contacted with the agent.

[0039a] In one aspect, there is provided an *in vitro* method for inducing a human embryonic stem cell-like DNA methylation pattern in one or more human induced pluripotent stem (iPS) cells, comprising contacting the one or more human iPS cells with an agent that increases expression of Zscan4 in the one or more human iPS cells, wherein increased expression of Zscan4 induces a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells as compared to one or more corresponding human iPS cells that are not contacted with the agent.

[0039b] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human induced pluripotent stem (iPS) cells, in the manufacture of a medicament for inducing a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells, wherein increased expression of Zscan4 induces a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells that are contacted with the agent as compared to one or more corresponding human iPS cells that are not contacted with the agent.

[0040] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating one or more human oocyte cells, by contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, where increased expression of Zscan4 rejuvenates the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

[0040a] In one aspect, there is provided an *in vitro* method of rejuvenating one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 rejuvenates the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

[0040b] In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human oocyte cells, in the manufacture of a medicament for rejuvenating the one or more human oocyte cells, wherein increased expression of Zscan4 rejuvenates the one or more human oocyte cells that are contacted with the agent as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

[0041] Other embodimentsaspects of the present disclosure relate to a method of increasing genome stability of one or more human oocyte cells, by contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, where increased expression of Zscan4 increases genome stability in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent. In one aspect, there is provided an *in vitro* method of increasing genome stability of one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 increases genome stability in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent. In another aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human oocyte cells, in the manufacture of a medicament for increasing genome stability of the one or more human oocyte cells, wherein increased expression of Zscan4 increases genome stability in the one or more human oocyte cells that are contacted with the agent as compared to one or more corresponding human oocyte cells that are not contacted with the agent. Other embodimentsaspects of the present disclosure relate to a method of correcting one or more karyotype abnormalities in one or more human oocyte cells, by contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, where increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent. In one aspect, there is provided an *in vitro* method of correcting one or more karyotype abnormalities in one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent. In another aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human oocyte cells, in the manufacture of a medicament for correcting one or more karyotype abnormalities in the one or more human oocyte cells, wherein increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more human oocyte cells that are contacted with the agent as compared to one or more corresponding human oocyte cells that are not contacted with the agent. In some embodiments, the one or more human oocyte cells are isolated from a subject prior to contacting with the agent that increases expression of Zscan4. In some embodiments, after contacting with the agent that increases expression of Zscan4 the one or more human oocyte cells undergo *in vitro* fertilization.

[0042] Other aspects of the present disclosure relate to an *in vitro* method of increasing genome stability of one or more fertilized human oocytes, ~~by~~ comprising contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, wherein increased expression of Zscan4 increases genome stability in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes ~~embryo~~ that are not contacted with the agent. Other aspects of the present

disclosure relate to an *in vitro* method of correcting one or more karyotype abnormalities in one or more fertilized human oocytes, by contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, where increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes that are not contacted with the agent. In some embodiments, the one or more fertilized human oocytes were fertilized by *in vitro* fertilization. In some embodiments, prior to being fertilized, the one or more human oocytes were isolated from a subject. In some embodiments, the one or more fertilized oocytes are embryos between the one-cell stage and the blastocyst stage.

[0043] Other aspects of the present disclosure relate to a method of treating a disease or condition associated with a telomere abnormality, ~~by~~comprising: i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a telomere abnormality; ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, where increasing expression of Zscan4 induces telomere lengthening in the human bone marrow cells; and iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a telomere abnormality.

[0043a] In another aspect, there is provided use of human bone marrow cells in the manufacture of a medicament for engrafting into a subject to treat a disease or condition associated with a telomere abnormality, wherein the subject is one suffering from the disease or condition associated with a telomere abnormality, wherein the human bone marrow cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces telomere lengthening in the human bone marrow cells.

[0044] Other aspects of the present disclosure relate to a method of treating a disease or condition associated with a chromosome abnormality, ~~by~~comprising: i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a chromosome abnormality; ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the human bone marrow cells; and iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a chromosome abnormality.

[0044a] In one aspect, there is provided use of human bone marrow cells in the manufacture of a medicament for engrafting into a subject to treat a disease or condition associated with a chromosome abnormality, wherein subject is one suffering from the disease or condition associated with a chromosome abnormality, wherein the human bone marrow cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the human bone marrow cells.

[0045] In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is one or more diseases or conditions selected from diseases of telomere shortening, bone marrow failure syndromes, age-related telomere shortening diseases or disorders, and premature aging diseases or disorders. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is a disease of telomere shortening selected from dyskeratosis congenita, Hoyeraal-Hreidarsson syndrome, Revesz syndrome, Coats plus syndrome, idiopathic pulmonary fibrosis, liver cirrhosis, pancreatic

fibrosis, Alzheimer's disease, and osteoarthritis. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is a bone marrow failure syndrome selected from Fanconi anemia, amegakaryocytic thrombocytopenia, aplastic anemia, Diamond Blackfan anemia, dyskeratosis congenita, paroxysmal nocturnal hemoglobinuria (PNH), Pearson syndrome, Shwachman Diamond syndrome, thrombocytopenia, and myelodysplastic syndrome. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is an age-related telomere shortening disease or disease, a premature aging disease or disease, or both selected from Werner syndrome, Bloom's syndrome, Hutchinson-Gilford progeria syndrome, Cockayne syndrome, Xeroderma pigmentosa, Ataxia telangiectasia, Rothmund Thomson syndrome, Trichothiodystrophy, Juberg-Marsidi syndrome, and Down syndrome.

[0046] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating a tissue or organ in a subject, by administering to a subject in need thereof an agent that increases expression of Zscan4 in the tissue or organ, where increasing expression of Zscan4 rejuvenates the tissue or organ. In one aspect, there is provided use of an agent that increases expression of Zscan4 in a tissue or organ, in the manufacture of a medicament for rejuvenating the tissue or organ in a subject in need thereof, wherein increasing expression of Zscan4 rejuvenates the tissue or organ.

[0047] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating a subject in need thereof, by administering to the subject an agent that increases expression of Zscan4, where increasing expression of Zscan4 rejuvenates the subject. In one aspect, there is provided use of an agent that increases expression of Zscan4 in the manufacture for rejuvenating a subject in need thereof, wherein increasing expression of Zscan4 rejuvenates the subject.

[0048] Other embodimentsaspects of the present disclosure relate to a method of extending lifespan of one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in one or more human cells in the subject, where increasing expression of Zscan4 extends the lifespan of the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent. In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for extending lifespan of the one or more human cells, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

[0049] Other embodimentsaspects of the present disclosure relate to a method of extending lifespan of a tissue or organ in a subject, by administering to a subject in need thereof an agent that increases expression of Zscan4 in the tissue or organ, where increasing expression of Zscan4 extends the lifespan of the tissue or organ. In one aspect, there is provided use of an agent that increases expression of Zscan4 in a tissue or organ, in the manufacture of a medicament for extending lifespan of the tissue or organ in a subject, wherein increasing expression of Zscan4 extends the lifespan of the tissue or organ.

[0050] Other embodimentsaspects of the present disclosure relate to a method of extending lifespan of a subject, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where increasing expression of Zscan4

extends the lifespan of the one or more human cells, thereby extending the lifespan of the subject. In one aspect, there is provided use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for extending lifespan of the subject, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells, thereby extending the lifespan of the subject.

[0051] Other aspects of the present disclosure relate to a method of extending lifespan of a subject in need thereof, ~~by~~comprising: i. isolating one or more human cells from the subject; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells; and iii. administering the contacted one or more human cells to the subject to extend the lifespan of the subject. In one aspect, there is provided use of one or more human cells in the manufacture of a medicament for extending lifespan of a subject in need thereof, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells.

[0052] Other aspects of the present disclosure relate to a method for determining one or more Zscan4-induced effects in one or more human cells, ~~by~~comprising: i. contacting the one or more human cells with an agent that increases expression of Zscan4 in one or more human cells; ii. measuring expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells; and iii. comparing the expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells to the expression levels of SERPINB4, DNMT3L, and/or DUX4 in one or more corresponding human cells that are not contacted with the agent, wherein an increase in the expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells indicates the presence of one or more Zscan4-induced effects in the one or more human cell.

