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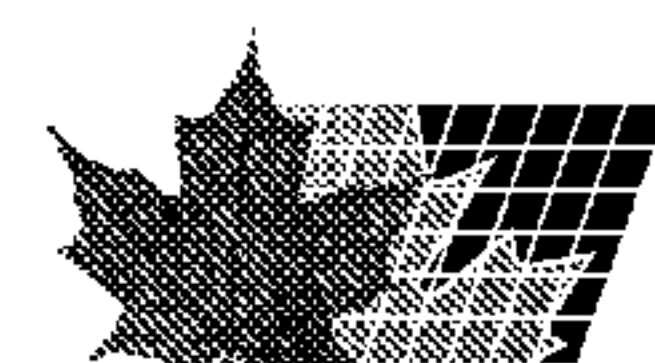
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(54) Titre : CORNEE SYNTHETIQUE PRODUITE A PARTIR DE CELLULES SOUCHES RETINIENNES
(54) Title: SYNTHETIC CORNEA FROM RETINAL STEM CELLS

(57) **Abrégé/Abstract:**

Methods of producing synthetic corneas are disclosed which are differentiated from retinal stem cells (rSC) derived from parthenogenetically activated human oocytes, including that such synthetic corneas are produced in the absence of a 3-D scaffold. Isolated synthetic corneas, produced by the disclosed methods, are also described.



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(54) Title: SYNTHETIC CORNEA FROM RETINAL STEM CELLS

(57) Abstract: Methods of producing synthetic corneas are disclosed which are differentiated from retinal stem cells (rSC) derived from parthenogenetically activated human oocytes, including that such synthetic corneas are produced in the absence of a 3-D scaffold. Isolated synthetic corneas, produced by the disclosed methods, are also described.

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SYNTHETIC CORNEA FROM RETINAL STEM CELLS

FIELD OF THE INVENTION

[0001] The invention relates generally to embryonic stems cells (ES), and more specifically to a process for obtaining synthetic corneas.

BACKGROUND INFORMATION

[0002] Human embryonic stem cells (hES) cells are pluripotent cells that can differentiate into an array of cell types. When injected into immune-deficient mice, embryonic stem cells form differentiated tumors (teratomas). However, embryonic stem cells that are induced *in vitro* to form embryoid bodies (EBs) provide a source of embryonic stem cell lines that are amenable to differentiation into multiple cell types characteristic of several tissues under certain growth conditions. For example, hES have been differentiated into endoderm, ectoderm, and mesoderm derivatives.

[0003] Human ES cells and their differentiated progeny are important sources of human cells for therapeutic transplantation and for drug testing and development. Required by both of these goals is the provision of sufficient cells that are differentiated into tissue types suitable for a patient's needs or the appropriate pharmacological test. Associated with this is a need for an efficient and reliable method of producing differentiated cells from embryonic stem cells.

[0004] hES and hEG cells offer remarkable scientific and therapeutic possibilities, involving potential for generating more specialized cells or tissues. Ethical concerns about the sources of hES and hEG cells, however, and fears that use of nuclear transfer (NT) for research could lead to use of NT to produce a human being, have fostered a great deal of public discussion and debate.

[0005] Parthenogenic activation of mammalian oocytes may be used as an alternative to fertilization by sperm/NT to prepare oocytes for embryonic stem cell generation. Parthenogenic activation is the production of embryonic cells, with or without eventual development into an adult, from a female gamete in the absence of any contribution from a male gamete.

[0006] Currently, a focus of stem cell research is the development of artificial organs, rehabilitation devices, or prosthesis to replace natural body tissues. This development generally envisages the use of biocompatible materials for engineering stem cells to control expansion/differentiation; i.e., the use of 3-D scaffolds (e.g., PLG scaffolds, chitosan scaffolds, PCL/PEG scaffolds) to create devices which mimic tissue-like function by providing mechanical support for proliferation.

[0007] Alternatively, transplantation of cultured stem cells or differentiated stem cells is envisioned as a therapeutic modality. These methods are generally known as in vivo tissue engineering or in situ generation. While much of the work in this area purports the direct transplantation of cultured cells, as a practical matter, such modalities often require seeding differentiated stem cells within porous scaffold biomaterials (e.g., cardiomyocytes derived from stem cells and gels or porous alginate).

SUMMARY OF THE INVENTION

[0008] The present invention relates to the seminal discovery of a method of producing a 3-dimensional sensory system organ obtained from stem cells derived from parthenogenically activated human oocytes. The method of the invention does not require the use of external scaffolding. As disclosed in one embodiment, the sensory organ is a synthetic cornea.

[0010] In one embodiment, an isolated retinal-stem cell derived synthetic cornea is disclosed. In a related aspect, the retinal stem cell is obtained from a parthenogenetically activated human oocyte. In another related aspect, the cornea is terminally differentiated. In another aspect, the cornea is histocompatible with the oocyte donor, including that the cornea comprises homoplasmic mitochondrial DNA, and is transplantable in humans.

[0011] In another embodiment, a method of producing a synthetic cornea is disclosed, including parthenogenetically activating a human oocyte, where activation includes contacting the oocyte with an ionophore at high O₂ tension and contacting the oocyte with a serine-threonine kinase inhibitor under low O₂ tension, cultivating the activated oocyte at low O₂ tension until blastocyst formation, transferring the blastocyst to a layer of feeder cells, and culturing the transferred blastocyst under high O₂ tension, mechanically isolating an inner cell mass (ICM) from trophectoderm of the blastocyst and culturing the cells of the ICM on a layer of feeder cells under high O₂ tension, where retinal stem cells can be identified in the culture by human embryonic stem cell markers (hES) and neuron specific markers, and where

the identified retinal stem cells are optionally isolated, culturing the isolated stem cells in media comprising serum replacement (M/SR), plasmonate, and at least one mitogen that activates the gp130/STAT pathway and/or the MAP kinase pathway on a fibroblast feeder layer treated with a DNA synthesis inhibitor, culturing the mitogen treated cells in M/SR comprising plasmonate (M/SRP), without added mitogen, to near confluence, where about 1/2 volume of the M/SRP is replaced with M/SR periodically until the near confluent cells develop pigmentation and a domed appearance, and transferring the pigmented cells in M/SR to a gelatin coated substrate, where about 1/2 volume of the M/SR is replaced with M/SR periodically until a synthetic cornea develops. Optionally, the retinal cells can be cultured as an enriched rather than isolated population of cells.

[0012] In one aspect, the mitogen is selected from leukemia inhibitory factor (LIF), bFGF, and a combination thereof. In another aspect, the DNA synthesis inhibitor is an alkylating agent, including, but not limited to, mitomycin C. In a related aspect, the feeder cells are human.

[0013] In one embodiment, a method of treating a subject in need thereof is disclosed, including replacing a cornea of the subject with a synthetic cornea. In one aspect, the subject has a disease which effects the cornea such as keratitis, corneal ulcer, corneal abrasion, snow blindness, arc eye, Thygeson's superficial punctate keratopathy, Fuchs' dystrophy, keratoconus, keratpconjunctivitis sicca, corneal infections, or corneal dystrophy. In another aspect, the subject has an injured cornea.

[0014] In another embodiment, a method of identifying an agent that affects the cornea of an eye is disclosed including contacting a retinal-stem cell derived synthetic cornea with an agent and observing a change to the cornea in the presence and absence of the agent, where a change to the cornea is indicative of an agent that affects the cornea.

[0015] In one aspect, the agent has a therapeutic effect on the cornea. In another aspect, the agent has an adverse effect on the cornea. In a related aspect, the change to the cornea includes modulation of gene expression, modulation of protein expression, change in opacity, change in plasticity, change in hardness, change in light phase velocity, and change in shape.

[0016] In one embodiment, a method for replacement of a cornea of an eye with the synthetic cornea is disclosed including surgically excising the cornea from the eye, inserting

the synthetic cornea into the area of the removed cornea, and allowing the synthetic cornea to interface with tissue underlying the excision to anchor the synthetic cornea to the eye.

[0017] In a related aspect, the method further includes separating a portion of the outer surface of a cornea thereby forming a corneal flap and a corneal bed, the corneal flap having an anterior surface and a posterior surface, the corneal bed having a shaped anterior surface, implanting the synthetic cornea on the corneal bed, the cornea having an anterior surface and a posterior surface, and replacing the portion of the cornea that was separated.

[0018] In another embodiment, a method of delivering an effective amount of an agent to the eye of a subject is disclosed including transforming at least a portion of the cells comprising the synthetic cornea with a nucleic acid vehicle, where the vehicle encodes the agent, identifying a population of cells comprising the synthetic cornea which express the agent encoded by the nucleic acid, and replacing cornea cells of the subject with transformed cells of the synthetic cornea, where the replaced cells deliver the agent to the eye of the subject.

[0019] In a related aspect, the replacing step includes replacing the cornea of the subject with the synthetic cornea.

[0020] Exemplary methods and compositions according to this invention are described in greater detail below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] Figure 1A shows a micrograph of the surface marker expression of alkaline phosphatase for the parthenogenically derived hES cells.

[0022] Figure 1B shows a micrograph of the expression for the surface marker Oct4.

[0023] Figure 1C shows a micrograph of the expression for the surface marker SSEA-1.

[0024] Figure 1D shows a micrograph of the expression for the surface marker SSEA-3.

[0025] Figure 1E shows a micrograph of the expression for the surface marker SSEA-4.

[0026] Figure 1F shows a micrograph of the expression for the surface marker TRA-1-60.

[0027] Figure 1G shows a micrograph of the expression for the surface marker TRA-1-81.

[0028] Figure 2A shows the analysis of telomerase activity for the parthenogenically derived hES cells. 500, 1000, and 10000 (units) of extract was used to perform the analysis. Δ H-heat treated test extract (negative control); positive control-telomerase positive cells; CHAPS-lysis buffer; TSR8-control template.

[0029] Figure 2B shows a micrograph of embryoid body formation from parthenogenically derived hES cells, 9 day culture.

[0030] Figure 2C shows a micrograph of embryoid body formation from parthenogenically derived hES cells, 10 day culture.

[0031] Figure 2D illustrates the karyotype of parthenogenically derived hES cells.

[0032] Figure 2E shows the results from DNA finger printing analysis of parthenogenically derived hES cells. 1- DNA from the blood of the oocyte donor; 2 – DNA from the parthenogenic hES cells derived from the same donor; 3 - DNA from human feeder fibroblasts.

[0033] Figure 3 shows Northern blot for characterizing the expression of genes associated with genomic imprinting. DNA probes: SNRPN, Peg1_2, Peg1_A, H19, and GAPDH (as an internal control). NSF, neonatal skin fibroblasts; hES, human embryonic stem cell line derived from fertilized oocytes; 1, phESC-1; 2, phESC-3, 3, phESC-4, 4, phESC-5; 5, phESC-6; 6 phESC-7. NSF RT-, hES RT-, 1 RT- are negative controls.

[0034] Figure 4 shows the differentiation of phESC into derivatives of all three germ layers. Ectoderm differentiation is presented by positive immunocytochemical staining for neuron specific markers 68 (A), NCAM (B), beta III-tubulin (C) and glial cell marker GFAP (D, M). Differentiated cells were positive for mesodermal markers: muscle specific alpha actinin (G) and desmin (J), endothelial markers PECAM-1 (E) and VE-Cadherin (F). Endoderm differentiation is presented by positive staining for alpha-fetoprotein (H, L). The phESC produce pigmented epithelial-like cells (I, K). Magnification (I) x 100; (A-H, J-M), x 400.

[0035] Figure 5 shows the characterization of phESC lines for specific markers. Undifferentiated colonies of phESC on human feeder layer cells (A-F), negative staining for SSEA-1 (G-L), expression of cell surface markers SSEA-3 (M-R), SSEA-4 (S-X). Magnification (A) to (E) x 100; (F) x 200; (G) to (X) x 400. Alkaline phosphatase positive

staining of phESC colonies on feeder cells (A-F), OCT-4 (G-L), TRA-1-60 (K-R) and TRA-1-81 (S-X). Magnification (A, B, O, R) x 100; (C-F, M, S, X) x 200; (G-L, N, P, Q, T-W) x 400.

[0036] Figure 6 demonstrates that phESC cells possess high levels of telomerase activity by comparison with positive control cells: "+"-extract from 500 cells; "-"-heat treated cell extract with inactivated telomerase; "Control +"-telomerase positive cell extract (applied with TRAPEZE Kit); "B"-CHAPS lysis buffer, primer-dimer/PCR contamination control; TSR8-telomerase quantitative control template (0.1 and 0.2 amole/ μ l); "M"-marker, DNA ladder.

[0037] Figure 7 shows the G-banded karyotyping of phESC lines. The phESC-1 (A), phESC-3 (B), phESC-4 (C), phESC-5 (D) and phESC-6 (E) lines have normal 46, XX karyotype. The phESC-7 line has 47, XXX karyotype (F).

[0038] Figure 8 shows a synthetic cornea obtained from stems cells derived from parthenogenetically activated human oocytes.

DETAILED DESCRIPTION OF THE INVENTION

[0039] Before the present composition, methods, and culturing methodologies are described, it is to be understood that this invention is not limited to particular compositions, methods, and experimental conditions described, as such compositions, methods, and conditions may vary. It is also to be understood that the terminology used herein is for purposes of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only in the appended claims.

[0040] As used in this specification and the appended claims, the singular forms "a", "an", and "the" include plural references unless the context clearly dictates otherwise. Thus, for example, references to "the method" includes one or more methods, and/or steps of the type described herein which will become apparent to those persons skilled in the art upon reading this disclosure and so forth.

[0041] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the invention, as it will be understood that

modifications and variations are encompassed within the spirit and scope of the instant disclosure. All publications mentioned herein are incorporated herein by reference in their entirety.

[0042] "Differentiation" refers to a change that occurs in cells to cause those cells to assume certain specialized functions and to lose the ability to change into certain other specialized functional units. Cells capable of differentiation may be any of totipotent, pluripotent or multipotent cells. Differentiation may be partial or complete with respect to mature adult cells.

[0043] Gynogenesis refers to the production of an embryo containing a discernible trophectoderm and inner cell mass that results upon activation of a cell, such as an oocyte, or other embryonic cell type, containing mammalian DNA of all female origin, preferably human female origin, e.g., human or non-human primate oocyte DNA. Such female mammalian DNA may be genetically modified, e.g., by insertion, deletion or substitution of at least one DNA sequence, or may be unmodified. For example, the DNA may be modified by the insertion or deletion of desired coding sequences, or sequences that promote or inhibit embryogenesis. Typically, such an embryo will be obtained by in vitro activation of an oocyte that contains DNA of all female origin. Gynogenesis is inclusive of parthenogenesis which is defined below. It also includes activation methods where the spermatozoal DNA does not contribute to the DNA in the activated oocyte.

[0044] In a related aspect, oocytes are obtained from superovulating subjects prepared for IVF. "Superovulation" techniques, such as treatment of a female subject with hormones, used in IVF are designed to stimulate the ovaries to produce several eggs (oocytes) rather than the usual single egg as in a natural cycle.

[0045] The medications required to boost egg production may include, but are not limited to the following: Lupron (gonadotropin releasing hormone-agonist), Orgalutran, Antagon or Cetrotide (gonadotropin releasing hormone-antagonist), Follistim, Bravelle or Gonal-F (FSH, follicle stimulating hormone), Repronex (combination of FSH and LH, luteinizing hormone), and Pregnyl or Novarel (hCG, human chorionic gonadotropin).

[0046] In a related aspect, collection of eggs can be performed under transvaginal ultrasound guidance. To accomplish this, a needle is inserted (e.g., under IV sedation)

through the vaginal wall into the ovaries using ultrasound to locate each follicle. The follicular fluid is drawn up into a test tube to obtain the eggs.

[0047] “Parthenogenesis” (“parthenogenically activated” and “parthenogenetically activated” is used interchangeably) the process by which activation of the oocyte occurs in the absence of sperm penetration, and refers to the development of an early stage embryo comprising trophectoderm and inner cell mass that is obtained by activation of an oocyte or embryonic cell, e.g., blastomere, comprising DNA of all female origin. In a related aspect, a “parthenote” refers to the resulting cell obtained by such activation. In another related aspect, “blastocyst” refers to a cleavage stage of a fertilized or activated oocyte comprising a hollow ball of cells made of outer trophoblast cells and an inner cell mass (ICM). In a further related aspect, “blastocyst formation” refers to the process, after oocyte fertilization or activation, where the oocyte is subsequently cultured in media for a time to enable it to develop into a hollow ball of cells made of outer trophoblast cells and ICM (e.g., 5 to 6 days).

[0048] “Pluripotent cell” refers to a cell derived from an embryo produced by activation of a cell containing DNA of all female or male origin that can be maintained in vitro for prolonged, theoretically indefinite period of time in an undifferentiated state, that can give rise to different differentiated tissue types, i.e., ectoderm, mesoderm, and endoderm. The pluripotent state of the cells is preferably maintained by culturing inner cell mass or cells derived from the inner cell mass of an embryo produced by androgenetic or gynogenetic methods under appropriate conditions, for example, by culturing on a fibroblast feeder layer or another feeder layer or culture that includes leukemia inhibitory factor (LIF). The pluripotent state of such cultured cells can be confirmed by various methods, e.g., (i) confirming the expression of markers characteristic of pluripotent cells; (ii) production of chimeric animals that contain cells that express the genotype of the pluripotent cells; (iii) injection of cells into animals, e.g., SCID mice, with the production of different differentiated cell types in vivo; and (iv) observation of the differentiation of the cells (e.g., when cultured in the absence of feeder layer or LIF) into embryoid bodies and other differentiated cell types in vitro.