[0053] In some embodiments that may be combined with any of the preceding embodiments, the increased expression of Zscan4 is transient. In some embodiments that may be combined with any of the preceding embodiments, the agent increases Zscan4 expression for about 1 hour to about 23 hours. In some embodiments that may be combined with any of the preceding embodiments, the agent increases Zscan4 expression for about 1 day to about 10 days. In some embodiments that may be combined with any of the preceding embodiments, the agent interacts directly with endogenous Zscan4 to increase expression of Zscan4. In some embodiments that may be combined with any of the preceding embodiments, the agent is an isolated nucleic acid molecule encoding Zscan4. In some embodiments that may be combined with any of the preceding embodiments, the isolated nucleic acid molecule is a synthetic mRNA. In some embodiments that may be combined with any of the preceding embodiments, the isolated nucleic acid molecule contains a vector. In some embodiments that may be combined with any of the preceding embodiments, the vector is a viral vector. In some embodiments that may be combined with any of the preceding embodiments, the viral vector is a paramyxovirus vector, a retrovirus vector, a lentivirus vector or an adenovirus vector. In some embodiments that may be

protein is encapsulated in a nanoparticle. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4 protein is a mouse Zscan4 protein, a human ZSCAN4 protein, or a homolog thereof. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4 protein is selected from a Zscan4a protein, a Zscan4b protein, a Zscan4c protein, a Zscan4d protein, a Zscan4e protein, and a Zscan4f protein. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4 protein contains an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to an amino acid sequence selected from SEQ ID NOs: 11-20 and 31-40. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4 protein is a human ZSCAN4 protein. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4 protein contains an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to SEQ ID NO: 17. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4 protein is a Zscan4-ERT2 fusion protein. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4 protein is a Zscan4-ΔC protein. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4-ΔC protein contains a mouse Zscan4 protein, a human ZSCAN4 protein, or a homolog thereof, and where the Zscan4 protein contains a deletion of at least one zinc finger domain. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4-ΔC protein contains a Zscan4 protein selected from a Zscan4a protein, a Zscan4b protein, a Zscan4c protein, a Zscan4d protein, a Zscan4e protein, and a Zscan4f protein, and where the Zscan4 protein contains a deletion of at least one zinc finger domain. In some embodiments that may be combined with any of the preceding embodiments, the Zscan4-ΔC protein contains a human ZSCAN4 protein, and where the Zscan4 protein contains a deletion of at least one zinc finger domain. In some embodiments that may be combined with any of the preceding embodiments, the agent is a retinoid, an agent that induces oxidative stress, or both.

[0054] Other embodimentsaspects of the present disclosure relate to a method of increasing telomere length in one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the human cell, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where

increased expression of Zscan4 induces telomere lengthening in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0055] Other embodimentsaspects of the present disclosure relate to a method of treating a subject in need of telomere lengthening, by contacting one or more human cells in the subject with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 induces telomere lengthening in the one or more human cells.

[0056] Other embodimentsaspects of the present disclosure relate to a method of treating a subject in need of telomere lengthening, by: i. isolating one or more human cells in need of telomere lengthening from the subject; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and iii. administering the contacted one or more human cells to the subject.

[0057] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a telomere abnormality, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces telomere lengthening in the one or more human cells to treat the disease or condition associated with a telomere abnormality.

[0058] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a telomere abnormality, by: i. isolating one or more human cells from a subject suffering from a disease or condition associated with a telomere abnormality; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a telomere abnormality.

[0059] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a chromosome abnormality, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells to treat the disease or condition associated with a chromosome abnormality.

[0060] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a chromosome abnormality, by: i. isolating one or more human cells from a subject suffering from a disease or condition associated with a chromosome abnormality; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells; and iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a chromosome abnormality.

[0061] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a karyotype abnormality, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells to treat the disease or condition associated with a karyotype abnormality.

[0062] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a karyotype abnormality, by: i. isolating one or more human cells from a subject suffering from a disease or condition associated with a karyotype abnormality; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells; and iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a karyotype abnormality.

ataxia, spinal muscular atrophy, Steele- Richardson-Olszewski disease, Tabes dorsalis, and toxic encephalopathy.

[0064] Other embodimentsaspects of the present disclosure relate to a method of treating a cancer, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more cancer cells in the subject, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 represses growth of the one or more cancer cells, thereby treating the cancer. Other embodimentsaspects of the present disclosure relate to a method of improving responsiveness to chemotherapy in a cancer patient, by administering to a subject in need thereof an agent that reduces expression of endogenous ZSCAN4 in one or more cancer stem cells in the subject, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where reducing expression of endogenous ZSCAN4 reduces or eliminates resistance to one or more chemotherapeutic agents in the one or more cancer stem cells, thereby improving responsiveness to the one or more chemotherapeutic agents in the subject. In some embodiments, the agent that reduces expression of endogenous ZSCAN4 is an siRNA or shRNA specific for ZSCAN4. In some embodiments, the cancer selected from cancers of the heart (e.g. angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma, myxoma, rhabdomyoma, fibroma, lipoma and teratoma), lung cancers (e.g., bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma); gastrointestinal tract cancers (e.g., esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma); stomach cancers (carcinoma, lymphoma, leiomyosarcoma); pancreatic cancers (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma); small bowel cancers (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma); large bowel cancers (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); genitourinary tract cancers (e.g., kidney (adenocarcinoma, Wilms' tumor, nephroblastoma, lymphoma, leukemia); bladder and urethra cancers (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma); prostate cancers (adenocarcinoma, sarcoma); testis cancers (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); liver cancers (e.g., hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma); bone cancers (e.g., osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma,

chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor, chordoma, osteochondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors); nervous system cancers (e.g., skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma, pinealoma, glioblastoma multiforme, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord (neurofibroma, meningioma, glioma, sarcoma)); gynecological cancers (e.g., uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma, serous cystadenocarcinoma, mucinous cystadenocarcinoma, endometrioid tumors, Brenner tumor, clear cell carcinoma, unclassified carcinoma, granulosa-theca cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, embryonal rhabdomyosarcoma, fallopian tubes (carcinoma)); hematologic cancers (e.g., blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma)); skin cancers (e.g., malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles, dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis); and adrenal gland cancers (e.g., neuroblastoma).

[0065] Other embodimentsaspects of the present disclosure relate to a method of increasing genome stability of one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 increases genome stability in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0066] Other embodimentsaspects of the present disclosure relate to a method of increasing DNA repair capacity of one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 increases DNA repair capacity in

the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0067] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 rejuvenates the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0068] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating skin, treating atopic dermatitis, and/or a skin lesion, by topically administering to the skin of a subject in need thereof an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4,.

[0069] Other embodimentsaspects of the present disclosure relate to a method of treating hair loss, by topically administering to the scalp of a subject in need thereof an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4.

[0070] Other embodimentsaspects of the present disclosure relate to a method of preventing hair graying, treating hair graying, or both, by administering to one or more hair follicles of a subject in need thereof an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4.

[0071] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating a cornea, by administering to a cornea of a subject in need thereof an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4.

[0072] Other embodimentsaspects of the present disclosure relate to a method of treating dry eye, by administering to a cornea of a subject in need thereof an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4.

[0073] Other embodimentsaspects of the present disclosure relate to a method of treating idiopathic pulmonary fibrosis, by administering to a lung of a subject in need thereof an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4.

[0074] Other embodimentsaspects of the present disclosure relate to a method of treating atherosclerosis, a coronary heart disease, or both, by administering to the bloodstream of a subject in need thereof an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4.

[0075] Other embodimentsaspects of the present disclosure relate to a method of providing resistance to one or more genotoxic agents in one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 increases resistance to one or more genotoxic agents in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent. In some embodiments, the genotoxic agent is mitomycin C or cisplatin.

[0076] In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are human adult cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are adult stem cells, tissue stem cells, progenitor cells, or induced pluripotent stem cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are one or more adult stem cells, tissue stem cells, or progenitor cells selected from hematopoietic stem cells, mesenchymal stem cells, adipose stem cells, neuronal stem cells, and germ stem cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are somatic cells, mature cells, or differentiated cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are somatic cells, mature cells, or differentiated cells. In some embodiments that may be combined with any of the preceding embodiments, the one or more human cells are one or more somatic cells, mature cells, or differentiated cells selected from epidermal cells, fibroblasts, lymphocytes, hepatocytes, epithelial cells, myocytes, chondrocytes, osteocytes, adipocytes, cardiomyocytes, pancreatic β cells, keratinocytes, erythrocytes, peripheral blood cells, neurocytes, astrocytes, germ cells, sperm cells, and oocytes.

[0077] Other embodimentsaspects of the present disclosure relate to a method for inducing a human embryonic stem cell-like DNA methylation pattern in one or more human induced pluripotent stem (iPS) cells, by contacting the one or more human iPS cells with an agent that increases expression of Zscan4 in the one or more human iPS cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 induces a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells as compared to one or more corresponding human iPS cells that are not contacted with the agent.

[0078] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating one or more human oocyte cells, by contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 rejuvenates the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

[0079] Other embodimentsaspects of the present disclosure relate to a method of increasing genome stability of one or more human oocyte cells, by contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 increases genome stability in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent. Other embodimentsaspects of the present disclosure relate to a method of correcting one or more karyotype abnormalities in one or more human oocyte cells, by contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent. In some embodiments, the one or more human oocyte cells are isolated from a subject prior to contacting with the agent that increases expression of Zscan4. In some embodiments, after contacting with the agent that increases expression of Zscan4 the one or more human oocyte cells undergo *in vitro* fertilization.

[0080] Other embodimentsaspects of the present disclosure relate to an *in vitro* method of increasing genome stability of one or more fertilized human oocytes, by contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 increases genome stability in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes embryo that are not contacted with the agent. Other embodimentsaspects of the present disclosure relate to an *in vitro* method of correcting one or more karyotype abnormalities in one or more fertilized human oocytes, by contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes that are not contacted with the agent. In some embodiments, the one or more fertilized human oocytes were fertilized by *in vitro* fertilization. In some embodiments, prior to being fertilized, the one or more human oocytes were isolated from a subject. In some embodiments, the one or more fertilized oocytes are embryos between the one-cell stage and the blastocyst stage.

[0081] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a telomere abnormality, by: i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a telomere abnormality; ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces telomere lengthening in the human bone marrow cells; and iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a telomere abnormality.

[0082] Other embodimentsaspects of the present disclosure relate to a method of treating a disease or condition associated with a chromosome abnormality, by: i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a chromosome abnormality; ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, where the agent is a synthetic mRNA molecule encoding Zscan4

or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 induces correction of the chromosome abnormality in the human bone marrow cells; and iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a chromosome abnormality.

[0083] In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is one or more diseases or conditions selected from diseases of telomere shortening, bone marrow failure syndromes, age-related telomere shortening diseases or disorders, and premature aging diseases or disorders. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is a disease of telomere shortening selected from dyskeratosis congenita, Hoyeraal-Hreidarsson syndrome, Revesz syndrome, Coats plus syndrome, idiopathic pulmonary fibrosis, liver cirrhosis, pancreatic fibrosis, Alzheimer's disease, and osteoarthritis. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is a bone marrow failure syndrome selected from Fanconi anemia, amegakaryocytic thrombocytopenia, aplastic anemia, Diamond Blackfan anemia, dyskeratosis congenita, paroxysmal nocturnal hemoglobinuria (PNH), Pearson syndrome, Shwachman Diamond syndrome, thrombocytopenia, and myelodysplastic syndrome. In some embodiments that may be combined with any of the preceding embodiments, the disease or condition is an age-related telomere shortening disease or disease, a premature aging disease or disease, or both selected from Werner syndrome, Bloom's syndrome, Hutchinson-Gilford progeria syndrome, Cockayne syndrome, Xeroderma pigmentosa, Ataxia telangiectasia, Rothmund Thomson syndrome, Trichothiodystrophy, Juberg-Marsidi syndrome, and Down syndrome.

[0084] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating a tissue or organ in a subject, by administering to a subject in need thereof an agent that increases expression of Zscan4 in the tissue or organ, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 rejuvenates the tissue or organ.

[0085] Other embodimentsaspects of the present disclosure relate to a method of rejuvenating a subject in need thereof, by administering to the subject an agent that increases expression of Zscan4, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 rejuvenates the subject.

[0086] Other embodimentsaspects of the present disclosure relate to a method of extending lifespan of one or more human cells, by contacting the one or more human cells with an agent that increases expression of Zscan4 in one or more human cells in the subject, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 extends the lifespan of the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

[0087] Other embodimentsaspects of the present disclosure relate to a method of extending lifespan of a tissue or organ in a subject, by administering to a subject in need thereof an agent that increases expression of Zscan4 in the tissue or organ, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 extends the lifespan of the tissue or organ.

[0088] Other embodimentsaspects of the present disclosure relate to a method of extending lifespan of a subject, by administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 extends the lifespan of the one or more human cells, thereby extending the lifespan of the subject.

[0089] Other embodimentsaspects of the present disclosure relate to a method of extending lifespan of a subject, by: i. isolating one or more human cells from the subject; ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4, and where increasing expression of Zscan4 extends the lifespan of the one or more human cells; and iii. administering the contacted one or more human cells to the subject to extend the lifespan of the subject.

[0090] Other embodimentsaspects of the present disclosure relate to a method for determining one or more Zscan4-induced effects in one or more human cells, by: i. contacting the one or more human cells with an agent that increases expression of Zscan4 in one or more human cells, where the agent is a synthetic mRNA molecule encoding Zscan4 or a viral vector, preferably a Sendai viral vector, encoding Zscan4; ii. measuring expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells; and iii. comparing the expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells to the expression levels of SERPINB4,

CLAIMS

What is claimed:

1. A method of increasing telomere length in one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the human cell, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

2. A method of treating a subject in need of telomere lengthening, comprising contacting one or more human cells in the subject with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells.

3. A method of treating a subject in need of telomere lengthening, comprising:

i. isolating one or more human cells in need of telomere lengthening from the subject;

ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and

iii. administering the contacted one or more human cells to the subject.

4. A method of treating a disease or condition associated with a telomere abnormality, comprising administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells to treat the disease or condition associated with a telomere abnormality.

5. A method of treating a disease or condition associated with a telomere abnormality, comprising:

i. isolating one or more human cells from a subject suffering from a disease or condition associated with a telomere abnormality;

ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and

iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a telomere abnormality.

6. A method of treating a disease or condition associated with a chromosome abnormality, comprising administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells to treat the disease or condition associated with a chromosome abnormality.

7. A method of treating a disease or condition associated with a chromosome abnormality, comprising:

i. isolating one or more human cells from a subject suffering from a disease or condition associated with a chromosome abnormality;

ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells; and

iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a chromosome abnormality.

8. A method of treating a disease or condition associated with a karyotype abnormality, comprising administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells to treat the disease or condition associated with a karyotype abnormality.

9. A method of treating a disease or condition associated with a karyotype abnormality, comprising:

i. isolating one or more human cells from a subject suffering from a disease or condition associated with a karyotype abnormality;

ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells; and

iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a karyotype abnormality.

10. The method of claim 8 or claim 9, wherein the karyotype abnormality is selected from the group consisting of a chromosome nullisomy, a chromosome monosomy, a chromosome trisomy, a chromosome tetrasomy, and a chromosome pentasomy.

11. The method of claim 8 or claim 9, wherein the karyotype abnormality is selected from the group consisting of trisomy 21, trisomy 16, trisomy 18, trisomy 13, monosomy X, XXX aneuploidy, XXY aneuploidy, XYY aneuploidy, and 1p36 duplication.

12. The method of claim 8 or claim 9, wherein the disease or condition associated with a karyotype abnormality is selected from the group consisting of dup(17)(p11.2p11.2) syndrome, Pelizaeus-Merzbacher disease, dup(22)(q11.2q11.2) syndrome, cat-eye syndrome, Cri-du-chat syndrome, Wolf-Hirschhorn, Williams-Beuren syndrome, Charcot-Marie-Tooth disease, Hereditary neuropathy with liability to pressure palsies, Smith-Magenis syndrome, Neurofibromatosis, Alagille syndrome, Velocardiofacial syndrome, DiGeorge syndrome, Steroid sulfatase deficiency, Kallmann syndrome, Microphthalmia with linear skin defects, Adrenal hypoplasia, Glycerol kinase deficiency, Pelizaeus-Merzbacher disease, Testis-determining factor on Y, Azoospermia (factor a), Azoospermia (factor b), Azoospermia (factor c), and 1p36 deletion.

13. The method of any one of claims 4-12, wherein the disease or condition is one or more diseases or conditions selected from the group consisting of diseases of telomere shortening, bone marrow failure syndromes, age-related telomere shortening diseases or disorders, and premature aging diseases or disorders.

14. The method of any one of claims 4-9, wherein the disease or condition is a disease of telomere shortening selected from the group consisting of dyskeratosis congenita, Hoyeraal-Hreidarsson syndrome, Revesz syndrome, Coats plus syndrome, idiopathic pulmonary fibrosis, liver cirrhosis, pancreatic fibrosis, Alzheimer's disease, and osteoarthritis.

15. The method of any one of claims 4-9, wherein the disease or condition is a bone marrow failure syndrome selected from the group consisting of Fanconi anemia, amegakaryocytic thrombocytopenia, aplastic anemia, Diamond Blackfan anemia, dyskeratosis congenita, paroxysmal nocturnal hemoglobinuria (PNH), Pearson syndrome, Shwachman Diamond syndrome, thrombocytopenia, and myelodysplastic syndrome.

16. The method of any one of claims 4-9, wherein the disease or condition is an age-related telomere shortening disease or disorder, a premature aging disease or disorder, or both selected from the group consisting of Werner syndrome, Bloom's syndrome, Hutchinson-Gilford progeria syndrome, Cockayne syndrome, Xeroderma pigmentosa, Ataxia telangiectasia, Rothmund Thomson syndrome, Trichothiodystrophy, Juberg-Marsidi syndrome, and Down syndrome.

17. The method of any one of claims 4-9, wherein the disease or condition is one or more diseases or conditions selected from the group consisting of immunological deficiencies, an autoimmune disease, an autoimmune disorder, chronic ulcers, atherosclerosis, cancer, a neurologic injury, a degenerative disorder, a neurodegenerative disorder, wound healing, muscle repair, cardiac muscle repair, cartilage replacement, arthritis, osteoarthritis, tooth regeneration, blindness, age-related blindness due to proliferative decline of retinal pigmented epithelial cells, deafness, bone marrow failure, bone marrow transplant, diabetes, muscular dystrophy, Duchenne muscular dystrophy, a genetic disease, a genetic mutation, and DNA damage.

18. The method of any one of claims 4-9, wherein the disease or condition is a cancer selected from the group consisting of cancers of the heart (e.g. angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma, myxoma, rhabdomyoma, fibroma, lipoma and teratoma), lung cancers (e.g., bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma); gastrointestinal tract cancers (e.g., esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma); stomach cancers (carcinoma, lymphoma, leiomyosarcoma); pancreatic cancers (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma); small bowel cancers (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma); large bowel cancers (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); genitourinary tract cancers (e.g., kidney (adenocarcinoma, Wilms' tumor, nephroblastoma, lymphoma, leukemia); bladder and urethra cancers (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma); prostate cancers (adenocarcinoma, sarcoma); testis cancers (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); liver cancers (e.g., hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma); bone cancers (e.g., osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor, chordoma, osteochondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors); nervous system cancers (e.g., skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma, pinealoma, glioblastoma multiforme, oligodendroglioma,

schwannoma, retinoblastoma, congenital tumors), spinal cord (neurofibroma, meningioma, glioma, sarcoma)); gynecological cancers (e.g., uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma, serous cystadenocarcinoma, mucinous cystadenocarcinoma, endometrioid tumors, Brenner tumor, clear cell carcinoma, unclassified carcinoma, granulosa-theca cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, embryonal rhabdomyosarcoma, fallopian tubes (carcinoma)); hematologic cancers (e.g., blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma)); skin cancers (e.g., malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles, dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis); and adrenal gland cancers (e.g., neuroblastoma).