[0049] “Diploid cell” refers to a cell, e.g., an oocyte or blastomere, having a diploid DNA content of all male or female origin.

[0050] “Haploid cell” refers to a cell, e.g., an oocyte or blastomere, having a haploid DNA content, where the haploid DNA is of all male or female origin.

[0051] “Activation” refers to a process where a fertilized or unfertilized oocyte, for example, but not limited to, in metaphase II of meiosis, undergoes a process typically including separation of the chromatid pairs, extrusion of the second polar body, resulting in an oocyte having a haploid number of chromosomes, each with one chromatid. Activation includes methods whereby a cell containing DNA of all male or female origin is induced to develop into an embryo that has a discernible inner cell mass and trophectoderm, which is useful for producing pluripotent cells but which is itself is likely to be incapable of developing into a viable offspring. Activation may be carried out, for example, under one of the following conditions: (i) conditions that do not cause second polar body extrusion; (ii) conditions that cause polar body extrusion but where the polar body extrusion is inhibited; or (iii) conditions that inhibit first cell division of the haploid oocyte.

[0052] “Metaphase II” refers to a stage of cell development where the DNA content of a cell consists of a haploid number of chromosomes with each chromosome represented by two chromatids.

[0053] In one embodiment, metaphase II oocytes are activated/cultured by incubating oocytes under various O₂ tension gas environments. In a related aspect, the low O₂ tension gas environment is created by a gas mixture comprising an O₂ concentration of about 2%, 3%, 4%, or 5%. In a further related aspect, the gas mixture comprises about 5% CO₂. Further, the gas mixture comprises about 90% N₂, 91% N₂, or 93% N₂. This gas mixture is to be distinguished from 5% CO₂ air, which is approximately about 5% CO₂, 20% O₂, and 75% N₂.

[0054] “O₂ tension” refers to the partial pressure (pressure exerted by a single component of a gas mixture) of oxygen in a fluid (i.e., liquid or gas). Low tension is when the partial pressure of oxygen (pO₂) is low and high tension is when the pO₂ is high.

[0055] “Defined-medium conditions” refer to environments for culturing cells where the concentration of components therein required for optimal growth are detailed. For example, depending on the use of the cells (e.g., therapeutic applications), removing cells from conditions that contain xenogenic proteins is important; i.e., the culture conditions are animal-free conditions or free of non-human animal proteins. In a related aspect, “in vitro fertilization (IVF) media” refers to a nutrient system which contains chemically defined substances on or in which fertilized oocytes can be grown.

[0056] “Extracellular matrix (ECM) substrates” refer to a surface beneath cells which supports optimum growth. For example, such ECM substrates include, but are not limited to, Matrigel, laminin, gelatin, and fibronectin substrates. In a related aspect, such substrates may comprise collagen IV, entactin, heparin sulfate proteoglycan, to include various growth factors (e.g., bFGF, epidermal growth factor, insulin-like growth factor-1, platelet derived growth factor, nerve growth factor, and TGF- β -1).

[0057] “Embryo” refers to an embryo that results upon activation of a cell, e.g., oocyte or other embryonic cells containing DNA of all male or female origin, which optionally may be modified, that comprises a discernible trophectoderm and inner cell mass, which cannot give rise to a viable offspring and where the DNA is of all male or female origin. The inner cell mass or cells contained therein are useful for the production of pluripotent cells as defined previously.

[0058] “Inner cell mass (ICM)” refers to the inner portion of an embryo which gives rise to fetal tissues. Herein, these cells are used to provide a continuous source of pluripotent cells in vitro. Further, the ICM includes the inner portion of the embryo that results from androgenesis or gynogenesis, i.e., embryos that result upon activation of cells containing DNA of all male or female origin. Such DNA, for example, will be human DNA, e.g., human oocyte or spermatozoal DNA, which may or may not have been genetically modified.

[0059] “Trophectoderm” refers to another portion of early stage embryo which gives rise to placental tissues, including that tissue of an embryo that results from androgenesis or gynogenesis, i.e., embryos that result from activation of cells that contain DNA of all male or female origin, e.g., human ovarian or spermatozoan.

[0060] “Differentiated cell” refers to a non-embryonic cell that possesses a particular differentiated, i.e., non-embryonic, state. The three earliest differentiated cell types are endoderm, mesoderm, and ectoderm.

[0061] “Substantially identical” refers to a quality of sameness regarding a particular characteristic that is so close as to be essentially the same within the ability to measure difference (e.g., by HLA typing, SNP analysis, and the like).

[0062] “Histocompatible” refers to the extent to which an organism will tolerate a graft of a foreign tissue.

[0063] “Genomic imprinting” refers to the mechanism by which a number of genes throughout the genome are monoallelically expressed according to their parental origin.

[0064] “Synthetic” refers to the characteristic of an object whose production is by defined artificial manipulation.

[0065] “Homoplasmy,” including grammatical variations thereof, refers to the presence of the same type of the mitochondrial DNA (mtDNA) within a cell or individual.

[0066] “Heteroplasmy,” including grammatical variations thereof, refers to the presence of a mixture of more than one type of mitochondrial DNA (mtDNA) within a cell or individual.

[0067] “Uniparental” refers to one or more cells or individuals from which another arises and to which it remains subsidiary.

[0068] “Mechanically isolating” refers to the process of separating cell aggregates by physical forces. For example, such a process would exclude the use of enzymes (or other cell cleavage products) which might contain non-human materials.

[0069] In one embodiment, stem cells can be generated by methods known in the art, for example, but not limited to, the methods as described by Thomson (see, e.g., U.S. Pat. No. 7,029, 913; U.S. Pat. No. 6,200,806; U.S. Pat. No. 6,887,706; U.S. Pat. No. 5,843,780), Uchida (see, e.g., U.S. Pat. No. 7,083,977; U.S. Pat. No. 7,049,141), Carpenter (see, e.g., U.S. Pat. No. 6,777,233), Anderson et al. (see, e.g., U.S. Pat. No. 5,589,376), Hogan (see, e.g., U.S. Pat. No. 5,453,357), Naktsuji et al. (see, e.g., U.S. Pat. No. 7,083,977), and Khilian (see, e.g., U.S. Pat. No. 5,449,620), which are incorporated herein by reference. In one aspect, retinal stem cells are obtained by methods known in the art (see, e.g., U.S. Pat. No. 6,117,675).

[0070] In another embodiment, stem cells are generated from a parthenogenetically activated human oocyte. In one aspect, a synthetic cornea is obtained from a retinal stem cell differentiated from stem cells derived from a parthenogenetically activated human oocyte.

[0071] In another aspect, the synthetic cornea of the present invention can be used as a replacement for subjects having refractive error, such as those subjects which are nearsighted, farsighted, or have astigmatism. Refractive errors occur when the curve of the cornea is irregularly shaped (too steep or too flat).

[0072] The cornea is a unique, transparent structure that covers the iris, pupil, and anterior chamber, providing most of the eye's optical power. Together with the lens, the cornea refracts light and, as a result, aids in focusing. The cornea contributes more to the total refraction than the lens does, but, whereas the curvature of the lens can be adjusted to "tune" focus, the curvature of the cornea is fixed. The cornea has no blood vessels, its nourishment is obtained via diffusion from the tear fluid, the aqueous humor, and neurotrophins supplied by nerve fibers that innervate it. Thus, for example, disturbances in circulation of these fluids or inflammatory processes play a large role in the pathogenesis of corneal abnormalities.

[0073] The cornea is composed mostly of dense connective tissue. However, the collagen fibers are arranged in a parallel pattern, allowing light waves to constructively interfere, thus letting light pass through relatively uninhibited.

[0074] The changes associated with aging of the cornea include increased opacity, increased anterior surface curvatures, and possibly changes in refractive index distribution. Various refractive eye surgery techniques change the shape of the cornea in order to reduce the need for corrective lenses or otherwise improve the refractive state of the eye. In many techniques, reshaping of the cornea is performed by photoablation using an excimer laser.

[0075] If the corneal stroma develops visually significant opacity, irregularity, or edema, a cadaveric donor cornea can be transplanted. Because there are no blood vessels in the cornea, it is relatively shielded-off from immuno-response, thus the incidence of rejection of donated corneas is relatively low (approximately 20%).

[0076] There are also synthetic corneas (keratoprotheses), however, these are typically plastic inserts or may be composed of biocompatible synthetic materials that encourage tissue in-growth into the synthetic cornea, thereby promoting biointegration. Alternatively, orthokeratology offers the use of specialized hard or rigid gas-permeable contact lenses to transiently reshape the cornea in order to improve the refractive state of the eye or reduce the need for eyeglasses and contact lenses.

[0077] The cornea has unmyelinated nerve endings sensitive to touch, temperature, and chemicals; a touch of the cornea causes an involuntary reflex to close the eyelid. Because transparency is of prime importance, the cornea does not have blood vessels; it receives nutrients via diffusion from the tear fluid at the outside and the aqueous humour at the inside and also from neurotrophins supplied by nerve fibers that innervate it. In humans, the cornea

has a diameter of about 11.5 mm and a thickness of 0.5 mm - 0.6 mm in the center and 0.6 mm - 0.8 mm at the periphery. In humans, the refractive power of the cornea is approximately 43 dioptres, roughly three-fourths of the eye's total refractive power. Transparency, avascularity, and immunologic privilege make the cornea a special tissue.

[0078] The corneal tissue is arranged in five basic layers: epithelium, Bowman's layer, stroma, Descemet's membrane and endothelium, each having a separate function. The epithelium is the outermost layer of the cornea, comprising about 10% of the tissue's thickness. The epithelium functions primarily to: (1) block passage of foreign materials, such as dust, water, and bacteria, into the eye and other layers of the cornea; and (2) provide a smooth surface that absorbs oxygen and cell nutrients from tears, then distributes these nutrients to the rest of the cornea. The epithelium is filled with thousands of tiny nerve endings that make the cornea extremely sensitive to pain when rubbed or scratched. The part of the epithelium that serves as the foundation one which the epithelial cells anchor and organize themselves is called the basement membrane.

[0079] Lying directly below the basement membrane of the epithelium is a transparent sheet known as Bowman's layer. It is composed of strong layered protein (collagen) fibers. Once injured, Bowman's layer can form a scar as it heals. If these scars are large and centrally located, some vision loss can occur.

[0080] Beneath the Bowman's layer is the stroma, which comprises 90% of the cornea's thickness. It consists primarily of water (78%) and collagen (16%), and does not contain any blood vessels. Collagen give the cornea it strength, elasticity, and form. The collagen's unique shape, arrangement, and spacing are essential in producing the cornea's light conducting transparency.

[0081] Under the stroma is Descemet's membrane, a thin but strong sheet of tissue that serves as a protective barrier against infection and injury. Descemet's membrane is composed of collagen fibers (different from those of stroma) and is made by the endothelial cells that lie below it. Descemet's membrane is regenerated readily after injury.

[0082] The endothelium is the extremely thin, innermost layer of the cornea. Endothelial cells are essential in keeping the cornea clear. Normally, fluid leaks slowly from inside the eye into the middle corneal layer (stroma). The endothelium's primary task is to pump this excel fluid out of the stroma. Without this pumping action, the stroma would swell with

water, become hazy, and ultimately opaque. Once endothelium cells are destroyed by disease or trauma, they are lost forever. If too many endothelial cells are destroyed, corneal edema and blindness ensue, with corneal transplantation the only available therapy.

[0083] The human cornea proteome has been characterized. About 52% (28 of 54) of the corneal extracellular proteins are common plasma proteins when the identified immunoglobulin chains and complement C3 are included. This group of corneal proteins also contain different serpins (α -1-antichymotrypsin, α -1-antitrypsin, and antithrombin III), α -1-microglobulin, different apolipoproteins, fibrinogen, haptoglobin, hemopexin, albumin, amyloid P-component, tetranectin, transferrin, transthyretin, and vitamin D-binding protein. Thus, these proteins are either synthesized by the corneal cells or originate from blood and enter the cornea with the bulk flow from the ciliary arteries located in the corneoscleral limbus area.

[0084] When the cornea is curved too much, faraway objects will appear blurry because they are focused in front of the retina: i.e., myopia or nearsightedness. Myopia affects over 25% of all adults. Hyperopia, or farsightedness, is the opposite of myopia. Distant objects are clear, and objects appear blurry close-up (i.e., images focus on a point beyond the retina). Astigmatism is a condition in which the uneven curvature of the cornea blurs and distorts both distant and near objects. In astigmatism, the cornea is shaped like the back of a spoon, curved more in one direction than in another. This causes light rays to have more than one focal point and focus on two separate areas of the retina, distorting the visual image. Two thirds of adults who have myopia also have astigmatism.

[0085] Refractive errors are usually corrected by eyeglasses or contact lenses. Although refractive surgery is becoming an increasing popular option.

[0086] Additional disorders affecting the cornea include, but are not limited to, allergies, conjunctivitis, corneal infections, dry eye, Fuchs' dystrophy, herpes zoster, iridocorneal endothelial syndrome, keratoconus, lattice dystrophy, map-dot-fingerprint dystrophy, ocular herpes, Stevens-Johnson syndrome, pterygium, keratitis, corneal ulcer, corneal abrasion, snow blindness, arc eye, Thygeson's superficial punctate keratopathy, and keratconjunctivitis sicca.

[0087] As used herein, "corneal transplant," "corneal graft," or "penetrating keratoplasty," refers to a surgical procedure where a damaged or diseased cornea is replaced by cornea

tissue. In corneal transplant surgery, the surgeon removes the central portion of the diseased or injured cornea and replaces it with a clear cornea. The new cornea is placed in the opening and is sutured to the eye (see, e.g., Rapuano et al. Anterior Segment, The Requisites (Requisites in Ophthalmology), 1999, Mosby, Inc., Philadelphia, PA). Approximately 20% of corneal transplant patients reject their donor corneas. In one aspect of the present invention, the recipient of the synthetic cornea is the donor of the oocytes from which the cornea is derived. As such, the possibility of tissue rejection is minimized.

[0088] In one embodiment, a method for replacement of a cornea of an eye using the synthetic cornea includes surgically excising the cornea from the eye, inserting the synthetic cornea into the area of the removed cornea, and allowing the synthetic cornea to interface with tissue underlying the excision to anchor the synthetic cornea to the eye.

[0089] In a related aspect, the method includes separating a portion of the outer surface of a cornea thereby forming a corneal flap and a corneal bed, the corneal flap having an anterior surface and a posterior surface, the corneal bed having a shaped anterior surface, implanting the synthetic cornea on the corneal bed, the cornea having an anterior surface and a posterior surface, and replacing the portion of the cornea that was separated.

[0090] In another embodiment, a method delivering an effective amount of an agent to the eye of a subject using the synthetic cornea of the present invention includes transforming a portion of the cells comprising the synthetic cornea with a nucleic acid vehicle, where the vehicle encodes the agent, identifying a population of cells comprising the synthetic cornea which express the agent encoded by the nucleic acid, and replacing cornea cells of the subject with transformed cells of the synthetic cornea, where the replaced cells deliver the agent to the eye of the subject.

[0091] In a related aspect, the replacing step comprises replacing the cornea of the subject with the synthetic cornea. In a further related aspect, the subject can be a domesticated animal, including cats and dogs. Further, the subject may be human.

[0092] In the native environment, immature oocytes (eggs) from the ovary undergo a process of maturation which results in the progression through meiosis to metaphase II of meiosis. The oocytes then arrest at metaphase II. In metaphase II, the DNA content of the cell consists of a haploid number of chromosomes, each represented by two chromatids.

[0093] Such oocytes may be maintained indefinitely by cryopreserving by, for example, but not limited to, microinjection with a sugar.

[0094] In one embodiment, a method for producing human stem cells from a cryopreserved oocyte is provided, including microinjecting into the cytoplasm of the oocyte cell a cryopreservation agent, freezing the oocyte to a cryogenic temperature to cause it to enter a dormant state, storing the oocyte in the dormant state, thawing the oocyte, parthenogenically activating the oocyte at high O₂ tension, isolating an inner cell mass (ICM) from the activated oocyte, and culturing the cells of the ICM on a layer of human feeder cells, where culturing is carried out under low O₂ tension.

[0095] In one aspect, oocytes obtained as described are transferred to modified, isotonic IVF covered with embryo-tested mineral oil (Sigma), or any other suitable medium. If desired, the oocytes may be incubated with an extracellular sugar at the same concentration as the amount planned for microinjection. For example, to inject 0.1 M sugar, oocytes may be equilibrated in DMEM/F-12 with 0.1 M sugar. In one aspect, the cryopreservation agent comprises a lower Na⁺ concentration than standard DMEM (i.e., Na⁺ low media). In a related aspect, the cryopreservation agent comprises a higher K⁺ concentration than standard DMEM (i.e., K⁺ high). In a further related aspect, the cryopreservation agent comprises both a lower Na⁺ and higher K⁺ concentration than standard DMEM (i.e., Na⁺ low/ K⁺ high media). In one aspect, the cryopreservation agent comprises an organic buffer, including but not limited to, HEPES. In another aspect, the cryopreservation agent comprises moieties that inhibit apoptotic protein (e.g., capases).