19. The method of any one of claims 4-9 wherein the disease or condition is an autoimmune disease selected from the group consisting of thyroiditis, Goodpasture's disease, rheumatoid arthritis, juvenile oligoarthritis, collagen-induced arthritis, adjuvant-induced arthritis, Sjogren' s syndrome, multiple sclerosis, experimental autoimmune encephalomyelitis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, autoimmune gastric atrophy, pemphigus vulgaris, psoriasis, vitiligo, type 1 diabetes, non-obese diabetes, myasthenia gravis, Grave's disease, Hashimoto' s thyroiditis, sclerosing cholangitis, sclerosing sialadenitis, systemic lupus erythematosis, autoimmune thrombocytopenia purpura, Addison' s disease, systemic sclerosis, polymyositis, dermatomyositis, autoimmune hemolytic anemia, and pernicious anemia.

20. The method of any one of claims 4-9, wherein the disease or condition is a neurodegenerative disease selected from the group consisting of adrenoleukodystrophy (ALD), alcoholism, Alexander's disease, Alper's disease, Alzheimer's disease, amyotrophic lateral sclerosis, Lou Gehrig's Disease, ataxia telangiectasia, Batten disease, Spielmeyer-Vogt-Sjogren-Batten disease, bovine spongiform encephalopathy (BSE), Canavan disease, cerebral palsy, Cockayne syndrome, Corticobasal degeneration, Creutzfeldt-Jakob disease, familial fatal insomnia, frontotemporal lobar degeneration, Huntington's disease, HIV-associated dementia, Kennedy's disease, Krabbe's disease, Lewy body dementia, neuroborreliosis, Machado- Joseph disease, Spinocerebellar ataxia type 3, Multiple System Atrophy, multiple sclerosis, narcolepsy, Niemann Pick disease, Parkinson's disease, Pelizaeus-Merzbacher Disease, Pick's disease,

primary lateral sclerosis, prion diseases, progressive supranuclear palsy, Refsum's disease, Sandhoff disease, Schilder's disease, subacute combined degeneration of spinal cord secondary to Pernicious Anaemia, Spielmeyer-Vogt-Sjogren-Batten disease, Batten disease, spinocerebellar ataxia, spinal muscular atrophy, Steele- Richardson-Olszewski disease, Tabes dorsalis, and toxic encephalopathy.

21. A method of treating a cancer, comprising administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more cancer cells in the subject, wherein increasing expression of Zscan4 represses growth of the one or more cancer cells, thereby treating the cancer.

22. A method of improving responsiveness to chemotherapy in a cancer patient, comprising administering to a subject in need thereof an agent that reduces expression of endogenous ZSCAN4 in one or more cancer stem cells in the subject, wherein reducing expression of endogenous ZSCAN4 reduces or eliminates resistance to one or more chemotherapeutic agents in the one or more cancer stem cells, thereby improving responsiveness to the one or more chemotherapeutic agents in the subject.

23. The method of claim 22, wherein the agent that reduces expression of endogenous ZSCAN4 is an siRNA or shRNA specific for ZSCAN4.

24. The method of any one of claims 21-23, wherein the cancer selected from the group consisting of cancers of the heart (e.g. angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma, myxoma, rhabdomyoma, fibroma, lipoma and teratoma), lung cancers (e.g., bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma); gastrointestinal tract cancers (e.g., esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma); stomach cancers (carcinoma, lymphoma, leiomyosarcoma); pancreatic cancers (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma); small bowel cancers (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma); large bowel cancers (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); genitourinary tract cancers (e.g., kidney (adenocarcinoma, Wilms' tumor, nephroblastoma, lymphoma, leukemia); bladder and urethra cancers (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma); prostate cancers (adenocarcinoma, sarcoma); testis cancers (seminoma, teratoma, embryonal carcinoma, teratocarcinoma,

choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); liver cancers (e.g., hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma); bone cancers (e.g., osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor, chordoma, osteochondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors); nervous system cancers (e.g., skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma, pinealoma, glioblastoma multiforme, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord (neurofibroma, meningioma, glioma, sarcoma)); gynecological cancers (e.g., uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma, serous cystadenocarcinoma, mucinous cystadenocarcinoma, endometrioid tumors, Brenner tumor, clear cell carcinoma, unclassified carcinoma, granulosa-theca cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, embryonal rhabdomyosarcoma, fallopian tubes (carcinoma)); hematologic cancers (e.g., blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma)); skin cancers (e.g., malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles, dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis); and adrenal gland cancers (e.g., neuroblastoma).

25. A method of increasing genome stability of one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases genome stability in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

26. A method of increasing DNA repair capacity of one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases DNA repair capacity

in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

27. A method of rejuvenating one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 rejuvenates the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

28. A method of rejuvenating skin, treating atopic dermatitis, and/or a skin lesion, comprising topically administering to the skin of a subject in need thereof an agent that increases expression of Zscan4.

29. A method of treating hair loss, comprising topically administering to the scalp of a subject in need thereof an agent that increases expression of Zscan4.

30. A method of preventing hair graying, treating hair graying, or both, comprising administering to one or more hair follicles of a subject in need thereof an agent that increases expression of Zscan4.

31. A method of rejuvenating a cornea, comprising administering to a cornea of a subject in need thereof an agent that increases expression of Zscan4.

32. A method of treating dry eye, comprising administering to a cornea of a subject in need thereof an agent that increases expression of Zscan4.

33. A method of treating idiopathic pulmonary fibrosis, comprising administering to a lung of a subject in need thereof an agent that increases expression of Zscan4.

34. A method of treating atherosclerosis, a coronary heart disease, or both, comprising administering to the bloodstream of a subject in need thereof an agent that increases expression of Zscan4.

35. A method of providing resistance to one or more genotoxic agents in one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases resistance to one or more genotoxic agents in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

36. The method of claim 35, wherein the genotoxic agent is mitomycin C or cisplatin.

37. The method of any one of claims 1-36, wherein the one or more human cells are human adult cells.

38. The method of any one of claims 1-36, wherein the one or more human cells are adult stem cells, tissue stem cells, progenitor cells, or induced pluripotent stem cells.

39. The method of any one of claims 1-36, wherein the one or more human cells are one or more adult stem cells, tissue stem cells, or progenitor cells selected from the group consisting of hematopoietic stem cells, mesenchymal stem cells, adipose stem cells, neuronal stem cells, and germ stem cells.

40. The method of any one of claims 1-36, wherein the one or more human cells are somatic cells, mature cells, or differentiated cells.

41. The method of any one of claims 1-36, wherein the one or more human cells are one or more somatic cells, mature cells, or differentiated cells selected from the group consisting of epidermal cells, fibroblasts, lymphocytes, hepatocytes, epithelial cells, myocytes, chondrocytes, osteocytes, adipocytes, cardiomyocytes, pancreatic β cells, keratinocytes, erythrocytes, peripheral blood cells, neurocytes, astrocytes, germ cells, sperm cells, and oocytes.

42. A method for inducing a human embryonic stem cell-like DNA methylation pattern in one or more human induced pluripotent stem (iPS) cells, comprising contacting the one or more human iPS cells with an agent that increases expression of Zscan4 in the one or more human iPS cells, wherein increased expression of Zscan4 induces a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells as compared to one or more corresponding human iPS cells that are not contacted with the agent.

43. A method of rejuvenating one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 rejuvenates the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

44. A method of increasing genome stability of one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4

in the one or more human oocyte cells, wherein increased expression of Zscan4 increases genome stability in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

45. A method of correcting one or more karyotype abnormalities in one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

46. The method of any one of claims 43-45, wherein the one or more human oocyte cells are isolated from a subject prior to contacting with the agent that increases expression of Zscan4.

47. The method of any one of claims 43-46, wherein after contacting with the agent that increases expression of Zscan4 the one or more human oocyte cells undergo *in vitro* fertilization.

48. An *in vitro* method of increasing genome stability of one or more fertilized human oocytes, comprising contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, wherein increased expression of Zscan4 increases genome stability in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes that are not contacted with the agent.

49. An *in vitro* method of correcting one or more karyotype abnormalities in one or more fertilized human oocytes, comprising contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, wherein increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes that are not contacted with the agent.

50. The method of claim 48 or claim 49, wherein the one or more fertilized human oocytes were fertilized by *in vitro* fertilization.

51. The method of claim 50, wherein prior to being fertilized, the one or more human oocytes were isolated from a subject.

52. The method of any one of claims 48-51, wherein the one or more fertilized oocytes are embryos between the one-cell stage and the blastocyst stage.

53. A method of treating a disease or condition associated with a telomere abnormality, comprising:

i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a telomere abnormality;

ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces telomere lengthening in the human bone marrow cells; and

iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a telomere abnormality.

54. A method of treating a disease or condition associated with a chromosome abnormality, comprising:

i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a chromosome abnormality;

ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the human bone marrow cells; and

iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a chromosome abnormality.

55. The method of claim 53 or claim 54, wherein the disease or condition is one or more diseases or conditions selected from the group consisting of diseases of telomere shortening, bone marrow failure syndromes, age-related telomere shortening diseases or disorders, and premature aging diseases or disorders.

56. The method of claim 53 or claim 54, wherein the disease or condition is a disease of telomere shortening selected from the group consisting of dyskeratosis congenita, Hoyeraal-Hreidarsson syndrome, Revesz syndrome, Coats plus syndrome, idiopathic pulmonary fibrosis, liver cirrhosis, pancreatic fibrosis, Alzheimer's disease, and osteoarthritis.

57. The method of claim 53 or claim 54, wherein the disease or condition is a bone marrow failure syndrome selected from the group consisting of Fanconi anemia, amegakaryocytic

thrombocytopenia, aplastic anemia, Diamond Blackfan anemia, dyskeratosis congenita, paroxysmal nocturnal hemoglobinuria (PNH), Pearson syndrome, Shwachman Diamond syndrome, thrombocytopenia, and myelodysplastic syndrome.

58. The method of claim 53 or claim 54, wherein the disease or condition is an age-related telomere shortening disease or disease, a premature aging disease or disease, or both selected from the group consisting of Werner syndrome, Bloom's syndrome, Hutchinson-Gilford progeria syndrome, Cockayne syndrome, Xeroderma pigmentosa, Ataxia telangiectasia, Rothmund Thomson syndrome, Trichothiodystrophy, Juberg-Marsidi syndrome, and Down syndrome.

59. A method of rejuvenating a tissue or organ in a subject, comprising administering to a subject in need thereof an agent that increases expression of Zscan4 in the tissue or organ, wherein increasing expression of Zscan4 rejuvenates the tissue or organ.

60. A method of rejuvenating a subject in need thereof, comprising administering to the subject an agent that increases expression of Zscan4, wherein increasing expression of Zscan4 rejuvenates the subject.

61. A method of extending lifespan of one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in one or more human cells in the subject, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

62. A method of extending lifespan of a tissue or organ in a subject, comprising administering to a subject in need thereof an agent that increases expression of Zscan4 in the tissue or organ, wherein increasing expression of Zscan4 extends the lifespan of the tissue or organ.

63. A method of extending lifespan of a subject, comprising administering to a subject in need thereof an agent that increases expression of Zscan4 in one or more human cells in the subject, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells, thereby extending the lifespan of the subject.

64. A method of extending lifespan of a subject in need thereof, comprising:

i. isolating one or more human cells from the subject;

ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells; and

iii. administering the contacted one or more human cells to the subject to extend the lifespan of the subject.

65. A method for determining one or more Zscan4-induced effects in one or more human cells, comprising:

i. contacting the one or more human cells with an agent that increases expression of Zscan4 in one or more human cells;

ii. measuring expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells; and

iii. comparing the expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells to the expression levels of SERPINB4, DNMT3L, and/or DUX4 in one or more corresponding human cells that are not contacted with the agent, wherein an increase in the expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells indicates the presence of one or more Zscan4-induced effects in the one or more human cell.

66. The method of any one of claims 1-65, wherein the increased expression of Zscan4 is transient.

67. The method of any one of claims 1-66, wherein the agent increases Zscan4 expression for about 1 hour to about 23 hours.

68. The method of any one of claims 1-66, wherein the agent increases Zscan4 expression for about 1 day to about 10 days.

69. The method of any one of claims 1-68, wherein the agent interacts directly with endogenous Zscan4 to increase expression of Zscan4.

70. The method of any one of claims 1-68, wherein the agent is an isolated nucleic acid molecule encoding Zscan4.

71. The method of claim 70, wherein the isolated nucleic acid molecule is a synthetic mRNA.

72. The method of claim 70, wherein the isolated nucleic acid molecule comprises a vector.

73. The method of claim 72, wherein the vector is a viral vector.

74. The method of claim 73, wherein the viral vector is a paramyxovirus vector, a retrovirus vector, a lentivirus vector, or an adenovirus vector.

75. The method of claim 73, wherein the viral vector is a paramyxovirus vector.

76. The method of claim 75, wherein the paramyxovirus vector is a Sendai virus vector.

77. The method of claim 72, wherein the vector is a plasmid vector.

78. The method of any one of claims 72-77, wherein the vector encodes Zscan4 operably linked to a promoter.

79. The method of claim 78, wherein the promoter is a constitutive promoter.

80. The method of claim 78, wherein the promoter is an inducible promoter.

81. The method of any one of claims 70-80, wherein the Zscan4 is a Zscan4-ERT2 fusion protein.

82. The method of any one of claims 70-80, wherein the Zscan4 is a Zscan4-ΔC protein.

83. The method of claim 82, wherein the Zscan4-ΔC protein comprises a deletion of at least one zinc finger domain.

84. The method of any one of claims 70-83, wherein the Zscan4 is mouse Zscan4, human ZSCAN4, or a homolog thereof.

85. The method of any one of claims 70-83, wherein the Zscan4 is selected from the group consisting of Zscan4a, Zscan4b, Zscan4c, Zscan4d, Zscan4e, and Zscan4f.

86. The method of any one of claims 70-83, wherein the isolated nucleic acid molecule comprises a nucleotide sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to a nucleotide sequence selected from the group consisting of SEQ ID Nos: 1-10 and 21-30.

87. The method of any one of claims 70-83, wherein the Zscan4 is human ZSCAN4.

88. The method of any one of claims 70-83, wherein the isolated nucleic acid molecule comprises a nucleotide sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to SEQ ID NO: 7.

89. The method of any one of claims 1-68, wherein the agent is a Zscan4 protein.

90. The method of claim 89, wherein the Zscan4 protein is fused to a cell-penetrating peptide.

91. The method of claim 90, wherein the cell-penetrating peptide comprises a protein transduction domain.

92. The method of claim 90 or claim 91, wherein the cell-penetrating peptide comprises a poly-arginine peptide tag.

93. The method of claim 89, wherein the Zscan4 protein is encapsulated in a nanoparticle.

94. The method of any one of claims 89-93, wherein the Zscan4 protein is a mouse Zscan4 protein, a human ZSCAN4 protein, or a homolog thereof.

95. The method of any one of claims 89-93, wherein the Zscan4 protein is selected from the group consisting of a Zscan4a protein, a Zscan4b protein, a Zscan4c protein, a Zscan4d protein, a Zscan4e protein, and a Zscan4f protein.

96. The method of any one of claims 89-93, wherein the Zscan4 protein comprises an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 11-20 and 31-40.

97. The method of any one of claims 89-93, wherein the Zscan4 protein is a human ZSCAN4 protein.

98. The method of any one of claims 89-93, wherein the Zscan4 protein comprises an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least

87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to SEQ ID NO: 17.

99. The method of any one of claims 89-98, wherein the Zscan4 protein is a Zscan4-ERT2 fusion protein.

100. The method of any one of claims 89-93, wherein the Zscan4 protein is a Zscan4-ΔC protein.

101. The method of claim 100, wherein the Zscan4-ΔC protein comprises a mouse Zscan4 protein, a human ZSCAN4 protein, or a homolog thereof, and wherein the Zscan4 protein comprises a deletion of at least one zinc finger domain.

102. The method of claim 100, wherein the Zscan4-ΔC protein comprises a Zscan4 protein selected from the group consisting of a Zscan4a protein, a Zscan4b protein, a Zscan4c protein, a Zscan4d protein, a Zscan4e protein, and a Zscan4f protein, and wherein the Zscan4 protein comprises a deletion of at least one zinc finger domain.

103. The method of claim 100, wherein the Zscan4-ΔC protein comprises a human ZSCAN4 protein, and wherein the ZSCAN4 protein comprises a deletion of at least one zinc finger domain.

104. The method of any one of claims 1-68, wherein the agent is a retinoid or an agent that induces oxidative stress.

CLAIMS

What is claimed:

1. An *in vitro* method of increasing telomere length in one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the human cell, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

2. Use of an agent that increases expression of Zscan4 in a human cell, in the manufacture of a medicament for increasing telomere length in one or more human cells, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

3. Use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for treating a subject in need of telomere lengthening, wherein increased expression of Zscan4 induces telomere lengthening in the one or more human cells that are contacted with the agent.

4. A method of treating a subject in need of telomere lengthening, comprising:
   i. isolating one or more human cells in need of telomere lengthening from the subject;
   ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and
   iii. administering the contacted one or more human cells to the subject.

5. Use of one or more human cells in the manufacture of a medicament for treating a subject in need of telomere lengthening, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells.

6. Use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for treating a disease or condition associated with a telomere abnormality in the subject, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells to treat the disease or condition associated with a telomere abnormality.

7. A method of treating a disease or condition associated with a telomere abnormality, comprising:
   i. isolating one or more human cells from a subject suffering from a disease or condition associated with a telomere abnormality;
   ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells; and
   iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a telomere abnormality.

8. Use of one or more human cells in the manufacture of a medicament for treating a disease or condition associated with a telomere abnormality in a subject suffering from the disease or

condition associated with a telomere abnormality, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces telomere lengthening in the one or more human cells.