[0096] Alternatively, the oocytes may be optionally equilibrated with any other substantially non-permeable solute, such as NaCl, to decrease their cell volume prior to microinjection. This initial decrease in cell volume may result in a smaller final volume of the microinjected oocytes compared to oocytes not incubated in a hypertonic media prior to microinjection. This smaller final volume may minimize any potential adverse effect from the swelling of the oocytes. This general procedure for the preparation of cells for microinjection may also be used for other cell types (e.g., activated oocytes, hES cells, and the like).

[0097] The oocytes are then microinjected with a cryopreservation agent. Microinjection equipment and procedures are well characterized in the art and microinjection equipment known for use in injecting small molecules into cells may be used with the invention. In an

exemplary microinjection step, oocytes can be microinjected at a pressure of 10 psi for 30 milliseconds. Another example of a standard microinjection technique is the method described by Nakayama and Yanagimachi (Nature Biotech. 16:639-642, 1998).

[0098] A cryopreservation agent useful in this process includes any chemical that has cryo-protective properties and is ordinarily non-permeable. In particular, the cryopreservation agent can include sugars either alone or mixed together with other traditional cryopreservation agents. Carbohydrate sugars such as trehalose, sucrose, fructose, and raffinose, may be microinjected to concentrations less than or equal to about 1.0 M, and more preferably, less than or equal to about 0.4 M. In one aspect, the concentration is between 0.05 and 0.20 M, inclusive. Additionally, an extracellular sugar or traditional cryopreservation agent may be added prior to storage. If the cells were incubated in a hypertonic solution prior to microinjection, the substantially non-permeable solute may be allowed to remain in the media after microinjection or may be removed from the media by washing the cells with media containing a lower concentration, or none, of this solute.

[0099] Certain sugars or polysaccharides which ordinarily do not permeate cell membranes because they are too large to pass through the membrane have superior physiochemical and biological properties for cryopreservation purposes. While these sugars ordinarily do not permeate cell membranes on their own, using the method as described, these ordinarily non-permeating sugars may be microinjected intracellularly to result in a beneficial effect.

[0100] Non-permeating sugars having a stabilizing or preserving effect on cells that are especially useful as the cryopreservation agent in the present method include sucrose, trehalose, fructose, dextran, and raffinose. Among these sugars, trehalose, a non-reducing disaccharide of glucose, has been shown to be exceptionally effective in stabilizing cell structures at low concentrations. The addition of extracellular glycolipids or glycoproteins may also stabilize the cell membrane.

[0101] Following the microinjection of the cryopreservation agent, the cells are prepared for storage. A variety of methods for freezing and/or drying may be employed to prepare the cells for storage. In particular, three approaches are described herein: vacuum or air drying, freeze drying, and freeze-thaw protocols. Drying processes have the advantage that the stabilized biological material may be transported and stored at ambient temperatures.

[0102] Typically, oocytes loaded with 1 to 2M DMSO are cooled at a very slow cooling rate (0.3 to 0.5°C/min) to an intermediate temperature (-60°C. to -80°C.) before plunging in liquid nitrogen for storage. The sample can then be stored at this temperature.

[0103] The suspended material can then be stored at cryopreservation temperatures, for example, by leaving the vials in liquid nitrogen (LN₂), for the desired amount of time.

[0104] Protocols for vacuum or air drying and for freeze drying proteins are well characterized in the art (Franks et al., "Materials Science and the Production of Shelf-Stable Biologicals," BioPharm, October 1991, p. 39; Shalaev et al., "Changes in the Physical State of Model Mixtures during Freezing and Drying: Impact on Product Quality," Cryobiol. 33, 14-26 (1996)) and such protocols may be used to prepare cell suspensions for storage with the method as described. In addition to air drying, other convective drying methods that may be used to remove water from cell suspensions include the convective flow of nitrogen or other gases.

[0105] An exemplary evaporative vacuum drying protocol useful with the method of the invention may include placing 20µl each into wells on 12 well plates and vacuum drying for 2 hours at ambient temperature. Of course, other drying methods could be used, including drying the cells in vials. Cells prepared in this manner may be stored dry, and rehydrated by diluting in DMEM or any other suitable media.

[0106] A method of the invention using freeze drying to prepare the cells for storage begins with freezing the cell suspension. While prior art freezing methods may be employed, the simple plunge freezing method described herein for the freeze-thaw method may also be used for the freezing step in the freeze drying protocol.

[0107] After freezing, a two stage drying process may be employed. In the first stage, energy of sublimation is added to vaporize frozen water. Secondary drying is performed after the pure crystalline ice in the sample has been sublimated. Freeze dried cells can be stored and hydrated in the same manner as described above for vacuum drying. Viable cells may then be recovered.

[0108] After the recovery of cells from a frozen or dried state, any external cryopreservation agent may be optionally removed from the culture media. For example, the media may be diluted by the addition of the corresponding media with a lower concentration of cryopreservation agent. For example, the recovered cells may be incubated for

approximately five minutes in media containing a lower concentration of sugar than that used for cell storage. For this incubation, the media may contain the same sugar that was used as the cryopreservation agent; a different cryopreservation agent, such as galactose; or any other substantially non-permeable solute. To minimize any osmotic shock induced by the decrease in the osmolarity of the media, the concentration of the extracellular cryopreservation agent may be slowly decreased by performing this dilution step multiple times, each time with a lower concentration of cryopreservation agent. These dilution steps may be repeated until there is no extracellular cryopreservation agent present or until the concentration of cryopreservation agent or the osmolarity of the media is reduced to a desired level.

[0109] The parthenogenetically activated oocytes, blastocysts, ICM, and autologous stem cells can be stored or "banked" in a manner that allows the cells to be revived as needed in the future. An aliquot of the parthenogenetically activated oocytes and autologous stem cells can be removed at any time, to be grown into cultures of many undifferentiated cells and then differentiated into a particular cell type or tissue type, and may then be used to treat a disease or to replace malfunctioning tissues in a subject. Since the cells are parthenogenetically derived from the donor, the cells can be stored so that an individual or close relative can have access to cells for an extended period of time.

[0110] In one embodiment, a cell bank is provided for storing parthenogenetically activated oocytes, blastocysts, ICM, and/or autologous stem cell samples. In another embodiment, methods for administering such a cell bank are provided. U.S. Published Patent Application No. 20030215942, which is incorporated by reference herein in its entirety, provides an example of a stem cell bank system.

[0111] Using methods such as those described above, the isolation and in vitro propagation of parthenogenetically activated oocytes, blastocysts, ICM, and autologous stem cell samples and their cryopreservation facilitates the establishment of a "bank" of transplantable human stem cells. Because it is possible to store smaller aliquots of cells, the banking procedure could take up a relatively small space. Therefore, the cells of many individuals could be stored or "banked" on a short term or long term basis, with relatively little expense.

[0112] In one embodiment, a portion of the sample is made available for testing, either before or after processing and storage.

[0113] This invention also provides methods of recording the parthenogenetically activated oocyte, blastocyst, ICM, and/or autologous stem cell samples so that when a sample needs to be located, it can be easily retrieved. Any indexing and retrieval system can be used to fulfill this purpose. Any suitable type of storage system can be used so that the parthenogenetically activated oocytes, blastocysts, ICM, and/or autologous stem cells can be stored. The samples can be designed to store individual samples, or can be designed to store hundreds, thousands, and even millions of different cell samples.

[0114] The stored parthenogenetically activated oocyte, blastocyst, ICM, and/or autologous stem cell samples can be indexed for reliable and accurate retrieval. For example, each sample can be marked with alphanumeric codes, bar codes, or any other method or combinations thereof. There may also be an accessible and readable listing of information enabling identification of each parthenogenetically activated oocyte, blastocyst, ICM, and/or autologous stem cell sample and its location in the bank and enabling identification of the source and/or type the cell sample, which is outside of the bank. This indexing system can be managed in any way known in the art, e.g., manually or non-manually, e.g. a computer and conventional software can be used.

[0115] In one embodiment, the cell samples are organized using an indexing system so that the sample will be available for the donor's use whenever needed. In other embodiments, the cell samples can be utilized by individuals related to the original donor. Once recorded into the indexing system, the cell sample can be made available for matching purposes, e.g., a matching program will identify an individual with matching type information and the individual will have the option of being provided the matching sample.

[0116] The storage banking system can comprise a system for storing a plurality of records associated with a plurality of individuals and a plurality of cell samples. Each record may contain type information, genotypic information or phenotypic information associated with the cell samples or specific individuals. In one embodiment, the system will include a cross-match table that matches types of the samples with types of individuals who wish to receive a sample.

[0117] In one embodiment, the database system stores information for each parthenogenetically activated oocyte, blastocyst, ICM, and/or autologous stem cell sample in the bank. Certain information is stored in association with each sample. The information may be associated with a particular donor, for example, an identification of the donor and the

donor's medical history. For example, each sample may be HLA typed and the HLA type information may be stored in association with each sample. The information stored may also be availability information. The information stored with each sample is searchable and identifies the sample in such a way that it can be located and supplied to the client immediately.

[0118] Accordingly, embodiments of the invention utilize computer-based systems that contain information such as the donor, date of submission, type of cells submitted, types of cell surface markers present, genetic information relating to the donor, or other pertinent information, and storage details such as maintenance records and the location of the stored samples, and other useful information.

[0119] The term "a computer-based system" refers to the hardware, software, and any database used to store, search, and retrieve information about the stored cells. The computer-based system preferably includes the storage media described above, and a processor for accessing and manipulating the data. The hardware of the computer-based systems of this embodiment comprises a central processing unit (CPU) and a database. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable.

[0120] In one embodiment, the computer system includes a processor connected to a bus that is connected to a main memory (preferably implemented as RAM) and a variety of secondary storage devices, such as a hard drive and removable medium storage device. The removable medium storage device can represent, for example, a floppy disk drive, a DVD drive, an optical disk drive, a compact disk drive, a magnetic tape drive, etc. A removable storage medium, such as a floppy disk, a compact disk, a magnetic tape, etc. containing control logic and/or data recorded therein can be inserted into the removable storage device. The computer system includes appropriate software for reading the control logic and/or the data from the removable medium storage device once inserted in the removable medium storage device. Information relating to the parthenogenetically activated oocyte, blastocyst, ICM, and/or autologous stem cell can be stored in a well known manner in the main memory, any of the secondary storage devices, and/or a removable storage medium. Software for accessing and processing these data (such as search tools, compare tools, etc.) reside in main memory during execution.

[0121] As used herein, "a database" refers to memory that can store any useful information relating to the parthenogenetically activated oocyte and/or autologous stem cell collections and the donors.

[0122] The data relating to the stored parthenogenetically activated oocyte, blastocyst, ICM, and/or autologous stem cell can be stored and manipulated in a variety of data processor programs in a variety of formats. For example, the data can be stored as text in a word processing file, such as Microsoft WORD or WORDPERFECT, an ASCII file, an html file, or a pdf file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE.

[0123] A "search program" refers to one or more programs that are implemented on the computer-based system to search for details or compare information relating to the cryopreserved samples within a database. A "retrieval program" refers to one or more programs that can be implemented on the computer-based system to identify parameters of interest in the database. For example, a retrieval program can be used to find samples that fit a particular profile, samples having specific markers or DNA sequences, or to find the location of samples corresponding to particular individuals.

[0124] There is no upper limit on the number of cell samples that can be stored in one cell bank. In one embodiment, hundreds of products from different individuals will be stored at one bank or storage facility. In another embodiment, up to millions of products may be stored in one storage facility. A single storage facility may be used to store parthenogenetically activated oocyte and/or autologous stem cell samples, or multiple storage facilities may be used.

[0125] In some embodiments of the present invention, the storage facility may have a means for any method of organizing and indexing the stored cell samples, such as, for example, automated robotic retrieval mechanisms and cell sample manipulation mechanisms. The facility may include micromanipulation devices for processing cell samples. Known conventional technologies can be used for efficient storage and retrieval of the cell samples. Exemplary technologies include but are not limited to Machine Vision, Robotics, Automated Guided Vehicle System, Automated Storage and Retrieval Systems, Computer Integrated Manufacturing, Computer Aided Process Planning, Statistical Process Control, and the like.

[0126] The type information or other information associated with the individual in need of a sample may be recorded into a system that can be used to identify an appropriate matching product, such as, for example, a database system, an indexing system, and the like. Once recorded in the system, a match can be made between the type of the individual and a donor cell sample. In preferred embodiments, the donor sample is from the same individual as the individual in need of the sample. However, similar but not identical donor/recipient matches can also be used. The matching sample is available for the individual possessing the matching type identifier. In one embodiment of this invention, the individual's identification information is stored in connection with the cell sample. In some embodiments, the matching process occurs around the time of harvesting the sample, or can occur at any time during processing, storage, or when a need arises. Accordingly, in some embodiments of the invention, the matching process occurs before the individual is in actual need of the cell sample.

[0127] When the parthenogenetically activated oocyte, blastocyst, ICM, and/or autologous stem cell sample is needed by an individual, it may be retrieved and made available for research, transplantation or other purposes within minutes, if desired. The sample may also be further processed to prepare it for transplantation or other needs.

[0128] Normally, the oocyte is ovulated at this stage and fertilized by the sperm. The sperm initiates the completion of meiosis in a process called activation. During activation, the pairs of chromatids separate, the second polar body is extruded, and the oocyte retains a haploid number of chromosomes, each with one chromatid. The sperm contributes the other haploid complement of chromosomes to make a full diploid cell with single chromatids. The chromosomes then progress through DNA synthesis during the first cell cycle. These cells then develop into embryos.

[0129] By contrast, embryos described herein are developed by artificial activation of cells, typically mammalian oocytes or blastomeres containing DNA of all male or female origin. As discussed in the background of the invention, many methods have been reported in the literature for artificial activation of unfertilized oocytes. Such methods include physical methods, e.g., mechanical methods such as pricking, manipulation or oocytes in culture, thermal methods such as cooling and heating, repeated electric pulses, enzymatic treatments, such as trypsin, pronase, hyaluronidase, osmotic treatments, ionic treatments such as with divalent cations and calcium ionophores, such as ionomycin and A23187, the use of

anesthetics such as ether, ethanol, tetracaine, lignocaine, procaine, phenothiazine, tranquilizers such as thioridazine, trifluoperazine, fluphenazine, chlorpromazine, the use of protein synthesis inhibitors such as cycloheximide, puromycin, the use of phosphorylation inhibitors, e.g., protein kinase inhibitors such as staurosporine, 2-aminopurine, shingosine, and DMAP, combinations thereof, as well as other methods.

[0130] Such activation methods are well known in the art and are discussed U.S. Pat. No. 5,945,577, incorporated herein by reference.

[0131] In one embodiment, a human cell in metaphase II, typically an oocyte or blastomere comprising DNA of all male or female origin, is artificially activated for effecting artificial activation of oocytes.

[0132] In a related aspect, the activated cell, e.g., oocyte, which is diploid, is allowed to develop into an embryo that comprises a trophectoderm and an inner cell mass. This can be effected using known methods and culture media that facilitate blastocyst development.

[0133] After the gynogenetic embryos have been cultured to produce a discernable trophectoderm and inner cell mass, the cells of the inner cell mass are then used to produce the desired pluripotent cell lines. This can be accomplished by transferring cells derived from the inner cell mass or the entire inner cell mass onto a culture that inhibits differentiation. This can be effected by transferring the inner cell mass cells onto a feeder layer that inhibits differentiation, e.g., fibroblasts or epithelial cells, such as fibroblasts derived from postnatal human tissues, etc., or other cells that produce LIF. Other factors/components may be employed to provide appropriate culture conditions for maintaining cells in the undifferentiated state including, but not limited to, addition of conditioned media (Amit et al., *Developmental Biol* (2000) 227:271-278), bFGF and TGF- β 1 (with or without LIF) (Amit et al., *Biol Reprod* (2004) 70:837-845), factors which activate the gp130/STAT3 pathway (Hoffman and Carpenter, *Nature Biotech* (2005) 23(6):699-708), factors which activate the PI3K/Akt, PKB pathway (Kim et al., *FEBS Lett* (2005) 579:534-540), factors that are members of the bone morphogenetic protein (BMP) super-family (Hoffman and Carpenter (2005), *supra*), and factors which activate the canonical/ β -catenin Wnt signaling pathway (e.g., GSK-3-specific inhibitor; Sato et al., *Nat Med* (2004) 10:55-63). In a related aspect, such factors may comprise culture conditions that include feeder cells and/or ECM substrates (Hoffman and Carpenter (2005), *supra*).

[0134] In one aspect, the inner cell mass cells are cultured on human postnatal foreskin or dermal fibroblast cells or other cells which produce leukemia inhibitory factor, or in the presence of leukemia inhibitory factor. In a related aspect, feeder cells are inactivated prior to seeding with the ICM. For example, the feeder cells can be mitotically inactivated using an antibiotic. In a related aspect, the antibiotic can be, but is not limited to, mytomycin C.

[0135] Culturing will be effected under conditions that maintain the cells in an undifferentiated, pluripotent state, for prolonged periods, theoretically indefinitely. In one embodiment, oocytes are parthenogenically activated with calcium ionophores under high O₂ tension followed by contacting the oocytes with a serine-threonine kinase inhibitor under low O₂ tension. The resulting ICM from the parthenogenically activated oocytes are cultured under high O₂ tension, where the cells, for example, are maintained using a gas mixture comprising 20% O₂. In one aspect, culturable refers to being capable of, or fit for, being cultivated. In a related aspect, ICM isolation is carried out mechanically after four days of blastocyst cultivation, where the cultivation is carried out on feeder cells. Such cultivation, for example, eliminates the need to use materials derived from animal sources, as would be the case for immunosurgery.