9. Use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for treating a disease or condition associated with a chromosome abnormality in the subject, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells to treat the disease or condition associated with a chromosome abnormality.

10. A method of treating a disease or condition associated with a chromosome abnormality, comprising:

i. isolating one or more human cells from a subject suffering from a disease or condition associated with a chromosome abnormality;
ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells; and
iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a chromosome abnormality.

11. Use of one or more human cells in the manufacture of a medicament for treating a disease or condition associated with a chromosome abnormality in a subject suffering from the disease or condition associated with a chromosome abnormality, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the one or more human cells.

12. Use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for treating a disease or condition associated with a karyotype abnormality in the subject, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells to treat the disease or condition associated with a karyotype abnormality.

13. A method of treating a disease or condition associated with a karyotype abnormality, comprising:

i. isolating one or more human cells from a subject suffering from a disease or condition associated with a karyotype abnormality;
ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells; and
iii. administering the contacted one or more human cells to the subject to treat the disease or condition associated with a karyotype abnormality.

14. Use of one or more human cells in the manufacture of a medicament for treating a disease or condition associated with a karyotype abnormality in a subject suffering from the disease or condition associated with a karyotype abnormality, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 induces correction of the karyotype abnormality in the one or more human cells.

15. The method of claim 13 or use of claim 12 or 14, wherein the karyotype abnormality is selected from the group consisting of a chromosome nullisomy, a chromosome monosomy, a chromosome trisomy, a chromosome tetrasomy, and a chromosome pentasomy.

16. The method of claim 13 or use of claim 12 or 14, wherein the karyotype abnormality is selected from the group consisting of trisomy 21, trisomy 16, trisomy 18, trisomy 13, monosomy X, XXX aneuploidy, XXY aneuploidy, XYY aneuploidy, and 1p36 duplication.

17. The method of claim 13 or use of claim 12 or 14, wherein the disease or condition associated with a karyotype abnormality is selected from the group consisting of dup(17)(p11.2p11.2) syndrome, Pelizaeus-Merzbacher disease, dup(22)(q11.2q11.2) syndrome, cat-eye syndrome, Cri-du-chat syndrome, Wolf-Hirschhorn, Williams-Beuren syndrome, Charcot-Marie-Tooth disease, Hereditary neuropathy with liability to pressure palsies, Smith-Magenis syndrome, Neurofibromatosis, Alagille syndrome, Velocardiofacial syndrome, DiGeorge syndrome, Steroid sulfatase deficiency, Kallmann syndrome, Microphthalmia with linear skin defects, Adrenal hypoplasia, Glycerol kinase deficiency, Pelizaeus-Merzbacher disease, Testis-determining factor on Y, Azoospermia (factor a), Azoospermia (factor b), Azoospermia (factor c), and 1p36 deletion.

18. The method of any one of claims 7, 10, 13 and 15-17, or use of any one of claims 6, 8, 9, 11, 12, 14 and 15-17, wherein the disease or condition is one or more diseases or conditions selected from the group consisting of diseases of telomere shortening, bone marrow failure syndromes, age-related telomere shortening diseases or disorders, and premature aging diseases or disorders.

19. The method of any one of claims 7, 10 and 13, or use of any one of claims 6, 8, 9, 11, 12 and 14, wherein the disease or condition is a disease of telomere shortening selected from the group consisting of dyskeratosis congenita, Hoyeraal-Hreidarsson syndrome, Revesz syndrome, Coats plus syndrome, idiopathic pulmonary fibrosis, liver cirrhosis, pancreatic fibrosis, Alzheimer's disease, and osteoarthritis.

20. The method of any one of claims 7, 10 and 13, or use of any one of claims 6, 8, 9, 11, 12 and 14, wherein the disease or condition is a bone marrow failure syndrome selected from the group consisting of Fanconi anemia, amegakaryocytic thrombocytopenia, aplastic anemia, Diamond Blackfan anemia, dyskeratosis congenita, paroxysmal nocturnal hemoglobinuria (PNH), Pearson syndrome, Shwachman Diamond syndrome, thrombocytopenia, and myelodysplastic syndrome.

21. The method of any one of claims 7, 10 and 13, or use of any one of claims 6, 8, 9, 11, 12 and 14, wherein the disease or condition is an age-related telomere shortening disease or disorder, a premature aging disease or disorder, or both selected from the group consisting of Werner syndrome, Bloom's syndrome, Hutchinson-Gilford progeria syndrome, Cockayne syndrome, Xeroderma pigmentosa, Ataxia telangiectasia, Rothmund Thomson syndrome, Trichothiodystrophy, Juberg-Marsidi syndrome, and Down syndrome.

22. The method of any one of claims 7, 10 and 13, or use of any one of claims 6, 8, 9, 11, 12 and 14, wherein the disease or condition is one or more diseases or conditions selected from the group consisting of immunological deficiencies, an autoimmune disease, an autoimmune disorder, chronic ulcers, atherosclerosis, cancer, a neurologic injury, a degenerative disorder, a neurodegenerative disorder, wound healing, muscle repair, cardiac muscle repair, cartilage replacement, arthritis, osteoarthritis, tooth regeneration, blindness, age-related blindness due to proliferative decline of retinal pigmented epithelial cells, deafness, bone marrow failure, bone marrow transplant, diabetes, muscular dystrophy, Duchenne muscular dystrophy, a genetic disease, a genetic mutation, and DNA damage.

23. The method of any one of claims 7, 10 and 13, or use of any one of claims 6, 8, 9, 11, 12 and 14, wherein the disease or condition is a cancer selected from the group consisting of cancers of the heart (e.g. angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma, myxoma, rhabdomyoma, fibroma, lipoma and teratoma), lung cancers (e.g., bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma); gastrointestinal tract cancers (e.g., esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma); stomach cancers (carcinoma, lymphoma, leiomyosarcoma); pancreatic cancers (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma); small bowel cancers (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma); large bowel cancers (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); genitourinary tract cancers (e.g., kidney (adenocarcinoma, Wilms' tumor, nephroblastoma, lymphoma, leukemia); bladder and urethra cancers (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma); prostate cancers (adenocarcinoma, sarcoma); testis cancers (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); liver cancers (e.g., hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma); bone cancers (e.g., osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor, chordoma, osteochondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors); nervous system cancers (e.g., skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma, pinealoma, glioblastoma multiforme, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord (neurofibroma, meningioma,

glioma, sarcoma)); gynecological cancers (e.g., uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma, serous cystadenocarcinoma, mucinous cystadenocarcinoma, endometrioid tumors, Brenner tumor, clear cell carcinoma, unclassified carcinoma, granulosa-theca cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, embryonal rhabdomyosarcoma, fallopian tubes (carcinoma)); hematologic cancers (e.g., blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma)); skin cancers (e.g., malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles, dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis); and adrenal gland cancers (e.g., neuroblastoma).

24. The method of any one of claims 7, 10 and 13, or use of any one of claims 6, 8, 9, 11, 12 and 14, wherein the disease or condition is an autoimmune disease selected from the group consisting of thyroiditis, Goodpasture's disease, rheumatoid arthritis, juvenile oligoarthritis, collagen-induced arthritis, adjuvant-induced arthritis, Sjogren' s syndrome, multiple sclerosis, experimental autoimmune encephalomyelitis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, autoimmune gastric atrophy, pemphigus vulgaris, psoriasis, vitiligo, type 1 diabetes, non-obese diabetes, myasthenia gravis, Grave's disease, Hashimoto' s thyroiditis, sclerosing cholangitis, sclerosing sialadenitis, systemic lupus erythematosis, autoimmune thrombocytopenia purpura, Addison' s disease, systemic sclerosis, polymyositis, dermatomyositis, autoimmune hemolytic anemia, and pernicious anemia.

25. The method of any one of claims 7, 10 and 13, or use of any one of claims 6, 8, 9, 11, 12 and 14, wherein the disease or condition is a neurodegenerative disease selected from the group consisting of adrenoleukodystrophy (ALD), alcoholism, Alexander's disease, Alper's disease, Alzheimer's disease, amyotrophic lateral sclerosis, Lou Gehrig's Disease, ataxia telangiectasia, Batten disease, Spielmeyer-Vogt-Sjogren-Batten disease, bovine spongiform encephalopathy (BSE), Canavan disease, cerebral palsy, Cockayne syndrome, Corticobasal degeneration, Creutzfeldt-Jakob disease, familial fatal insomnia, frontotemporal lobar degeneration, Huntington's disease, HIV-associated dementia, Kennedy's disease, Krabbe's disease, Lewy body dementia, neuroborreliosis, Machado- Joseph disease, Spinocerebellar ataxia type 3, Multiple System Atrophy, multiple sclerosis, narcolepsy, Niemann Pick disease, Parkinson's disease, Pelizaeus-Merzbacher Disease, Pick's disease, primary lateral sclerosis, prion diseases, progressive supranuclear palsy, Refsum's disease, Sandhoff disease, Schilder's disease, subacute

combined degeneration of spinal cord secondary to Pernicious Anaemia, Spielmeyer-Vogt-Sjogren-Batten disease, Batten disease, spinocerebellar ataxia, spinal muscular atrophy, Steele-Richardson-Olszewski disease, Tabes dorsalis, and toxic encephalopathy.

26. Use of an agent that increases expression of Zscan4 in one or more cancer cells in a subject, in the manufacture of a medicament for treating a cancer in the subject, wherein increasing expression of Zscan4 represses growth of the one or more cancer cells, thereby treating the cancer.

27. Use of an agent that reduces expression of endogenous ZSCAN4 in one or more cancer stem cells in a cancer patient, in the manufacture of a medicament for improving responsiveness to chemotherapy in the cancer patient, wherein reducing expression of endogenous ZSCAN4 reduces or eliminates resistance to one or more chemotherapeutic agents in the one or more cancer stem cells, thereby improving responsiveness to the one or more chemotherapeutic agents in the cancer patient.

28. The use of claim 27, wherein the agent that reduces expression of endogenous ZSCAN4 is an siRNA or shRNA specific for ZSCAN4.

29. The use of any one of claims 26-28, wherein the cancer selected from the group consisting of cancers of the heart (e.g. angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma, myxoma, rhabdomyoma, fibroma, lipoma and teratoma), lung cancers (e.g., bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma); gastrointestinal tract cancers (e.g., esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma); stomach cancers (carcinoma, lymphoma, leiomyosarcoma); pancreatic cancers (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma); small bowel cancers (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma); large bowel cancers (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); genitourinary tract cancers (e.g., kidney (adenocarcinoma, Wilms' tumor, nephroblastoma, lymphoma, leukemia); bladder and urethra cancers (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma); prostate cancers (adenocarcinoma, sarcoma); testis cancers (seminoma, teratoma, embryonal carcinoma, teratocarcinoma,

choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); liver cancers (e.g., hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma); bone cancers (e.g., osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma,

chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor, chordoma, osteochondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors); nervous system cancers (e.g., skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma, pinealoma, glioblastoma multiforme, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord (neurofibroma, meningioma, glioma, sarcoma)); gynecological cancers (e.g., uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma, serous cystadenocarcinoma, mucinous cystadenocarcinoma, endometrioid tumors, Brenner tumor, clear cell carcinoma, unclassified carcinoma, granulosa-theca cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, embryonal rhabdomyosarcoma, fallopian tubes (carcinoma)); hematologic cancers (e.g., blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma)); skin cancers (e.g., malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles, dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis); and adrenal gland cancers (e.g., neuroblastoma).

30. An *in vitro* method of increasing genome stability of one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases genome stability in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

31. Use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for increasing genome stability of the one or more human cells, wherein increased expression of Zscan4 increases genome stability in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent

32. An *in vitro* method of increasing DNA repair capacity of one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases DNA repair capacity

in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

33. Use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for increasing DNA repair capacity of the one or more human cells, wherein increased expression of Zscan4 increases DNA repair capacity in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent

34. An *in vitro* method of rejuvenating one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 rejuvenates the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

35. Use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for rejuvenating the one or more human cells, wherein increased expression of Zscan4 rejuvenates the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

36. Use of an agent that increases expression of Zscan4 in the manufacture of a medicament for rejuvenating skin, treating atopic dermatitis, and/or a skin lesion, wherein the medicament is to be topically administered to a subject in need thereof.

37. Use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating hair loss, wherein the medicament is to be topically administered to the scalp of a subject in need thereof.

38. Use of an agent that increases expression of Zscan4 in the manufacture of a medicament for preventing hair graying, treating hair graying, or both, wherein the medicament is to be administered to one or more hair follicles of a subject in need thereof.

39. Use of an agent that increases expression of Zscan4 in the manufacture of a medicament for rejuvenating a cornea in a subject in need thereof.

40. Use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating dry eye in a subject in need thereof.

41. Use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating idiopathic pulmonary fibrosis, wherein the medicament is to be administered to a lung of a subject in need thereof.

42. Use of an agent that increases expression of Zscan4 in the manufacture of a medicament for treating atherosclerosis, a coronary heart disease, or both, wherein the medicament is to be administered to the bloodstream of a subject in need thereof.

43. An *in vitro* method of providing resistance to one or more genotoxic agents in one or more human cells, comprising contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increased expression of Zscan4 increases resistance to one or more genotoxic agents in the one or more human cells as compared to one or more corresponding human cells that are not contacted with the agent.

44. Use of an agent that increases expression of Zscan4 in one or more human cells, in the manufacture of a medicament for providing resistance to one or more genotoxic agents in the one or more human cells, wherein increased expression of Zscan4 increases resistance to one or more

genotoxic agents in the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

45. The method of claim 43 or use of claim 44, wherein the genotoxic agent is mitomycin C or cisplatin.

46. The method or use of any one of claims 1-45, wherein the one or more human cells are human adult cells.

47. The method or use of any one of claims 1-45, wherein the one or more human cells are adult stem cells, tissue stem cells, progenitor cells, or induced pluripotent stem cells.

48. The method or use of any one of claims 1-45, wherein the one or more human cells are one or more adult stem cells, tissue stem cells, or progenitor cells selected from the group consisting of hematopoietic stem cells, mesenchymal stem cells, adipose stem cells, neuronal stem cells, and germ stem cells.

49. The method or use of any one of claims 1-45, wherein the one or more human cells are somatic cells, mature cells, or differentiated cells.

50. The method or use of any one of claims 1-45, wherein the one or more human cells are one or more somatic cells, mature cells, or differentiated cells selected from the group consisting of epidermal cells, fibroblasts, lymphocytes, hepatocytes, epithelial cells, myocytes, chondrocytes, osteocytes, adipocytes, cardiomyocytes, pancreatic β cells, keratinocytes, erythrocytes, peripheral blood cells, neurocytes, astrocytes, germ cells, sperm cells, and oocytes.

51. An *in vitro* method for inducing a human embryonic stem cell-like DNA methylation pattern in one or more human induced pluripotent stem (iPS) cells, comprising contacting the one or more human iPS cells with an agent that increases expression of Zscan4 in the one or more human iPS cells, wherein increased expression of Zscan4 induces a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells as compared to one or more corresponding human iPS cells that are not contacted with the agent.

52. Use of an agent that increases expression of Zscan4 in one or more human induced pluripotent stem (iPS) cells, in the manufacture of a medicament for inducing a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells, wherein increased expression of Zscan4 induces a human embryonic stem cell-like DNA methylation pattern in the one or more human iPS cells that are contacted with the agent as compared to one or more corresponding human iPS cells that are not contacted with the agent.

53. An *in vitro* method of rejuvenating one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 rejuvenates the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

54. Use of an agent that increases expression of Zscan4 in one or more human oocyte cells, in the manufacture of a medicament for rejuvenating the one or more human oocyte cells, wherein increased expression of Zscan4 rejuvenates the one or more human oocyte cells that are

contacted with the agent as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

55. An *in vitro* method of increasing genome stability of one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 increases genome stability in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

56. Use of an agent that increases expression of Zscan4 in one or more human oocyte cells, in the manufacture of a medicament for increasing genome stability of the one or more human oocyte cells, wherein increased expression of Zscan4 increases genome stability in the one or more human oocyte cells that are contacted with the agent as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

57. An *in vitro* method of correcting one or more karyotype abnormalities in one or more human oocyte cells, comprising contacting the one or more human oocyte cells with an agent that increases expression of Zscan4 in the one or more human oocyte cells, wherein increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more human oocyte cells as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

58. Use of an agent that increases expression of Zscan4 in one or more human oocyte cells, in the manufacture of a medicament for correcting one or more karyotype abnormalities in the one or more human oocyte cells, wherein increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more human oocyte cells that are contacted with the agent as compared to one or more corresponding human oocyte cells that are not contacted with the agent.

59. The method of any one of claims 53, 55 and 57, or the use of any one of claims 54, 56 and 58, wherein the one or more human oocyte cells are isolated from a subject prior to contacting with the agent that increases expression of Zscan4.

60. The method of any one of claims 53, 55, 57 and 59, or the use of any one of claims 54, 56, 58 and 59, wherein after contacting with the agent that increases expression of Zscan4 the one or more human oocyte cells undergo *in vitro* fertilization.

61. An *in vitro* method of increasing genome stability of one or more fertilized human oocytes, comprising contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, wherein increased expression of Zscan4 increases genome stability in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes that are not contacted with the agent.

62. An *in vitro* method of correcting one or more karyotype abnormalities in one or more fertilized human oocytes, comprising contacting the one or more fertilized human oocytes with an agent that increases expression of Zscan4 in the one or more fertilized human oocytes, wherein increased expression of Zscan4 induces correction of the one or more karyotype abnormalities in the one or more fertilized human oocytes as compared to one or more corresponding fertilized human oocytes that are not contacted with the agent.

63. The method of claim 61 or claim 62, wherein the one or more fertilized human oocytes were fertilized by *in vitro* fertilization.

64. The method of claim 63, wherein prior to being fertilized, the one or more human oocytes were isolated from a subject.

65. The method of any one of claims 61-64, wherein the one or more fertilized oocytes are embryos between the one-cell stage and the blastocyst stage.

66. A method of treating a disease or condition associated with a telomere abnormality, comprising:

i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a telomere abnormality;
ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces telomere lengthening in the human bone marrow cells; and
iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a telomere abnormality.

67. Use of human bone marrow cells in the manufacture of a medicament for engrafting into a subject to treat a disease or condition associated with a telomere abnormality, wherein the subject is one suffering from the disease or condition associated with a telomere abnormality, wherein the human bone marrow cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces telomere lengthening in the human bone marrow cells.