[0136] In a related aspect, culture media for the ICM is supplemented with non-animal sera, including but not limited to, human umbilical cord serum, where the serum is present in defined media (e.g., IVF, available from MediCult A/S, Denmark; Vitrolife, Sweden; or Zander IVF, Inc., Vero Beach, FL). In another aspect, the media and processes as provided are free of animal products. In a related aspect, animal products are those products, including serum, interferons, chemokines, cytokines, hormones, and growth factors, that are from non-human sources.

[0137] The pluripotent state of the cells produced by the present invention can be confirmed by various methods. For example, the cells can be tested for the presence or absence of characteristic ES cell markers. In the case of human ES cells, examples of such markers are identified supra, and include SSEA-4, SSEA-3, TRA-1-60 and TRA-1-81 and are known in the art.

[0138] Also, pluripotency can be confirmed by injecting the cells into a suitable animal, e.g., a SCID mouse, and observing the production of differentiated cells and tissues. Still another method of confirming pluripotency is using the subject pluripotent cells to generate chimeric animals and observing the contribution of the introduced cells to different cell types.

Methods for producing chimeric animals are well known in the art and are described in U.S. Pat. No. 6,642,433, incorporated by reference herein.

[0139] Yet another method of confirming pluripotency is to observe ES cell differentiation into embryoid bodies and other differentiated cell types when cultured under conditions that favor differentiation (e.g., removal of fibroblast feeder layers). This method has been utilized and it has been confirmed that the subject pluripotent cells give rise to embryoid bodies and different differentiated cell types in tissue culture.

[0140] The resultant pluripotent cells and cell lines, preferably human pluripotent cells and cell lines, which are derived from DNA of entirely female original, have numerous therapeutic and diagnostic applications. Such pluripotent cells may be used for cell transplantation therapies or gene therapy (if genetically modified) in the treatment of numerous disease conditions.

[0141] In this regard, it is known that mouse embryonic stem (ES) cells are capable of differentiating into almost any cell type, e.g., hematopoietic stem cells. Therefore, human pluripotent (ES) cells produced according to the invention should possess similar differentiation capacity. The pluripotent cells according to the invention will be induced to differentiate to obtain the desired cell types according to known methods. For example, human ES cells produced according to the invention may be induced to differentiate into hematopoietic stem cells, muscle cells, cardiac muscle cells, liver cells, islet cells, retinal cells, cartilage cells, epithelial cells, urinary tract cells, etc., by culturing such cells in differentiation medium and under conditions which provide for cell differentiation. Medium and methods which result in the differentiation of ES cells are known in the art as are suitable culturing conditions.

[0142] For example, Palacios et al, Proc. Natl Acad. Sci., USA, 92:7530-7537 (1995) teach the production of hematopoietic stem cells from an embryonic cell line by subjecting stem cells to an induction procedure comprising initially culturing aggregates of such cells in a suspension culture medium lacking retinoic acid followed by culturing in the same medium containing retinoic acid, followed by transferal of cell aggregates to a substrate which provides for cell attachment.

[0143] Moreover, Pedersen, J. Reprod. Fertil. Dev., 6:543-552 (1994) is a review article which references numerous articles disclosing methods for in vitro differentiation of

embryonic stem cells to produce various differentiated cell types including hematopoietic cells, muscle, cardiac muscle, nerve cells, among others.

[0144] Further, Bain et al, Dev. Biol., 168:342-357 (1995) teach in vitro differentiation of embryonic stem cells to produce neural cells which possess neuronal properties. These references are exemplary of reported methods for obtaining differentiated cells from embryonic or stem cells. These references and in particular the disclosures therein relating to methods for differentiating embryonic stem cells are incorporated by reference in their entirety herein. Thus, using known methods and culture medium, one skilled in the art may culture the subject ES cells, including genetically engineered or transgenic ES cells, to obtain desired differentiated cell types, e.g., neural cells, muscle cells, hematopoietic cells, etc. Pluripotent cells produced by the methods described herein may be used to obtain any desired differentiated cell type. Therapeutic usages of differentiated human cells are unparalleled. For example, human hematopoietic stem cells may be used in medical treatments requiring bone marrow transplantation. Such procedures are used to treat many diseases, e.g., late stage cancers such as ovarian cancer and leukemia, as well as diseases that compromise the immune system, such as AIDS. Hematopoietic stem cells can be obtained, e.g., by incorporating male or female DNA derived from a male or female cancer or AIDS patient with an enucleated oocyte, obtaining pluripotent cells as described above, and culturing such cells under conditions which favor differentiation, until hematopoietic stem cells are obtained. Such hematopoietic cells may be used in the treatment of diseases including cancer and AIDS.

[0145] Alternatively, the subject pluripotent cells may be used to treat a patient with a neurological disorder by culturing such cells under differentiation conditions that produce neural cell lines. Specific diseases treatable by transplantation of such human neural cells include, by way of example, Parkinson's disease, Alzheimer's disease, ALS and cerebral palsy, among others. In the specific case of Parkinson's disease, it has been demonstrated that transplanted fetal brain neural cells make the proper connections with surrounding cells and produce dopamine. This can result in long-term reversal of Parkinson's disease symptoms.

[0146] One object of the subject invention is that it provides an essentially limitless supply of pluripotent, human cells that can be used to produce differentiated cells suitable for autologous transplantation for the oocyte donor. Human embryonic stem cells and their differentiated progeny derived from blastocysts remaining after infertility treatments, or

created using NT, will likely be rejected by a recipient's immune system when used in allogenic cell transplantation therapy. Parthenogenically derived stem cells should result in differentiated cells that could alleviate the significant problem associated with current transplantation methods, i.e., rejection of the transplanted tissue which may occur because of host-vs-graft or graft-vs-host rejection relative to the oocyte donor. Conventionally, rejection is prevented or reduced by the administration of anti-rejection drugs such as cyclosporin. However, such drugs have significant adverse side-effects, e.g., immunosuppression, carcinogenic properties, as well as being very expensive. Cells produced by the methods as disclosed should eliminate, or at least greatly reduce, the need for anti-rejection drugs relative to the oocyte donor.

[0147] Another object of the subject invention is that it provides an essentially limitless supply of pluripotent, human cells that can be used to produce differentiated cells suitable for allogenic transplantation to members of the oocyte donor's family. The cells will be immunologically and genetically similar to those of the oocytes donor's direct family members and thus less likely to be rejected by the donor's family members.

[0148] Another object of this method is that parthenogenic activation of mammalian oocytes is a relatively simple procedure when compared to SCNT and results in the creation of stem cells with less cell manipulation.

[0149] Parthenogenic activation of mammalian oocytes has shown to be more efficient in the creation of stem cells than methods requiring manipulation of the oocyte or blastocyst.

[0150] One drawback of SCNT is that subjects with deficient mitochondrial respiratory chain activity present phenotypes with striking similarities to abnormalities commonly encountered in SCNT fetuses and offspring (Hiendleder et al, Repro Fertil Dev (2005) 17(1-2):69-83). Cells normally contain only one type of mitochondrial DNA (mtDNA), termed homoplasmy, however, heteroplasmy does exist, usually as a combination of mutant and wild-type mt DNA molecules or form a combination of wild-type variants (Spikings et al., Hum Repro Update (2006) 12(4):401-415). As heteroplasmy can result in mitochondrial disease, various mechanisms exist to ensure maternal-only transmission. However, with the increasing use of protocols which bypass normal mechanisms for homoplasmy maintenance (e.g., cytoplasmic transfer (CT) and SCNT), perturbed mitochondrial function may be intrinsic to stem cells derived from these sources.

[0151] In one aspect, as the parthenotes are uniparental, the possibility of heteroplasmy is minimized.

[0152] Other diseases and conditions treatable by cell therapy include, by way of example, spinal cord injuries, multiple sclerosis, muscular dystrophy, diabetes, liver diseases including acute diseases (viral hepatitis, drug overdoses (acetaminophen) and others), chronic diseases (chronic hepatitis and others (generally leading to cirrhosis)), heritable liver defects (hemophilia B, factor IX deficiency, bilirubin metabolism defects, urea cycle defects, lysosomal storage disease, α 1-antitrypsin deficiency and others), heart diseases, cartilage replacement, burns, foot ulcers, gastrointestinal diseases, vascular diseases, kidney disease, retinal disease, corneal disease, urinary tract disease, and aging related diseases and conditions.

[0153] This methodology can be used to replace defective genes, e.g., defective immune system genes, cystic fibrosis genes, or to introduce genes which result in the expression of therapeutically beneficial proteins such as growth factors, lymphokines, cytokines, enzymes, etc.

[0154] For example, the gene encoding brain derived growth factor may be introduced into human pluripotent cells produced according to the invention, the cells differentiated into neural cells and the cells transplanted into a Parkinson's patient to retard the loss of neural cells during such disease.

[0155] Also, the subject pluripotent human ES cells, may be used as an in vitro model of differentiation, in particular for the study of genes which are involved in the regulation of early development. Also, differentiated cell tissues and organs produced using the subject ES cells may be used in drug studies.

[0156] Further, the subject ES cells or differentiated cells derived therefrom may be used as nuclear donors for the production of other ES cells and cell colonies.

[0157] Still further, pluripotent cells obtained according to the present disclosure may be used to identify proteins and genes that are involved in embryogenesis. This can be effected, e.g., by differential expression, i.e., by comparing mRNAs that are expressed in pluripotent cells provided according to the invention to mRNAs that are expressed as these cells differentiate into different cell types, e.g., neural cells, myocytes, other muscle cells,

skin cells, etc. Thereby, it may be possible to determine what genes are involved in differentiation of specific cell types.

[0158] Further, ES cells and/or their differentiated progeny that have specific genetic defects, such as the genetic defect that leads to Duchene's Muscular Dystrophy, may be used as models to study the specific disease associated with the genetic defect.

[0159] Also, it is another object of the present disclosure to expose pluripotent cell lines produced according to the described methods to cocktails of different growth factors, at different concentrations and under different cell culture conditions such as cultured on different cell matrices or under different partial pressures of gases so as to identify conditions that induce the production and proliferation of desired differentiated cell types.

[0160] In one embodiment, a synthetic cornea is disclosed which is produced in vitro, in the absence of a mechanical support for control of differentiation and/or proliferation (i.e., the absence of 3-D scaffolding). In one aspect, a synthetic cornea is disclosed, including, but not limited to, a cornea that is terminally differentiated in vitro.

[0161] In another embodiment, the cornea is produced from parthenogenetically activated human oocytes, where stem cells derivitized from the parthenogenetically activated oocytes are artificially manipulated to produce the cornea.

[0162] In one aspect, the synthetic cornea is produced including culturing the isolated stem cells from parthenogenetically activated oocytes in media comprising serum replacement (M/SR), plasmonate, and at least one mitogen that activates the gp130/STAT pathway and/or MAP kinase pathway on a fibroblast feeder layer treated with a DNA inhibitor, culturing the mitogen treated cells in M/SR comprising plasmonate (M/SRP), without added mitogens, to near confluence, where 1/2 volume of the M/SRP is replaced with M/SR periodically until the near confluent cells develop pigmentation and a domed appearance, and transferring the pigmented/domed cells in M/SR to a gelatin coated substrate, where 1/2 volume of the M/SR is replaced with M/SR periodically until a floating cell mass develops, where the floating cell mass is the synthetic cornea. In a related aspect, the M/SR includes KO Hi glucose DMEM, streptomycin, non-essential amino acids, Glutamax-I, β -mecaptoethanol, and Serum Replacement. In another related aspect, M/SRP comprises the components of M/SR and plasmonate.

[0163] The following examples are intended to illustrate but not limit the invention.

EXAMPLE 1

Production of Human Parthenogenic Embryogenic Stem Cells

[0164] Materials and Methods

[0165] Donors voluntarily donated eggs and blood (for DNA analysis) with no financial payment. Donors signed comprehensive informed consent documents and were informed that all donated materials were to be used for research and not for reproductive purposes. Before ovarian stimulation, oocyte donors underwent medical examination for suitability according to FDA eligibility determination guidelines for donors of human cells, tissues, and cellular and tissue-based products (Food and Drug Administration. (Draft) Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue Based Products (HCT/Ps) dated May 2004) and order N 67 (02.26.03) of Russian Public Health Ministry. It included X-ray, blood and urine analysis, and liver function test. Donors were also screened for syphilis, HIV, HBV, and HCV.

[0166] Oocytes were obtained using standard hormonal stimulation to produce superovulation in the subject donor. Each donor egg underwent ovarian stimulation by FSH from the 3rd to the 13th days of their menstrual cycle. A total of 1500IU of FSh was given. From the 10th to the 14th day of the donor's menstrual cycle, gonadoliberein antagonist Orgalutran (Organon, Holland) was injected at 0.25 mg/day. From the 12th to the 14th day of the donor's menstrual cycle a daily injection of 75IU FSH + 75IU LH (Menopur, Ferring GmbH, Germany) was given. If an ultrasound examination displayed follicles between 18 and 20mm in diameter, a single 8000IU dose of hGC (Choragon, Ferring GmbH, Germany) was administered on the 14th day of the donor's menstrual cycle. Trans-vaginal puncture was performed 35 hours after hCG injection on approximately the 16th day. Follicular fluid was collected from the antral follicles of anesthetized donors by ultrasound-guided needle aspiration into sterile tubes.

[0167] Cumulus oocyte complexes (COCs) were picked from the follicular fluid, washed in Flushing Medium (MediCult) and then incubated in Universal IVF medium (MediCult, see Table 1) with a Liquid Paraffin (MediCult) overlay for 2 hours in a 20% O₂, 5% CO₂, at 37°C humidified atmosphere.

Table 1. IVF media.

COMPOSITION

Calcium Chloride

EDTA

Glucose

Human Serum Albumin

Magnesium Sulfate

Penicillin G

Potassium Chloride

Potassium di-Hydrogen Phosphate

Sodium Bicarbonate

Sodium Chloride

Sodium Lactate

Sodium Pyruvate

Water

[0168] Before activation, cumulus-oocyte complexes (COCs) were treated with SynVibro Hyadase (MediCult) to remove cumulus cells followed by incubation in Universal IVF medium with a paraffin overlay for 30 minutes.

[0169] From this point onward, the culture of oocytes and embryos was performed in a humidified atmosphere at 37°C using O₂-reduced gas mixture (90% N₂ + 5% O₂ + 5% CO₂), with the exception of the ionomycin treatment. The oocytes were activated by incubation in 5 µM ionomycin for 5 minutes in a CO₂ incubator at 37°C in a gas environment of 20% O₂, 5% CO₂, followed by culture with 1 mM 6-dimethylaminopurine (DMAP) for 4 hours in IVF medium, paraffin overlay, in a gas environment of 90% N₂, 5% O₂, and 5%CO₂ at 37° C. Activation and cultivation were carried out in 4-well plates (Nunc, A/S, Denmark) in 500 µl of medium overlaid with liquid paraffin oil (MediCult, A/S, Denmark).

[0170] Activated oocytes were cultivated in IVF medium in a gas environment comprising 5% O₂, 5% CO₂, and 90% N₂, and embryos generated from the activated oocytes were cultured in the same gas mixture.

[0171] Activated oocytes were allowed to incubate in IVF under the above conditions until fully expanded blastocysts containing an inner cell mass (ICM) at a Blastocyst Scoring

Modification of 1AA or 2AA (Shady Grove Fertility Center, Rockville, MD, and Georgia Reproductive Specialists, Atlanta, GA) was observed.

[0172] The zona pellucida was removed by 0.5% pronase (Sigma, St. Louis) treatment. The ICM from blastocysts was isolated by immuno-surgery where the blastocysts were incubated with horse antiserum to human spleen cells followed by exposure to guinea pig complement. Trophoectoderm cells were removed from the ICM by gently pipetting the treated blastocysts.

[0173] For the derivation of phESC from whole blastocysts, the blastocysts were placed on a feeder layer in medium designed for culture of phESC (i.e., VitroHES (Vitrolife) supplemented with 4ng/ml hrbFGF, 5ng/ml hrLIF and 10% human umbilical cord blood serum). When blastocysts attached and trophoplast cells spread, the ICM became visible. Through three to four days of additional culture, the ICM was isolated through mechanical slicing of the ICM from the trophoectoderm outgrowth using a finely drawn glass pipette. Further, the IMC cells were cultured on a feeder cell layer of mitotically inactivated post natal human dermal fibroblasts, in VITROHES™ media (e.g., DMEM/high glucose medium, VitroLife, Sweden) supplemented with 10% human umbilical cord blood serum, 5 ng/ml human recombinant LIF (Chemicon Int'l, Inc., Temecula, CA), 4 ng/ml recombinant human FGF (Chemicon Int'l, Inc., Temecula, CA) and penicillin-streptomycin (100U/100µg) in a 96-well plate in 5% CO₂ and 20% O₂ at 37°C. This gas mixture was used to culture stem cells. Human fibroblast cultures were made using non-animal materials. Inactivation of fibroblasts was carried out using 10 µg/ml mitomycin C (Sigma, St. Louis, MO) for 3 hours.