68. A method of treating a disease or condition associated with a chromosome abnormality, comprising:

i. isolating human bone marrow cells from a subject suffering from a disease or condition associated with a chromosome abnormality;
ii. contacting the human bone marrow cells with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the human bone marrow cells; and
iii. engrafting the contacted human bone marrow cells into the subject to treat the disease or condition associated with a chromosome abnormality.

69. Use of human bone marrow cells in the manufacture of a medicament for engrafting into a subject to treat a disease or condition associated with a chromosome abnormality, wherein subject is one suffering from the disease or condition associated with a chromosome abnormality, wherein the human bone marrow cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the human bone marrow cells, wherein increasing expression of Zscan4 induces correction of the chromosome abnormality in the human bone marrow cells.

70. The method of claim 66 or claim 68, or use of claim 67 or 69 wherein the disease or condition is one or more diseases or conditions selected from the group consisting of diseases of telomere shortening, bone marrow failure syndromes, age-related telomere shortening diseases or disorders, and premature aging diseases or disorders.

71. The method of claim 66 or claim 68, or use of claim 67 or 69 wherein the disease or condition is a disease of telomere shortening selected from the group consisting of dyskeratosis

congenita, Hoyeraal-Hreidarsson syndrome, Revesz syndrome, Coats plus syndrome, idiopathic pulmonary fibrosis, liver cirrhosis, pancreatic fibrosis, Alzheimer's disease, and osteoarthritis.

72. The method of claim 66 or claim 68, or use of claim 67 or 69 wherein the disease or condition is a bone marrow failure syndrome selected from the group consisting of Fanconi anemia, amegakaryocytic thrombocytopenia, aplastic anemia, Diamond Blackfan anemia, dyskeratosis congenita, paroxysmal nocturnal hemoglobinuria (PNH), Pearson syndrome, Shwachman Diamond syndrome, thrombocytopenia, and myelodysplastic syndrome.

73. The method of claim 66 or claim 68, or use of claim 67 or 69 wherein the disease or condition is an age-related telomere shortening disease or disease, a premature aging disease or disease, or both selected from the group consisting of Werner syndrome, Bloom's syndrome, Hutchinson-Gilford progeria syndrome, Cockayne syndrome, Xeroderma pigmentosa, Ataxia telangiectasia, Rothmund Thomson syndrome, Trichothiodystrophy, Juberg-Marsidi syndrome, and Down syndrome.

74. Use of an agent that increases expression of Zscan4 in a tissue or organ, in the manufacture of a medicament for rejuvenating the tissue or organ in a subject in need thereof, wherein increasing expression of Zscan4 rejuvenates the tissue or organ.

75. Use of an agent that increases expression of Zscan4 in the manufacture for rejuvenating a subject in need thereof, wherein increasing expression of Zscan4 rejuvenates the subject.

76. Use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for extending lifespan of the one or more human cells, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells that are contacted with the agent as compared to one or more corresponding human cells that are not contacted with the agent.

77. Use of an agent that increases expression of Zscan4 in a tissue or organ, in the manufacture of a medicament for extending lifespan of the tissue or organ in a subject, wherein increasing expression of Zscan4 extends the lifespan of the tissue or organ.

78. Use of an agent that increases expression of Zscan4 in one or more human cells in a subject, in the manufacture of a medicament for extending lifespan of the subject, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells, thereby extending the lifespan of the subject.

79. A method of extending lifespan of a subject in need thereof, comprising:

i. isolating one or more human cells from the subject;

ii. contacting the one or more human cells with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells; and

iii. administering the contacted one or more human cells to the subject to extend the lifespan of the subject.

80. Use of one or more human cells in the manufacture of a medicament for extending lifespan of a subject in need thereof, wherein the one or more human cells have been isolated from the subject and contacted with an agent that increases expression of Zscan4 in the one or more human cells, wherein increasing expression of Zscan4 extends the lifespan of the one or more human cells.

81. A method for determining one or more Zscan4-induced effects in one or more human cells, comprising:

i. contacting the one or more human cells with an agent that increases expression of Zscan4 in one or more human cells;

ii. measuring expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells; and

iii. comparing the expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells to the expression levels of SERPINB4, DNMT3L, and/or DUX4 in one or more corresponding human cells that are not contacted with the agent, wherein an increase in the expression levels of SERPINB4, DNMT3L, and/or DUX4 in the one or more human cells indicates the presence of one or more Zscan4-induced effects in the one or more human cell.

82. The method or use of any one of claims 1-81, wherein the increased expression of Zscan4 is transient.

83. The method or use of any one of claims 1-82, wherein the agent increases Zscan4 expression for about 1 hour to about 23 hours.

84. The method or use of any one of claims 1-82, wherein the agent increases Zscan4 expression for about 1 day to about 10 days.

85. The method or use of any one of claims 1-84, wherein the agent interacts directly with endogenous Zscan4 to increase expression of Zscan4.

86. The method or use of any one of claims 1-84, wherein the agent is an isolated nucleic acid molecule encoding Zscan4.

87. The method or use of claim 86, wherein the isolated nucleic acid molecule is a synthetic mRNA.

88. The method or use of claim 86, wherein the isolated nucleic acid molecule comprises a vector.

89. The method or use of claim 88, wherein the vector is a viral vector.

90. The method or use of claim 89, wherein the viral vector is a paramyxovirus vector, a retrovirus vector, a lentivirus vector, or an adenovirus vector.

91. The method or use of claim 89, wherein the viral vector is a paramyxovirus vector.

92. The method or use of claim 91, wherein the paramyxovirus vector is a Sendai virus vector.

93. The method or use of claim 88, wherein the vector is a plasmid vector.

94. The method or use of any one of claims 88-93, wherein the vector encodes Zscan4 operably linked to a promoter.

95. The method or use of claim 94, wherein the promoter is a constitutive promoter.

96. The method or use of claim 94, wherein the promoter is an inducible promoter.

97. The method or use of any one of claims 86-96, wherein the Zscan4 is a Zscan4-ERT2 fusion protein.

98. The method or use of any one of claims 86-96, wherein the Zscan4 is a Zscan4-ΔC protein.

99. The method or use of claim 98, wherein the Zscan4-ΔC protein comprises a deletion of at least one zinc finger domain.

100. The method or use of any one of claims 86-99, wherein the Zscan4 is mouse Zscan4, human ZSCAN4, or a homolog thereof.

101. The method or use of any one of claims 86-99, wherein the Zscan4 is selected from the group consisting of Zscan4a, Zscan4b, Zscan4c, Zscan4d, Zscan4e, and Zscan4f.

102. The method or use of any one of claims 86-99, wherein the isolated nucleic acid molecule comprises a nucleotide sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to a nucleotide sequence selected from the group consisting of SEQ ID Nos: 1-10 and 21-30.

103. The method or use of any one of claims 86-99, wherein the Zscan4 is human ZSCAN4.

104. The method or use of any one of claims 86-99, wherein the isolated nucleic acid molecule comprises a nucleotide sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to SEQ ID NO: 7.

105. The method or use of any one of claims 1-84, wherein the agent is a Zscan4 protein.

106. The method or use of claim 105, wherein the Zscan4 protein is fused to a cell-penetrating peptide.

107. The method or use of claim 106, wherein the cell-penetrating peptide comprises a protein transduction domain.

108. The method or use of claim 106 or claim 107, wherein the cell-penetrating peptide comprises a poly-arginine peptide tag.

109. The method or use of claim 105, wherein the Zscan4 protein is encapsulated in a nanoparticle.

110. The method or use of any one of claims 105-109, wherein the Zscan4 protein is a mouse Zscan4 protein, a human ZSCAN4 protein, or a homolog thereof.

111. The method or use of any one of claims 105-109, wherein the Zscan4 protein is selected from the group consisting of a Zscan4a protein, a Zscan4b protein, a Zscan4c protein, a Zscan4d protein, a Zscan4e protein, and a Zscan4f protein.

112. The method or use of any one of claims 105-109, wherein the Zscan4 protein comprises an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 11-20 and 31-40.

113. The method or use of any one of claims 105-109, wherein the Zscan4 protein is a human ZSCAN4 protein.

114. The method or use of any one of claims 105-109, wherein the Zscan4 protein comprises an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to SEQ ID NO: 17.

115. The method or use of any one of claims 105-114, wherein the Zscan4 protein is a Zscan4-ERT2 fusion protein.

116. The method or use of any one of claims 105-109, wherein the Zscan4 protein is a Zscan4-ΔC protein.

117. The method or use of claim 116, wherein the Zscan4-ΔC protein comprises a mouse Zscan4 protein, a human ZSCAN4 protein, or a homolog thereof, and wherein the Zscan4 protein comprises a deletion of at least one zinc finger domain.

118. The method or use of claim 116, wherein the Zscan4-ΔC protein comprises a Zscan4 protein selected from the group consisting of a Zscan4a protein, a Zscan4b protein, a Zscan4c protein, a Zscan4d protein, a Zscan4e protein, and a Zscan4f protein, and wherein the Zscan4 protein comprises a deletion of at least one zinc finger domain.

119. The method or use of claim 116, wherein the Zscan4-ΔC protein comprises a human ZSCAN4 protein, and wherein the ZSCAN4 protein comprises a deletion of at least one zinc finger domain.

120. The method or use of any one of claims 1-84, wherein the agent is a retinoid or an agent that induces oxidative stress.