[0174] In a separate method, immuno-surgery was performed by incubating blastocysts with horse antiserum to human spleen cells followed by exposure to rabbit complement. The trophoectoderm cells were removed from the ICM through gentle pipetting of the treated blastocysts. Further culturing of the isolated ICMs was performed on a feeder layer of neonatal human skin fibroblasts (HSF) obtained from a genetically unrelated individual (with parental consent) derived using medium containing human umbilical cord blood serum. The HSF feeder layer was mitotically inactivated using mitomycin C.

[0175] The medium for the culture of HSF consisted of 90% DMEM (high glucose, with L-glutamine (Invitrogen), 10% human umbilical cord blood serum and penicillin-streptomycin (100U/100mg) Invitrogen).

[0176] For the culture of ICM and phESC, VitroHES (Vitrolife) supplemented with 4ng/ml hrbFGF, 5ng/ml hrLIF and 10% human umbilical cord blood serum was used. The ICM was mechanically plated on a fresh feeder layer and cultured for three to four days. The first colony was mechanically cut and replated after five days of culture. All subsequent passages were made after five to six days in culture. For early passages, colonies were mechanically divided into clumps and replated. Further passing of phESC was performed with collagenase IV treatment and mechanical dissociation. The propagation of phESC was performed at 37°C, 5% CO₂ in a humidified atmosphere.

[0177] Oocyte activation

[0178] From the initial 4 donors, activated oocytes were cultivated in IVF medium in a gas environment comprising 5% O₂, 5% CO₂, and 90% N₂ and followed over five (5) days. Table 2 shows the progress of maturation of the activated oocytes. Each oocyte was separated in a 4-well plate.

Table 2. Cultured Activated Oocytes.*

	Day 1	Day 2	Day 3	Day 5
N1	1 pronucleus (pn), 1 polar body (pb)	2 blastomers (bl) equal, fragmentation (fr)-0%	4 bl equal, fr-2%	1 morula, fr-15%
N2	0 pn, 1 pb	4 bl not equal, fr-4%	5 bl not equal, fr-20%	4 bl not equal, fr-40%
N3	1 pn, 1 pb	2 bl not equal, fr-0%	6 bl equal, fr-0%	early blastocysts
N4	1 pn, 1 pb	4 bl equal, fr-10%	4 bl equal, fr-20%	Fully expanded blastocyst with good ICM 1AA

*Cells were incubated in M1 media (MediCult) on the first day and M2 media (MediCult) on days 2-5. Media was changed everyday. M1 and M2 contain human serum albumin, glucose and derived metabolites, physiological salts, essential amino acids, non-essential amino acids, vitamins, nucleotides, sodium bicarbonate, streptomycin (40 mg/l), penicillin (40,000 IU/l) and phenol red.

[0179] Inner cell masses were isolated from N4 and transferred to human fibroblast feeder cells as outlined above. N1 and N2 degenerated on Day 6. Further, on Day 6, N3 produced

fully expanded blastocyst with ICM 2AB. N3 was then transferred to human fibroblast feeder cells on Day 6. ICM from N4 was unchanged. N3 was used to isolate stem cells.

[0180] ICM cells were cultivated in NitroHES medium in a gas environment comprising 5% CO₂ and 95% N₂ and followed over forty-five (45) days. Table 2a shows the progress of N3 ICM cell cultivation.

Table 2a. Progress of N3-ICM Cultivation.*

Day 3	ICM transplanted on fresh feeder cells.
Day 8	Colony of cells divided mechanically into 6 pieces and cultivated in 3 wells of a 96-well plate-1st passage.
Day 14	From five (5) colonies of 1st passage, cells were mechanically divided, and 20 colonies of a 2nd passage were cultivated in 3 wells of a 24-well plate.
Day 20	Cells were plated in 35 mm dish-3rd passage.
Day 24	Five (5) 35 mm dishes were seeded with cells-4th passage. One dish was divided chemically with 5% pronase (Sigma) at room temperature.
Day 30	Twenty-five (25) 35 mm were seeded with cells-5th** passage.
Day 34	6th** cell passage.
Day 35	11 ampules were frozen from the 6th passage.
Day 37	7th** cell passage.
Day 44	12 ampules were frozen from the 7th passage.
Day 45	8th cell passage.

*Cells were grown on M2 media (MediaCult).

** These passages were made with pronase digestion.

[0181] Stem cell isolation.

[0182] From the oocyte from 5 donors, the use of MediCult media is followed by a culture under reduced oxygen allowed for the production of 23 blastocysts on the fifth or sixth day of culture. Eleven of the blastocysts had visible ICMs (Table 3).

Table 3. Generation of parthenotes and parthenogenetic embryonic stem cell lines.

Donor Number	Oocytes harvested	Oocytes donated	Normally activated oocytes	Parthenotes created	Blastocysts derived		Lines generated
					With ICM	Without visible ICM	
1	8	4	4	4	2	-	phESC-1 immunosurgery
2	15	8	8	8	3	3	phESC-3 phESC-4 phESC-5 all from whole blastocysts
3	27	14	12 ¹	11 ²	3	2	phESC-6 from whole blastocysts
4	22	11	10 ³	10	2	3	phESC-7 from whole blastocysts
5	20	9 ⁴	7	7	1	4	No cell line generated

¹-two oocytes were not activated; ²- one oocyte degenerated after activation; ³- one oocyte was not activated; ⁴- two oocytes were at metaphase stage I and were discarded.

[0183] These results indicate an approximate 57.5% success rate in the formation of blastocysts from parthenogenetically activated oocytes.

[0184] Immunohistochemical staining

[0185] For immunostaining, hES cell colonies and phESC cells on feeder layers were seeded onto micro cover glass, washed twice with PBS and fixed with 100% methanol for 5 minutes at -20°C. Cells were washed twice with PBS + 0.05% Tween-20 and permeabilized with PBS + 0.1% Triton X-100 for 10 minutes at room temperature. After cell washing, non-specific binding was blocked by incubation with blocking solution (PBS + 0.05% Tween-20 + four percent goat serum plus three percent human umbilical cord blood serum) for 30 minutes at room temperature (RT). Monoclonal antibodies were diluted in blocking solution and used for one hour at RT: SSEA-1 (MAB4301) (1:30), SSEA-3 (MAB4303) (1:10), SSEA-4 (MAB4304) (1:50), OCT-4 (MAB4305) (1:30), TRA-1-60 (MAB4360) (1:50), and TRA-1-81 (MAB4381) (1:50) from Chemicon. After the cells were washed, secondary antibodies Alexa Fluor 546 (orange-fluorescent) and 488 (green-fluorescent)

(Molecular Probes, Invitrogen) were diluted 1:1000 in PBS + 0.05% Tween-20 and applied for one hour at RT. Cells were washed and nuclei were stained with DAPI (Sigma) 0.1 µg/ml in PBS + 0.05% Tween-20 during ten minutes at RT. Cells were washed and mounted on slides with Mowiol (Calbiochem). Fluorescence images were visualized with a fluorescence microscope.

[0186] For the detection of mesodermal markers in three week old embryoid bodies or in contractile embryoid bodies, monoclonal mouse anti-desmina antibody anti-human alpha actinin antibody (Chemicon) as the muscle specific markers, and anti-human CD31/PECAM-1 antibody (R&D Systems), antihuman VE Cadherin (DC144) antibody (R&D Systems) as the endothelial markers were used.

[0187] For detection of the endodermal markers in embryoid bodies, monoclonal mouse anti-human alpha-fetoprotein antibody (R&D Systems) was used.

[0188] Alkaline phosphatase and telomerase activity

[0189] Alkaline phosphatase and telomerase activity were performed according to the manufacturer's specifications with AP kit and TRAPEZE Kit (Chemicon).

[0190] Karyotyping

[0191] To analyse the karyotype, hES cells were treated with 10 µg/ml Demecolcine (Sigma) for two hours, harvested with 0.05% trypsin/EDTA (Invitrogen) and centrifuged at 700 x rpm for three minutes. The pellet was resuspended in 5 ml of 0.56% KCl, and incubated for 15 minutes at RT. After repeated centrifugation, the supernatant was removed and cells were resuspended and fixed with 5 ml of an ice cold mixture of methanol/acetic acid (3:1) for five minutes at +4°C. The fixation of the cells was repeated twice, after that the cell suspension was placed onto microscope slides and the preparations were stained with Giemsa Modified Stain (Sigma). Metaphases from cells prepared in this manner were analyzed by a standard G-banding method. Quantity of 5/1000 metaphase spreads were revealed and 63 metaphases were analyzed.

[0192] Embryoid body formation

[0193] hES and phESC cell colonies were mechanically divided into clumps and placed in wells of a 24 well plate precoated with 1.5% agarose (Sigma) in medium containing 85%

Knockout DMEM, 15% human umbilical cord blood serum, 1 x MEM NEAA, 1 mM Glutamax, 0.055 mM β -mercaptoethanol, penicillin-streptomycin (50 U/50 mg), 4 ng/ml hrbFGF (all from Invitrogen, except serum). Human EBs were cultured for 14 days in suspension culture and placed on a culture dish to give outgrowth or cultivated in suspension for an additional week.

[0194] Neural differentiation was induced by the cultivation of two week old embryoid bodies attached to a culture dish surface over a period of a week in differentiation medium: DMEM/F12, B27, 2 mM Glutamax, penicillin-streptomycin (100U/100 μ g) and 20 ng/ml hrbFGF (all from Invitrogen). Some embryoid bodies gave rise to differentiated cells with neural morphology, others were dissected and additionally cultured to produce neurospheres.

[0195] Rhythmically beating embryoid bodies appeared spontaneously following five days of culture after plating on an adhesive surface in the same medium as was used for embryoid body generation.

[0196] Cornea formation

[0197] hES were grown in Growth Medium with mitogens, LIF and bFGF (on a >40% confluent mitomycin C treated human fibroblast feeder layer). Near confluent (i.e., when ES lose clear colony borders), culture medium is replaced with Growth Medium without addition of mitogens. Thereafter, 50% of the medium is replaced with EB medium every 2-3 days for a minimum of three weeks. At this time, pigmented cells develop in small balls or large domes and columns in the culture.

[0198] The medium was then removed from the culture and cells were vigorously washed with EB Medium to dislodge the desired cells. The EB Medium wash and harvested cells were then transferred to a separate culture vessel that had been coated with 0.1% gelatin. After two days, 50% of the medium in the transferred culture was replaced with EB Medium. Subsequently, 50% of the medium in the transferred culture was replaced every 3-4 days with EB Medium for a minimum of three weeks until small floating cell masses that resemble oil droplets became visible. At this point, care was taken not to disturb the floating cell mass or lens when medium is replaced. Fifty percent of the medium is removed and replaced every 3-4 days with a volume of EB medium sufficient to ensure the growing cornea was completely immersed in medium.

[0199] Growth Medium:

KO Hi Glucose DMEM
500 U/ml streptomycin
1% non-essential amino acids
2 mM Glutamax-I
0.1 mM β -mercaptoethanol
8% Serum Replacement
8% Plasmonate (Bayer, Res Triangle Park)
Mitogens:
 10ng/ml LIF
 5ng/ml bFGF

[0200] EB Medium:

KO Hi Glucose DMEM
500 U/ml streptomycin
1% non-essential amino acids
2 mM Glutamax-I
0.1 mM β -mercaptoethanol
13% Serum Replacement

[0201] Histological Examination

[0202] A specimen (10 mm clear/white translucent tissue sphere) was placed in 70% ethanol after being fixed in neutral buffered formalin (NBF). The sphere was bisected, and a portion was examined for gross description and a portion was examined by microscopy.

[0203] The specimen was stained with a battery of histological dyes, including mucin stains (e.g., periodic acid-Schiff [PAS]), biogenic amine stains, melanin stains, lipochrome pigment stains, stains for iron and calcium, urate stains, fat stains, connective tissue stains, giemsa stains, microorganism stains (e.g., acid fast bacilli, gomori methenamine silver stain, and the like). Subsequent to staining, the specimen was examined under light microscopy.

[0204] HLA typing

[0205] Genomic DNA was extracted from donor blood, hES, phESC cells, and human newborn skin fibroblasts (NSFs) with Dynabeads DNA Direct Blood from Dynal (Invitrogen). HLA typing was performed by PCR with allele-specific sequencing primers

(PCR-SSP, Protrans) according to the manufacturer's specifications. HLA class I genes (HLA A*, B*, Cw*) were typed with PROTRANS HLA A* B* Cw* defining A*01-A*80, B*07-B*83, Cw*01-Cw*18 regions. HLA class II genes (HLA DRB1*, DRB3*, DRB4*, DRB5*, DQA1*, DQB1*) were analysed with PROTRANS HLA DRB1* defining DRB1*01-DRB1*16 (DR1-DR18), DRB3*, DRB4*, DRB5* regions and PROTRANS HLA DQB1* DQA1* defining DQB1*02- DQB1*06 (DQ2-DQ9), DQA1*0101-DQA1*0601 regions. PCR amplification was achieved: at 94°C for 2 min; 10 cycles at 94°C for 10 sec, 65°C for 1 min; 20 cycles at 94°C for 10 sec, 61°C for 50 sec, 72°C for 30 sec. Amplified products were detected in 2% agarose gel.

[0206] Affimetrix SNP microarray analysis

[0207] Genomic DNA was isolated from blood, cumulus cells, phESC and NSF by phenol/chloroform extraction method. These DNA samples obtained from four Caucasian subjects were genotyped with Affimetrix Mapping 50K Hind 240 Array (part of Affimetrix GeneChip Mapping 100K kit). Initially, the dataset contained 57,244 binary SNP markers. Since the number of markers is more than would be necessary to identify the equivalency of genomic samples and to study heterozygosity, 15 (chromosomes 1-15) out of 22 autosomal chromosomes were chosen. The shorter seven chromosomes were removed to reduce the chance that no marker, or only a single marker for a given chromosome, is selected during random sampling. The 1,459 markers were analyzed by Relcheck (version 0.67, Copyright © 2000 Karl W. Broman, Johns Hopkins University, Licensed under GNU General Public License version 2 (June 1991)).

[0208] Genomic imprinting analysis

[0209] Total nucleic acid was prepared as described Li et al. (J Biol Chem (2002) 277(16):13518-13527). RNA and DNA were extracted from cells using Tri-reagent (Sigma) or by using an RNA preparation kit from Qiagen (Valencia, CA).

[0210] Northern blots containing RNA from the various samples (see FIG. 3) were blotted onto filters by standard methods (See, e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual, 1989, 2nd ed, Cold Spring Harbor Press). The Northern filter was hybridized with single stranded oligonucleotide probes that hybridized specifically to the mRNAs. The oligonucleotide probes were end-labeled with [$\gamma^{32}\text{P}$]ATP (Amersham Biosciences). The filters were subsequently washed three times for 10 min each with 0.2 X

SSC (1 X SSC = 0.15 M NaCl and 0.015 M sodium citrate) containing 0.1% SDS at 60°C and analyzed by PhosphorImager (Molecular Dynamics). The sequences of the oligonucleotide probes were obtained from sequences based on the following Accession Nos.: NP002393 (Peg1_2 and Peg1_A; for these genes, human *PEG1* is transcribed from two alternative promoters, resulting in the transcription of two isoforms, of which only one (isoform 1_2) is imprinted. Paternal expression isoform 1 occurs in conjunction with an unmethylated CpG island in exon 1 of the paternal allele, whereas the corresponding CpG island in the maternal gene (isoform 1_A) is fully methylated. See, e.g., Li et al. (2002), supra); CAG29346 (SNRPN); AF087017 (H19); NR_001564 (inactive X specific transcripts-XIST); and P04406 (GAPDH).

[0211] DNA fingerprinting analysis

[0212] Genomic DNA was isolated from blood, hES cells, and NSF cells through a phenol/chloroform extraction, digested with *HinfI* restriction enzyme (Fermentas) and loaded in a 0.8% agarose gel. Following electrophoresis, denatured DNA was transferred to a nylon membrane (Hybond N, Amersham) by Southern blotting and hybridized with ³²P-labeled (CAC)₅ oligonucleotide probe. Data were analysed after membrane exposition on X-ray film (Kodak XAR) using Cronex intensifying screens.

[0213] Monolocus PCR genotyping

[0214] 3' Apolipoprotein B hypervariable minisatellite locus (3'ApoB VNTR)

[0215] Chromosomal location: 2p23-p23

[0216] **GenBank locus and locus definition:** APOB, apolipoprotein B (including Ag(x) antigen) untranslated region

[0217] **Repeat sequence 5'-3':** (TATAATTAAATATT TTATAATTAAAATATT)_n
(SEQ ID NO: 1)

[0218] Allelic ladder size range (bases): 450 + 10 + 2 primer + links

[0219] VNTR ladder size range (# of repeats, according to Ludwig et al, 1989): 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52

[0220] **Other known alleles (# of repeats):** 25, 27, 28, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 54, 55

[0221] **Promega K562 DNA® Allele sizes (# of repeats):** 36/36

[0222] **PCR protocol:**

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 1'

Elongation and primer linking 60°C, 2'

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

The analysis may be done as described in Verbenko et al., Apolipoprotein B 3'-VNTR polymorphism in Eastern European populations. Eur J Hum Gen (2003) 11(1):444-451. See Table 4.

Table 4. Allele Frequencies for Russian Populations

Allele	Allele frequency	Number of Alleles observed
25	0.001	1
30	0.079	75
32	0.071	68
33	0.001	1
34	0.238	227
35	0.004	4
36	0.393	375
37	0.001	1
38	0.036	36
39	0.001	1
40	0.014	13
42	0.001	1
44	0.042	41
45	0.006	6
46	0.033	31
48	0.067	64
50	0.011	10
52	0.001	1

Homozygotes 94
Heterozygotes 333
Total samples 427

- [0223] D1S80 (pMCT118) hypervariable minisatellite locus (D1S80 VNTR)
- [0224] Chromosomal location: 1p35-36
- [0225] GenBank locus and locus definition: Human D1S80 and MCT118 gene
- [0226] **Repeat sequence 5'-3':** (GAAGACAGACCACAG)_n (SEQ ID NO: 2)
- [0227] Allelic ladder size range (bases): 387-762
- [0228] **VNTR ladder size range (# of repeats):** 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 34, 35, 36, 37, 40, 41
- [0229] Other known alleles (# of repeats): 13, 14, 15, 38, 39,>41
- [0230] Promega K562 DNA® Allele sizes (# of repeats): 18/29
- [0231] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 45"

Primer linking 60°C, 30"

Elongation 72°C, 45"

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

- [0232] The analysis may be done as described in Verbenko et al., Allele frequencies for D1S80 (pMCT118) locus in some Eastern European populations. J Forensic Sci (2003) 48(1):207-208. See Table 5.

Table 5. Allele Frequencies for Russian Populations

Allele	Allele frequency	Number of Alleles observed
18	0.280	33
20	0.017	2
21	0.009	1
22	0.042	5
23	0.017	2
24	0.390	46
25	0.017	2
26	0.025	3
28	0.068	8
29	0.009	1
30	0.034	4
31	0.059	7
33	0.017	2
34	0.008	1
36	0.008	1

Homozygotes 15
Heterozygotes 44
Total samples 59

[0233] D6S366

[0234] Chromosomal location: 6q21-qter

[0235] GenBank locus and locus definition: NA

[0236] Allelic ladder size range (bases): 150-162

[0237] STR ladder size range (# of repeats): 12, 13, 15

[0238] Other known alleles (# of repeats): 10, 11, 14, 16, 17

[0239] Promega K562 DNA® Allele sizes (# of repeats): 13/14

[0240] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 1'

Elongation and primer linking 60°C, 2'

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

[0241] The analysis may be done as described in Efremov et al., An expert evaluation of molecular genetic individualizing systems based on the HUMvWFII and D6S366 tetranucleotide tandem repeats. Sud Med Ekspert (1998) 41(2):33-36. See Table 6.

Table 6. Allele Frequencies for Russian Populations

Allele	Allele frequency	Number of Alleles observed
10	0.008	3
11	0.059	21
12	0.316	112
13	0.251	89
14	0.085	30
15	0.175	62
16	0.015	7
17	0.011	4
Total samples	177	

[0242] D16S539**[0243]** Chromosomal location: 16q24-qter**[0244]** GenBank locus and locus definition: NA**[0245]** Repeat sequence 5'-3': (AGAT)_n**[0246]** Allelic ladder size range (bases): 264-304**[0247]** STR ladder size range (# of repeats): 5, 8, 9, 10, 11, 12, 13, 14, 15

[0248] Promega K562 DNA® Allele sizes (# of repeats): 11/12

[0249] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 45"

Primer linking 64°C, 30"

Elongation 72°C, 30"

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

[0250] The analysis has been done as described in GenePrint® STR Systems (Silver Stain Detection) Technical Manual No. D004. Promega Corporation, Madison, WI USA: 1993-2001. See Table 7.

Table 7. Allele Frequencies for Caucasian-Americans

Allele	Allele frequency	Number of Alleles observed
6	0.000	0
7	0.000	0
8	0.026	11
9	0.107	45
10	0.079	33
11	0.319	134
12	0.269	113
13	0.167	70
14	0.031	13
15	0.002	1
Homozygotes	57	
Heterozygotes	153	
Total samples	210	

[0251] D7S820

[0252] Chromosomal location: 7q11.21-22

[0253] GenBank locus and locus definition: NA

[0254] Repeat sequence 5'-3': (AGAT)_n

[0255] Allelic ladder size range (bases): 215-247

[0256] VNTR ladder size range (# of repeats): 6, 7, 8, 9, 10, 11, 12, 13, 14

[0257] Promega K562 DNA® Allele sizes (# of repeats): 9/11

[0258] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 45"

Primer linking 64°C, 30"

Elongation 72°C, 30"

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

The analysis has been done as described in GenePrint® STR Systems (Silver Stain Detection) Technical Manual No. D004. Promega Corporation, Madison, WI USA: 1993-2001. See Table 8.

Table 8. Allele Frequencies for D7S820 in Different Populations

Allele	Allele frequency for Caucasian-Americans	Number of Alleles observed	Allele frequency for Russians	Number of Alleles observed
6	0.002	1	0.0012	1
7	0.010	4	0.0087	7
8	0.155	65	0.1928	155
9	0.152	64	0.1480	119
10	0.295	124	0.2524	203
11	0.195	82	0.2040	164
12	0.121	51	0.1580	127
13	0.057	24	0.0299	24
14	0.012	5	0.0050	4
Homozygotes	43		92	
Heterozygotes	167		310	
Total samples	210		402	

[0259] Human von Willebrand factor gene hypervariable microsatellite locus II (vWFII)

[0260] Chromosomal location: 12p13.3-12p13.2

[0261] **GenBank locus and locus definition:** HUMvWFII, Human von Willebrand factor gene

[0262] Repeat sequence 5'-3': (ATCT)_n/(AGAT)_n

[0263] Allelic ladder size range (bases): 154-178

[0264] STR ladder size range (# of repeats): 9, 11, 12, 13

[0265] Other known alleles (# of repeats): 8, 10, 14, 15

[0266] Promega K562 DNA® Allele sizes (# of repeats): 13/13

[0267] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 1'

Elongation and primer linking	60°C, 2'
Extension step:	72°C, 5'
Hold step:	4°C, unlimited time

[0268] The analysis has been done as described in Efremov et al., An expert evaluation of molecular genetic individualizing systems based on the HUMvWFII and D6S366 tetranucleotide tandem repeats. Sud Med Ekspert (1998) 41(2):33-36. See Table 9.

Table 9. Allele Frequencies for Russian Populations

Allele	Allele frequency	Number of Alleles observed
9	0.082	37
10	0.088	40
11	0.392	177
12	0.296	134
13	0.069	31
14	0.058	26
15	0.015	7
Total samples	226	

[0269] D13S317

[0270] Chromosomal location: 13q22-q31

[0271] GenBank locus and locus definition: NA

[0272] Repeat sequence 5'-3': (AGAT)_n

[0273] Allelic ladder size range (bases): 165-197

[0274] STR ladder size range (# of repeats): 8, 9, 10, 11, 12, 13, 14, 15

[0275] Other known alleles (# of repeats): 7

[0276] Promega K562 DNA® Allele sizes (# of repeats): 8/8

[0277] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation:	95°C, 2'
Cycling for 30 cycles:	
Denaturation	94°C, 45"
Primer linking	64°C, 30"
Elongation	72°C, 30"
Extension step:	72°C, 5'
Hold step:	4°C, unlimited time

[0278] The analysis has been done as described in GenePrint® STR Systems (Silver Stain Detection) Technical Manual No. D004. Promega Corporation, Madison, WI USA: 1993-2001. See Table 10.

Table 10. Allele Frequencies for D13S317 in Different Populations

Allele	Allele frequency for Caucasian-Americans	Number of Alleles observed	Allele frequency for Russians	Number of Alleles observed
7	0.000	0	0	0
8	0.143	60	0.1393	112
9	0.052	22	0.0883	71
10	0.052	22	0.0684	55
11	0.305	128	0.3706	298
12	0.307	129	0.2040	164
13	0.083	35	0.0871	70
14	0.057	24	0.0423	34
15	0.000	0	0	0
Homozygotes	61		90	
Heterozygotes	149		312	
Total samples	210		402	

[0279] Human vonWillebrand factor gene hypervariable microsatellite locus (vWA)

[0280] Chromosomal location: 12p12pter

[0281] **GenBank locus and locus definition:** HUMVWFA31, Human von Willebrand factor gene

[0282] Repeat sequence 5'-3': (AGAT)_n

[0283] Allelic ladder size range (bases): 139-167

[0284] STR ladder size range (# of repeats): 14, 16, 17, 18

[0285] Other known alleles (# of repeats): 11, 12, 13, 15, 19, 20, 21

[0286] Promega K562 DNA® Allele sizes (# of repeats): 16/16

[0287] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 1'

Elongation and primer linking 60°C, 2'

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

[0288] The analysis has been done as described in GenePrint® STR Systems (Silver Stain Detection) Technical Manual No. D004. Promega Corporation, Madison, WI USA: 1993-2001. See Table 11.

Table 11. Allele Frequencies for HUMVWA31 in Different Populations

Allele	Allele frequency for Caucasian-Americans	Number of Alleles observed	Allele frequency for Russians	Number of Alleles observed
13	0.000	0	0.0025	2
14	0.131	56	0.0796	64
15	0.082	35	0.0920	74
16	0.211	90	0.2127	171
17	0.265	113	0.2836	228
18	0.202	86	0.2251	181
19	0.087	37	0.0833	67
20	0.021	9	0.0199	16
21	0.000	0	0.0012	1
Homozygotes	38		70	
Heterozygotes	175		332	
Total samples	213		402	

[0289] Human c-fms proto-oncogene for CSF-1 receptor gene microsatellite locus(CSF1PO)

[0290] Chromosomal location: 5q33.3-34

[0291] **GenBank locus and locus definition:** HUMCSF1PO, Human c-fms proto-oncogene

[0292] Repeat sequence 5'-3': (AGAT)_n

[0293] Allelic ladder size range (bases): 295-327

[0294] STR ladder size range (# of repeats): 7, 8, 9, 10, 11, 12, 13, 14, 15

[0295] Other known alleles (# of repeats): 6

[0296] Promega K562 DNA® Allele sizes (# of repeats): 9/10

[0297] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 45"

Primer linking 64°C, 30"

Elongation 72°C, 30"

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

[0298] The analysis has been done as described in GenePrint® STR Systems (Silver Stain Detection) Technical Manual No. D004. Promega Corporation, Madison, WI USA: 1993-2001. See Table 12.

Table 12. Allele Frequencies for Caucasian-Americans

Allele	Allele frequency	Number of Alleles observed
6	0.000	0
7	0.000	0
8	0.002	1
9	0.033	14
10	0.251	108
11	0.309	133
12	0.330	142
13	0.060	26
14	0.014	6
15	0.000	0
Homozygotes	47	
Heterozygotes	168	
Total samples	215	

[0299] Human thyroid peroxidase gene microsatellite locus (TPOX)

[0300] Chromosomal location: 2p25.1-pter

[0301] **GenBank locus and locus definition:** HUMTPOX, Human thyroid peroxidase gene

[0302] Repeat sequence 5'-3': (AATG)_n

[0303] Allelic ladder size range (bases): 224-252

[0304] STR ladder size range (# of repeats): 6, 7, 8, 9, 10, 11, 12, 13

[0305] Other known alleles (# of repeats): none

[0306] Promega K562 DNA® Allele sizes (# of repeats): 8/9

[0307] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 45"

Primer linking	64°C, 30"
Elongation	72°C, 30"
Extension step:	72°C, 5'
Hold step:	4°C, unlimited time

[0308] The analysis has been done as described in GenePrint® STR Systems (Silver Stain Detection) Technical Manual No. D004. Promega Corporation, Madison, WI USA: 1993-2001. See Table 13.

Table 13. Allele Frequencies for Caucasian-Americans

Allele	Allele frequency	Number of Alleles observed
6	0.002	1
7	0.000	0
8	0.528	227
9	0.093	40
10	0.056	24
11	0.284	122
12	0.037	16
13	0.000	0
Homozygotes	76	
Heterozygotes	139	
Total samples	215	

[0309] Human tyrosine hydroxylase gene microsatellite locus (TH01)

[0310] Chromosomal location: 5q33.3-34

[0311] **GenBank locus and locus definition:** HUMTHO1, Human tyrosine hydroxylase gene

[0312] Repeat sequence 5'-3': (AATG)_n

[0313] Allelic ladder size range (bases): 179-203

[0314] STR ladder size range (# of repeats): 5, 6, 7, 8, 9, 10, 11

[0315] Other known alleles (# of repeats): 9.3

[0316] Promega K562 DNA® Allele sizes (# of repeats): 9.3/9.3

[0317] PCR protocol:

Thermal cycler: DNA Technology Ltd., Russia

Initial Incubation: 95°C, 2'

Cycling for 30 cycles:

Denaturation 94°C, 45"

Primer linking 64°C, 30"

Elongation 72°C, 30"

Extension step: 72°C, 5'

Hold step: 4°C, unlimited time

The analysis has been done as described in GenePrint® STR Systems (Silver Stain Detection) Technical Manual No. D004. Promega Corporation, Madison, WI USA: 1993-2001. See Table 14.

Table 14. Allele Frequencies for Caucasian-Americans

Allele	Allele frequency	Number of Alleles observed
5	0.007	3
6	0.237	101
7	0.148	63
8	0.117	50
9	0.155	66
9.3	0.331	141
10	0.005	2
11	0.000	0
Homozygotes	50	
Heterozygotes	163	
Total samples	213	

[0318] Results

[0319] The hES cells from this method display many features that are typical for embryonic stem cells: cytoplasmic lipid bodies, small cytoplasmic/nuclear ratio and clearly distinguishable nucleoli. The hES cell colonies display similar morphology to that reported previously for human embryonic stem cells derived after in vitro fertilization. The cells were immunoreactively positive for alkaline phosphatase (Fig 1A), octamer-binding transcription

factor 4 mRNA (Oct-4) (Fig 1B), stage-specific embryonic antigen 1 (SSEA-1) (Fig 1C), stage-specific embryonic antigen 3 (SSEA-3) (Fig 1D), stage-specific embryonic antigen 4 (SSEA-4) (Fig 1E), tumor rejection antigen 1-60 (TRA-1-60) (Fig 1F), tumor rejection antigen 1-81 (TRA-1-81) (Fig 1G), and negative for stage-specific embryonic antigen 1 (SSEA-1) (Fig 1C), (which is positive for mouse embryonic stem cells, but not for human). Telomerase activity is often correlated with replicative immortality and is typically expressed in germ cells, cancer cells, and a variety of stem cells, including stem cells, but absent in most somatic cell types. The cells prepared by this method after three months in in vitro proliferation maintained their undifferentiated morphology and displayed high levels of telomerase activity (Fig 2A). The pluripotency of the cells was investigated in vitro by embryoid body formation (Fig 2B, 2C), G-banded karyotyping shows that cells have normal human 46XX karyotype (Fig 2D).

[0320] DNA fingerprinting analysis was performed on the blood of the oocyte donor, on the ES cells, and on the HNSF feeder cells by Southern blotting and hybridization with a ³²P – labeled (CAC)_n oligonucleotide probe (Fig 2E), and monolocus polymerase chain reaction (PCR) with different locuses.

[0321] For monolocus PCR, genotyping revealed identical alleles for all loci (but one, D7S820) between blood (donor) DNA and OL1 DNA. See Table 15.

Table 15. Monolocus PCR genotyping.

NN	Locus definition	Chromosomal location	hES	NSF	Blood
1.	3'ApoB	2p24-p23	36/48	36/36	36/48
2.	D1S80	1p35-36	18/24	22/31	18/24
3.	D6S366	6q21-qter	13/15	17/17	13/15
4.	D16S359	16q24-qter	8/13	12/13	8/13
5.	D7S820	7q11.21-22	11/11	9/10	10/11
6.	vWFII	12p13.3-12p13.2	11/13	9/11	11/13
7.	D13S317	13q22-q31	9/12	11/12	9/12
8.	vWA	12p12pter	14/18	17/18	14/18
9.	CSF1PO	5q33.3-34	12/12	12/13	12/12
10.	TPOX	2p25.1-pter	8/11	8/11	8/11
11.	TH01	5q33.3-34	6/6	6/9,3	6/6

[0322] Heterozygosity (heterozygosis) of all heterozygous donor loci (but one, D7S820) was not changed in hES loci. Homozygosity (homozygosis) of D7S820 locus in hES DNA is a result of mutation (insertion of one AGAT monomer in microsatellite repeat) due to slipped-strand mispairing during DNA replication and DNA repair.

[0323] These results are in accordance with those obtained with multilocus DNA fingerprinting (when substantially identical fingerprint patterns for donor DNA and hES DNA were found).

[0324] Figure 2E demonstrated heterozygosity of hES cells and their identity with the oocyte donor's blood, and there was not similarity between the hES cells and the feeder cells. The DNA profile of hES cell line was confirmed by PCR-based haplotype analysis using polymorphic genes within the MHC class I and class II. Total genomic DNA from the oocyte donor blood cells, from hES cells, and feeder HNSFs were genotyped and compared. The data demonstrated that hES cells and cells from donor blood were indistinguishable from each other and therefore should be considered autologous, and both distinguished from DNA of the feeder cells (Table 16).

Table 16. HLA Typing.

	MHC I			MHC II		
	HLA-A	HLA-B	HLA-C	DRB1	DQB1	DQA1
pHES-1	A*01	B*15(63)	Cw*04	DRB1*12	DQB1*06	DQA1*01
	A*02	B*35	Cw*0708	DRB1*13	DQB1*03	DQA1*0505
Donor	A*01	B*15(63)	Cw*04	DRB1*12	DQB1*06	DQA1*01
	A*02	B*35	Cw*0708	DRB1*13	DQB1*03	DQA1*0505
HNSF	A*25	B*15(62)	Cw*12	DRB1*04	DQB1*06	DQA1*01
	A*32	B*18	Cw*12	DRB1*15	DQB1*03	DQA1*03

[0325] DNA fingerprinting and HLA typing analysis confirmed that the hES cells are heterozygous and contain the whole donor genetic material. These results coincide with data from parthenogenetic monkey stem cell lines (Vrana et al., Proc Natl Acad Sci USA (2003) 100(Suppl 1):11911-11916), and do not coincide with data from parthenogenetic mouse stem cell lines (Lin et al., Stem Cells (2003) 21:153-161), which contains half of the donor genetic material.

[0326] The phESC lines display a morphology expected in hES cells, forming colonies with tightly packed cells, prominent nucleoli and a small cytoplasm to nucleus ratio (FIG. 4). These cells express traditional hES markers SSEA-3, SSEA-4, TRA-1-60, TRA-1-81, and OCT-4, and do not express SSEA-1, a positive marker for undifferentiated mouse embryonic stem cells (FIG. 4). The cells derived from all lines demonstrate high levels of alkaline phosphatase and telomerase activity (FIG. 5 and FIG. 6). G-banded karyotyping showed that phESC lines have a normal human 46,XX karyotype, with the exception of the phESC-7 line (FIG. 7). Approximately 91% of cells from the phESC-7 line have a 47,XXX karyotype and 9% of the cells have a 48,XXX,+6 karyotype. A different degree of X chromosome heteromorphism was observed in the lines; approximately 12% of the phESC-1 and phESC-6 lines; 42% for the phESC-5 line; and 70, 80, and 86 % for the cell lines phESC7, phESC-3, and phESC-4, respectively (FIG. 7).

[0327] Comparative DNA profiling of was performed on all the phESC lines, the donor somatic cells and the feeder cells. These studies used Affimetrix SNP microarrays (Mapping 50K Hind 240 Arrays) to study chromosome changes and to confirm the genetic similarity of

the phESC to the donor's somatic cells. All paired genotype relationships between phESC lines and their associated donor somatic cells were identified as "full siblings", and all other combinations of pairs were identified as "unrelated". Internal controls identified the paired genotype relationship between split cultures derived from the same phESC line as "monozygotic twins" (Table 17, Database S1).

Table 17. Database S1.

Database S1 Identifying DNA samples from phESC and related donors												
genotype 1	genotype 2	putative relationship	inferred relationship	IBS 0	IBS 1	IBS 2	n_typed	MZtwins	LOD par/off	LOD fullsibs	LOD halvesibs	LOD unrelated
1	2	unrelated	unrelated	166	662	631	1459	-1503.03	-300.45	-23.15	-8.41	0
1	3	unrelated	unrelated	241	616	602	1459	-1560.65	-434.85	-28.04	-12.22	0
1	4	unrelated	unrelated	225	623	611	1459	-1535.94	-400.61	-31.39	-14.39	0
1	5	unrelated	unrelated	225	623	611	1459	-1535.94	-400.61	-31.39	-14.39	0
1	6	unrelated	unrelated	243	644	572	1459	-1642.35	-445.78	-31.74	-14.54	0
1	7	unrelated	unrelated	252	638	569	1459	-1641.11	-453.5	-29.25	-12.86	0
1	8	unrelated	unrelated	250	643	566	1459	-1656.02	-460.02	-32.86	-15.32	0
1	9	unrelated	unrelated	219	657	583	1459	-1605.31	-382.39	-27.37	-11.58	0
1	10	unrelated	unrelated	158	707	594	1459	-1591.43	-279.21	-26.37	-10.89	0
1	11	unrelated	unrelated	193	668	598	1459	-1584.71	-354.76	-29.65	-13.31	0
1	12	unrelated	unrelated	166	671	622	1459	-1523.1	-300.5	-30.53	-13.92	0
2	3	unrelated	full sibs	0	282	1177	1459	-440.02	-146.3	0	-167.42	-363.63
2	4	unrelated	unrelated	233	627	599	1459	-1569.66	-423.24	-28.24	-12.91	0
2	5	unrelated	unrelated	233	627	599	1459	-1569.66	-423.24	-28.24	-12.91	0
2	6	unrelated	unrelated	217	650	592	1459	-1584.75	-388.44	-22.62	-8.53	0
2	7	unrelated	unrelated	243	650	566	1459	-1645.94	-437.91	-23.23	-8.72	0
2	8	unrelated	unrelated	225	649	585	1459	-1603.18	-404.41	-27.04	-11.97	0
2	9	unrelated	unrelated	210	639	610	1459	-1532.75	-360.46	-24.72	-9.89	0
2	10	unrelated	unrelated	144	683	632	1459	-1491.18	-243.56	-16.82	-4.51	0
2	11	unrelated	unrelated	172	680	607	1459	-1556.46	-310.03	-23.5	-9.7	0
2	12	unrelated	unrelated	176	667	616	1459	-1538.57	-327.95	-27.31	-12.06	0
3	4	unrelated	unrelated	336	457	666	1459	-1391.57	-599.92	-30.6	-14.62	0
3	5	unrelated	unrelated	336	457	666	1459	-1391.57	-599.92	-30.6	-14.62	0
3	6	unrelated	unrelated	322	482	655	1459	-1415.98	-571.23	-26.08	-11.86	0
3	7	unrelated	unrelated	369	442	648	1459	-1432.05	-664.95	-27.39	-11.93	0
3	8	unrelated	unrelated	334	483	642	1459	-1449.86	-597.75	-31.68	-15.14	0
3	9	unrelated	unrelated	307	493	659	1459	-1395.19	-530.45	-24.56	-10	0
3	10	unrelated	unrelated	215	623	621	1459	-1503.92	-364.97	-17.26	-4.43	0
3	11	unrelated	unrelated	264	582	613	1459	-1531.91	-473.48	-28.41	-12.81	0
3	12	unrelated	unrelated	254	595	610	1459	-1544.73	-460.57	-29.92	-13.88	0
4	5	unrelated	MZ twins	0	0	1459	1459	0	-379.58	-45.47	-401.67	-677.74
4	6	unrelated	unrelated	334	475	650	1459	-1436.59	-599.55	-32.73	-15.19	0
4	7	unrelated	unrelated	365	439	655	1459	-1418.34	-656.01	-31.6	-14.56	0
4	8	unrelated	unrelated	329	486	644	1459	-1450.75	-586.4	-32.06	-14.88	0
4	9	unrelated	unrelated	332	466	661	1459	-1395.18	-590.12	-28.69	-12.94	0
4	10	unrelated	unrelated	245	606	608	1459	-1542.32	-438.93	-28.75	-12.74	0
4	11	unrelated	unrelated	273	569	617	1459	-1530.97	-492.84	-29.03	-12.34	0
4	12	unrelated	full sibs	0	224	1235	1459	-326.17	-162.34	0	-183.44	-393.46
5	6	unrelated	unrelated	334	475	650	1459	-1436.59	-599.55	-32.73	-15.19	0
5	7	unrelated	unrelated	365	439	655	1459	-1418.34	-656.01	-31.6	-14.56	0
5	8	unrelated	unrelated	329	486	644	1459	-1450.75	-586.4	-32.06	-14.88	0
5	9	unrelated	unrelated	332	466	661	1459	-1395.18	-590.12	-28.69	-12.94	0
5	10	unrelated	unrelated	245	606	608	1459	-1542.32	-438.93	-28.75	-12.74	0
5	11	unrelated	unrelated	273	569	617	1459	-1530.97	-492.84	-29.03	-12.34	0
5	12	unrelated	full sibs	0	224	1235	1459	-326.17	-162.34	0	-183.44	-393.46
6	7	unrelated	full sibs	45	176	1238	1459	-277.78	-217.21	0	-165.72	-390.62
6	8	unrelated	full sibs	44	187	1228	1459	-289.8	-201.32	0	-153.75	-365.51
6	9	unrelated	unrelated	333	481	645	1459	-1436.5	-595.4	-30.3	-13.77	0
6	10	unrelated	unrelated	240	601	618	1459	-1518.17	-425.03	-27.11	-11.53	0
6	11	unrelated	full sibs	0	164	1295	1459	-209.27	-191.66	0	-213.25	-440.56
6	12	unrelated	unrelated	234	615	610	1459	-1547.15	-416.14	-30.21	-13.64	0
7	8	unrelated	full sibs	38	225	1196	1459	-326.62	-150.16	0	-121.55	-334.09
7	9	unrelated	unrelated	359	473	627	1459	-1479.28	-642.41	-30.61	-14.47	0
7	10	unrelated	unrelated	252	623	584	1459	-1598.35	-443.81	-28.88	-13.09	0
7	11	unrelated	full sibs	0	230	1229	1459	-318.49	-137.93	0	-159.55	-389.58
7	12	unrelated	unrelated	265	583	611	1459	-1539.33	-472.91	-30.55	-13.87	0
8	9	unrelated	unrelated	347	480	632	1459	-1472.41	-625.68	-30.93	-14.31	0
8	10	unrelated	unrelated	244	614	601	1459	-1561.3	-434	-28.07	-12.37	0
8	11	unrelated	full sibs	0	175	1284	1459	-223.73	-178.56	0	-200.12	-428.04
8	12	unrelated	unrelated	236	610	613	1459	-1539.08	-417.14	-29.32	-13.14	0
9	10	unrelated	full sibs	0	228	1231	1459	-315.15	-152.88	0	-174.27	-392.91
9	11	unrelated	unrelated	269	567	623	1459	-1502.69	-479.57	-28.47	-12.55	0
9	12	unrelated	unrelated	245	612	602	1459	-1557.25	-438.53	-26.07	-11.15	0
10	11	unrelated	unrelated	187	635	637	1459	-1478.7	-328.06	-25.52	-10.6	0
10	12	unrelated	unrelated	181	662	616	1459	-1534.36	-329	-25.2	-10.6	0

DNA samples were numbered as follows: 1-human neonatal skin fibroblasts; 2-phESC-7 line donor; 3-phESC-7 line; 4-phESC-1 line; 5-phESC-1 line; 6-phESC-3 line; 7-phESC-4 line; 8-phESC-5 line; 9-phESC-6 line; 10-phESC-6 line donor; 11-phESC-3 to phESC-5 lines donor; and 12-phESC-1 line donor.

The result shows that only one pair (sample 4-5), has been identified as monozygotic (MZ) twins. Ten other pairs (samples 2-3, 4-12, 5-12, 6-7, 6-11, 7-8, 7-11, 8-11, 9-10) have been identified as full siblings, and all the other combination of pairs have been identified as unrelated. The IBS columns in the output display the number of markers at which the pair are both typed and share 0, 1, or 2 alleles identical by state (For MZ twins under ideal conditions of no genotyping errors, all markers must be placed under IBS=2). The output does not display P (observed markers | given relationship) directly, but it displays LOD score $-\log_{10} \{P(\text{observed markers} | \text{putative relationship}) / P(\text{observed markers} | \text{relationship for which maximum likelihood was obtained and thus the call was made})\}$ as a measure of similarity. The smaller the LOD score is, the less likely the putative relationship between two samples it.

[0328] Comparative analysis of 1,459 SNP markers revealed phESC heterozygosity and showed that changes had occurred in the phESC cell genotype in comparison to the related donor somatic cell genotype. Some segments of the somatic cell genome that had formerly been heterozygous became homozygous in the related phESC line genome. This heterozygous to homozygous pattern occurred in 11-15% of the phESC-1, PhESC-3, phESC-4, phESC-5 and phESC-6 lines, and was 19% for the phESC7 line (Database S2). Moreover, genetic differences were observed between the phESC and phESC-5 lines that had been derived from the same oocyte donor (Table 18, Database S2).

Table 18

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines																
ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor	
1	SNP_A-1697748	rs10752719	3744122	3.744122	0.436	A B	A B	B B	A B	A B	A B	B B	B B	B B	B B	
1	SNP_A-1743594	rs806104	5977200	5.9772	0.631	A B	A B	A A	A B	A B	A B	A B	A B	A A	A A	
1	SNP_A-1687843	rs301791	8402638	8.402638	0.274	A B	A B	B B	B B	B B	B B	A B	A B	A A	A B	
1	SNP_A-1647681	rs1474868	11978430	11.97843	0.333	B B	B B	A A	A A	A A	A A	A A	A A	A A	A A	
1	SNP_A-1673737	rs1417144	14211391	14.211391	0.548	A A	A A	A B	A B	A B	A B	A A	A A	A B	A B	
1	SNP_A-1747116	rs860379	18414756	18.414756	0.25	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B	
1	SNP_A-1662223	rs10492997	19514677	19.514677	0.631	A A	A A	B B	B B	B B	B B	A B	A B	A A	A A	
1	SNP_A-1662225	rs559346	28077956	28.077956	0.583	B B	A B	A B	A B	A B	A B	A B	A B	A A	A B	

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-1646469	rs4949455	31783886	31.783886	0.382	A	A	A	B	A	A	A	A	A	A
1	SNP_A-1695076	rs6661190	33872782	33.872782	0.274	B	B	B	B	B	B	B	B	B	A
1	SNP_A-1679571	rs4653029	34558585	34.558585	0.274	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1675060	rs7531479	36798680	36.79868	0.714	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1753902	rs1010805	37858235	37.858235	0.738	A	A	A	A	B	A	A	A	B	B
1	SNP_A-1691977	rs6693076	39972196	39.972196	0.441	A	A	B	A	B	B	B	B	B	B
1	SNP_A-1723259	rs407752	40472948	40.472948	0.333	B	B	B	A	B	B	B	B	B	B
1	SNP_A-1692103	rs7515340	41055964	41.055964	0.381	A	A	A	A	A	A	A	A	B	B
1	SNP_A-1696731	rs4660575	41902429	41.902429	0.429	B	B	B	B	B	B	A	A	B	A
1	SNP_A-1701070	rs1408412	42787470	42.78747	0.679	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1729559	rs1771551	45552736	45.552736	0.738	A	A	A	A	A	A	A	A	B	A
1	SNP_A-1670587	rs2245122	47358015	47.358015	0.598	A	A	A	A	A	A	B	B	B	B
1	SNP_A-1711898	rs1875645	50501900	50.5019	0.524	A	A	B	B	B	B	B	B	B	B
1	SNP_A-1645411	rs625643	54349188	54.349188	0.25	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1718210	rs10493206	56531172	56.531172	0.488	A	A	B	B	B	B	A	A	A	A
1	SNP_A-1752670	rs1831870	57339224	57.339224	0.524	A	A	A	A	B	A	B	B	B	B
1	SNP_A-1669308	rs852766	57998529	57.998529	0.564	A	A	A	A	A	A	A	A	A	B
1	SNP_A-1681141	rs1969772	58917123	58.917123	0.738	A	A	A	A	A	A	B	B	A	B
1	SNP_A-1690420	rs10489908	61576784	61.576784	0.738	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1727043	rs2765249	62441479	62.441479	0.75	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1646105	rs3861943	63439667	63.439667	0.405	B	B	B	B	B	B	A	A	A	A
1	SNP_A-1654674	rs592298	64000081	64.000081	0.25	B	B	B	B	B	B	A	A	B	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-1708628	rs746633	64503887	64.503887	0.692	A	A	B	B	B	B	B	B	A	A
1	SNP_A-1713897	rs1171279	65700514	65.700514	0.345	B	B	B	B	B	B	B	B	B	A
1	SNP_A-1717648	rs1280310	66928844	66.928844	0.655	A	A	A	B	A	A	A	A	A	A
1	SNP_A-1712508	rs1408956	67849084	67.849084	0.536	A	A	A	A	B	A	A	A	B	B
1	SNP_A-1688631	rs1413953	70834525	70.834525	0.571	B	B	A	A	A	A	B	B	A	B
1	SNP_A-1720162	rs1338655	73569634	73.569634	0.429	A	A	A	A	A	A	A	A	B	B
1	SNP_A-1697494	rs10493539	74427598	74.427598	0.25	A	A	B	B	B	B	B	B	A	A
1	SNP_A-1649261	rs277355	75002805	75.002805	0.345	B	B	B	B	B	B	A	A	B	A
1	SNP_A-1744876	rs1250876	75905253	75.905253	0.345	A	A	A	B	A	A	A	A	B	B
1	SNP_A-1739854	rs3928852	76926021	76.926021	0.607	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1687047	rs10493596	77438262	77.438262	0.718	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1732619	rs1248480	79071260	79.07126	0.357	B	B	A	A	A	A	B	B	B	B
1	SNP_A-1664985	rs2127436	79792017	79.792017	0.488	A	A	A	B	A	A	B	B	A	A
1	SNP_A-1644541	rs2389016	80511350	80.51135	0.738	A	A	B	B	A	B	B	B	A	B
1	SNP_A-1645927	rs10518660	82094088	82.094088	0.738	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1693780	rs6598991	82697988	82.697988	0.524	B	B	A	A	A	A	A	A	A	A
1	SNP_A-1674234	rs2268667	85505767	85.505767	0.321	B	B	B	A	B	B	B	B	B	B
1	SNP_A-1752288	rs306322	88673430	88.67343	0.726	A	A	A	A	A	A	B	B	B	B
1	SNP_A-1736094	rs1831298	90211840	90.21184	0.262	A	A	B	B	B	B	A	A	B	A
1	SNP_A-1711115	rs4233429	90811924	90.811924	0.25	B	B	A	B	A	A	B	B	B	B
1	SNP_A-1714794	rs665484	91375951	91.375951	0.512	A	A	A	A	A	A	A	A	B	B
1	SNP_A-1675488	rs490800	92304926	92.304926	0.369	B	B	A	B	A	A	A	A	B	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-1656572	rs6703310	93500761	93.500761	0.393	A	A	A	A	A	A	B	B	B	B
1	SNP_A-1755223	rs223237	96276742	96.276742	0.476	B	B	B	B	B	B	A	A	A	A
1	SNP_A-1691383	rs1911500	98291841	98.291841	0.738	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1725993	rs1838587	101983453	101.983453	0.525	A	A	B	A	B	B	B	B	A	B
1	SNP_A-1689489	rs7521799	102944538	102.944538	0.619	B	B	B	A	B	B	A	B	B	B
1	SNP_A-1684273	rs1576516	104210964	104.210964	0.452	B	B	A	A	A	A	B	B	A	A
1	SNP_A-1733369	rs1919894	107240697	107.240697	0.381	B	B	B	B	B	B	A	B	B	B
1	SNP_A-1715038	rs10494081	108114145	108.114145	0.667	A	A	A	A	A	A	A	A	B	A
1	SNP_A-1699288	rs2026485	108978565	108.978565	0.333	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1750726	rs6682717	110527665	110.527665	0.441	A	A	B	B	B	B	A	B	A	A
1	SNP_A-1648811	rs694180	111438255	111.438255	0.464	B	B	B	B	B	B	B	B	A	B
1	SNP_A-1753842	rs1936061	112187978	112.187978	0.595	A	A	A	A	A	A	B	A	B	B
1	SNP_A-1689065	rs2359417	113685242	113.685242	0.452	B	B	B	B	B	B	A	A	B	B
1	SNP_A-1746401	rs3767824	118152606	118.152606	0.429	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1688653	rs1766803	119095860	119.09586	0.366	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1708513	rs477992	119969618	119.969618	0.286	A	A	B	B	B	B	B	B	B	B
1	SNP_A-1701244	rs10494240	143040559	143.040559	0.321	B	B	A	A	A	A	B	B	A	B
1	SNP_A-1706430	rs10494267	148366991	148.366991	0.321	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1680305	rs2879490	149760236	149.760236	0.381	B	B	B	B	B	B	A	A	A	A
1	SNP_A-1723421	rs10494303	150706096	150.706096	0.571	B	B	A	A	A	A	A	A	A	A
1	SNP_A-1681003	rs884664	151516798	151.516798	0.702	A	A	A	A	A	A	B	A	A	A
1	SNP_A-1667931	rs10494315	154072954	154.072954	0.655	A	A	A	A	A	A	B	B	B	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A- 1647211	rs919477	155585918	155.585918	0.25	B	B	B	B	B	B	B	B	A
1	SNP_A- 1662451	rs1149392	157241261	157.241261	0.286	B	B	B	B	B	B	B	B	B
1	SNP_A- 1695012	rs6683968	158923070	158.92307	0.571	A	A	B	B	B	B	A	A	A
1	SNP_A- 1716490	rs869513	159832184	159.832184	0.607	A	A	A	A	A	A	A	A	A
1	SNP_A- 1727494	rs4656422	161688624	161.688624	0.25	B	B	A	A	B	B	B	B	B
1	SNP_A- 1646555	rs4657482	162563307	162.563307	0.405	B	B	B	B	B	B	B	B	B
1	SNP_A- 1743854	rs2093658	164086850	164.08685	0.317	A	A	A	A	B	B	A	A	A
1	SNP_A- 1681011	rs1358948	165590931	165.590931	0.31	B	B	B	B	B	B	A	A	A
1	SNP_A- 1751990	rs2205848	166407951	166.407951	0.31	B	B	B	B	B	B	B	B	A
1	SNP_A- 1736240	rs10494487	167046739	167.046739	0.298	B	B	B	B	B	B	B	B	B
1	SNP_A- 1674510	rs3753538	168481215	168.481215	0.691	A	A	A	A	A	A	A	A	B
1	SNP_A- 1719434	rs10489280	169204277	169.204277	0.488	A	A	B	B	B	B	A	A	B
1	SNP_A- 1753950	rs989423	171514180	171.51418	0.75	A	A	A	A	A	A	A	A	A
1	SNP_A- 1722081	rs1359587	172487558	172.487558	0.691	B	B	B	B	B	B	B	B	A
1	SNP_A- 1694706	rs2861746	173128066	173.128066	0.452	B	B	A	A	A	A	B	B	B
1	SNP_A- 1733825	rs2493119	175995013	175.995013	0.333	B	B	B	B	B	B	B	B	A
1	SNP_A- 1671505	rs1281294	178629596	178.629596	0.714	A	A	A	A	A	A	A	A	A
1	SNP_A- 1694118	rs2274984	179839103	179.839103	0.524	B	B	B	B	B	B	A	A	B
1	SNP_A- 1644471	rs1184639	180355276	180.355276	0.357	B	B	B	B	B	B	B	B	A
1	SNP_A- 1711261	rs2840274	180942462	180.942462	0.429	A	A	B	B	B	B	A	A	B
1	SNP_A- 1706912	rs170885	181673406	181.673406	0.512	B	B	A	A	A	A	B	B	B
1	SNP_A- 1703470	rs10489701	182242226	182.242226	0.595	A	A	B	B	B	B	A	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A- 1696277	rs10489756	182835425	182.835425	0.262	B	B	A	A	A	A	A	A	B	A
1	SNP_A- 1744486	rs726706	183604111	183.604111	0.429	A	A	B	B	B	B	B	B	A	A
1	SNP_A- 1693312	rs7543266	184360480	184.36048	0.595	A	A	A	A	A	A	A	A	A	A
1	SNP_A- 1739170	rs6665263	185050414	185.050414	0.452	B	B	B	B	B	B	B	B	A	A
1	SNP_A- 1726093	rs10494626	186275233	186.275233	0.464	A	A	B	B	B	B	B	B	B	A
1	SNP_A- 1658415	rs815160	186988747	186.988747	0.427	A	A	A	A	A	A	A	A	A	A
1	SNP_A- 1666089	rs1563191	187849406	187.849406	0.333	B	B	B	B	B	B	B	B	B	B
1	SNP_A- 1753798	rs1338034	188358939	188.358939	0.393	B	B	B	B	B	B	B	B	B	B
1	SNP_A- 1688981	rs4657868	190164348	190.164348	0.524	B	B	B	B	B	B	B	B	B	B
1	SNP_A- 1723115	rs10494707	191296870	191.29687	0.357	B	B	B	B	B	B	A	A	B	B
1	SNP_A- 1651749	rs822456	191826836	191.826836	0.439	B	B	B	B	B	B	B	B	A	A
1	SNP_A- 1642592	rs10494728	192402426	192.402426	0.25	A	A	B	B	B	B	A	A	B	B
1	SNP_A- 1658925	rs3762271	193802099	193.802099	0.6	B	B	A	A	A	A	B	B	A	A
1	SNP_A- 1687705	rs1927246	195048356	195.048356	0.702	A	A	A	B	A	A	A	A	A	A
1	SNP_A- 1725025	rs10494808	196821529	196.821529	0.548	B	B	A	A	A	A	B	B	B	B
1	SNP_A- 1665029	rs6667172	197375495	197.375495	0.5	B	B	A	A	A	A	A	A	A	B
1	SNP_A- 1747494	rs832174	197990176	197.990176	0.25	A	A	B	B	B	B	B	B	B	B
1	SNP_A- 1651207	rs7555556	199822633	199.822633	0.293	A	A	A	A	A	A	A	A	A	A
1	SNP_A- 1714962	rs10494844	200501548	200.501548	0.75	A	A	A	A	A	A	A	A	B	A
1	SNP_A- 1724123	rs10494852	201189443	201.189443	0.655	B	B	B	B	B	B	A	A	A	A
1	SNP_A- 1673439	rs311286	203999303	203.999303	0.286	A	A	B	B	B	B	B	B	B	B
1	SNP_A- 1669116	rs684431	204553812	204.553812	0.381	B	B	A	A	A	A	B	B	A	A

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-6	pC-6 donor	pC-7	pC-7 donor	
1	SNP_A-1650733	rs2358452	208747444	208.747444	0.707	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1651975	rs340840	210516282	210.516282	0.393	A	A	B	B	B	B	B	B	A	A
1	SNP_A-1683565	rs10494987	211525052	211.525052	0.691	B	B	A	A	A	A	A	A	A	A
1	SNP_A-1750462	rs10495003	212237742	212.237742	0.417	A	A	B	A	B	A	A	A	A	A
1	SNP_A-1683969	rs6604634	213109650	213.10965	0.524	B	B	A	A	A	A	B	B	A	A
1	SNP_A-1731002	rs10495045	213806233	213.806233	0.714	A	A	A	B	A	B	B	B	B	B
1	SNP_A-1677675	rs618171	215537693	215.537693	0.631	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1703136	rs10495156	217494419	217.494419	0.298	B	B	B	B	B	B	A	A	A	A
1	SNP_A-1711849	rs1338077	218118775	218.118775	0.321	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1755399	rs4481859	219121051	219.121051	0.512	A	A	A	A	A	A	B	B	B	B
1	SNP_A-1739524	rs10495236	221802391	221.802391	0.691	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1710164	rs710805	225430849	225.430849	0.429	A	A	B	A	B	A	A	A	A	A
1	SNP_A-1688357	rs1998067	226545242	226.545242	0.298	B	B	A	A	A	A	B	B	B	B
1	SNP_A-1732138	rs9286801	229119361	229.119361	0.476	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1747040	rs1892298	230387334	230.387334	0.714	A	A	A	A	A	A	A	B	A	A
1	SNP_A-1717898	rs2463190	232711157	232.711157	0.441	A	A	B	A	B	A	A	A	A	A
1	SNP_A-1710935	rs819639	233219640	233.21964	0.56	A	A	A	A	A	A	B	A	A	A
1	SNP_A-1755297	rs2819774	234214896	234.214896	0.691	A	A	A	A	A	A	B	A	A	A
1	SNP_A-1677233	rs6685861	235621137	235.621137	0.357	B	B	A	A	A	A	A	B	A	A
1	SNP_A-1679485	rs732160	236262770	236.26277	0.298	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1679759	rs1039529	238918670	238.91867	0.619	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1664943	rs879725	240732087	240.732087	0.464	B	B	A	A	A	A	A	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-1724627	rs1093961	241902498	241.902498	0.415	B	A	A	B	A	A	A	A	A	A
1	SNP_A-1672603	rs3844080	243632874	243.632874	0.655	B	B	A	A	A	A	B	A	A	A
2	SNP_A-1753456	rs10519439	108913	0.108913	0.274	B	B	B	B	B	B	A	A	B	B
2	SNP_A-1746820	rs6759198	2342478	2.342478	0.56	A	A	B	B	B	B	A	A	B	B
2	SNP_A-1697325	rs2119075	4395806	4.395806	0.607	A	A	A	B	B	B	B	B	B	B
2	SNP_A-1740868	rs963964	5206872	5.206872	0.321	B	B	B	B	B	B	B	B	B	B
2	SNP_A-1677893	rs1429220	5881639	5.881639	0.369	B	B	B	B	B	B	B	B	B	B
2	SNP_A-1650909	rs6727796	7605796	7.605796	0.512	B	B	A	A	A	A	B	B	A	A
2	SNP_A-1663651	rs9287698	8437894	8.437894	0.281	B	B	B	B	B	B	A	A	A	A
2	SNP_A-1647101	rs2271333	9323848	9.323848	0.5	A	A	A	A	A	A	B	B	B	B
2	SNP_A-1717786	rs2241113	10226344	10.226344	0.31	B	B	A	A	A	A	B	A	B	B
2	SNP_A-1706150	rs1686426	10899146	10.899146	0.5	B	B	B	B	B	B	B	B	B	B
2	SNP_A-1676173	rs4669806	12151350	12.15135	0.619	B	B	A	A	A	A	A	A	A	A
2	SNP_A-1664687	rs625842	12779571	12.779571	0.583	B	B	A	A	A	A	B	B	B	B
2	SNP_A-1696327	rs7568703	15041402	15.041402	0.571	A	A	B	B	B	B	B	B	A	A
2	SNP_A-1683239	rs4668968	15835884	15.835884	0.369	B	B	B	B	B	B	B	B	B	B
2	SNP_A-1677981	rs9306902	16971747	16.971747	0.631	A	A	A	A	A	A	A	A	A	A
2	SNP_A-1714454	rs10495699	19918971	19.918971	0.56	A	A	A	A	A	A	A	A	A	A
2	SNP_A-1668860	rs10495705	20662972	20.662972	0.564	A	A	A	A	A	A	B	B	A	A
2	SNP_A-1693698	rs7594267	23344557	23.344557	0.571	A	A	B	B	B	B	B	B	A	A
2	SNP_A-1751070	rs1275963	26804398	26.804398	0.643	A	A	A	A	A	A	A	A	A	A
2	SNP_A-1684619	rs2014701	30210694	30.210694	0.631	A	A	A	A	A	A	B	A	B	B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
2	SNP_A- 1648557	rs10490360	32207919	32.207919	0.441	B	B	A	A	A	A	B	B	A	A
2	SNP_A- 1671421	rs219145	33123165	33.123165	0.634	A	A	A	A	A	A	A	A	B	B
2	SNP_A- 1696185	rs10495796	34029149	34.029149	0.274	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1642658	rs2049638	34866446	34.866446	0.738	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1696029	rs1401242	35923474	35.923474	0.417	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1748242	rs2161905	36427824	36.427824	0.286	B	B	B	B	B	B	A	A	B	B
2	SNP_A- 1660238	rs975315	38407251	38.407251	0.631	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1719460	rs9309043	39939220	39.93922	0.643	B	B	A	A	B	A	B	B	B	B
2	SNP_A- 1714203	rs2059338	41186539	41.186539	0.714	A	A	A	A	B	A	A	A	B	B
2	SNP_A- 1690204	rs10495900	43528810	43.52881	0.369	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1740164	rs4276071	44121457	44.121457	0.417	B	B	A	A	A	A	B	B	B	B
2	SNP_A- 1685265	rs6708061	44721790	44.72179	0.357	B	B	B	B	B	B	A	A	A	A
2	SNP_A- 1680505	rs6737073	45442330	45.44233	0.286	B	B	B	B	B	B	A	A	B	B
2	SNP_A- 1680749	rs935661	45967008	45.967008	0.56	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1721531	rs7589621	46494033	46.494033	0.738	B	B	A	A	A	A	A	A	A	A
2	SNP_A- 1734011	rs6544955	47235732	47.235732	0.643	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1699364	rs10495972	49412546	49.412546	0.298	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1696353	rs10495987	50064931	50.064931	0.286	A	A	A	A	A	A	B	B	B	B
2	SNP_A- 1646009	rs10490176	50979585	50.979585	0.738	B	B	A	A	A	A	A	A	A	A
2	SNP_A- 1676509	rs1160297	53148971	53.148971	0.321	A	A	B	B	B	B	B	B	A	A
2	SNP_A- 1742892	rs843622	54460133	54.460133	0.524	B	B	A	A	A	A	B	B	A	A
2	SNP_A- 1704006	rs5008666	59390639	59.390639	0.65	A	A	B	B	B	B	A	A	A	B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
2	SNP_A- 1673301	rs1517401	63452358	63.452358	0.738	A	A	B	B	B	B	A	A	A	A
2	SNP_A- 1711471	rs2581047	64219699	64.219699	0.286	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1652253	rs2971828	66466238	66.466238	0.667	B	B	A	A	A	A	A	A	A	A
2	SNP_A- 1722279	rs9309400	67746695	67.746695	0.738	A	A	A	A	A	A	B	B	A	A
2	SNP_A- 1656216	rs10496165	68531740	68.53174	0.333	B	B	B	B	B	B	B	B	A	A
2	SNP_A- 1703772	rs2312209	69633766	69.633766	0.524	B	B	A	A	A	A	B	B	B	B
2	SNP_A- 1753748	rs10489986	70719802	70.719802	0.75	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1723065	rs6724782	73591645	73.591645	0.286	A	A	B	B	B	B	A	A	B	B
2	SNP_A- 1665193	rs730148	76269470	76.26947	0.408	B	B	A	A	A	A	A	A	B	B
2	SNP_A- 1718918	rs1446707	77141310	77.14131	0.429	B	B	A	A	A	A	A	A	B	B
2	SNP_A- 1749208	rs4852483	79513076	79.513076	0.75	A	A	B	B	B	B	A	A	A	A
2	SNP_A- 1745171	rs216616	80715814	80.715814	0.298	B	B	A	A	A	A	B	B	B	B
2	SNP_A- 1750234	rs9309572	81381197	81.381197	0.321	B	B	B	B	B	B	A	A	B	A
2	SNP_A- 1728812	rs7577293	85846940	85.84694	0.274	A	A	B	B	B	B	B	B	A	A
2	SNP_A- 1676217	rs9308826	99738211	99.738211	0.738	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1655416	rs9308849	101983905	101.983905	0.714	A	A	A	A	A	A	A	A	B	A
2	SNP_A- 1655538	rs956966	103046093	103.046093	0.512	A	A	B	B	B	B	A	B	B	B
2	SNP_A- 1690274	rs1869070	106074094	106.074094	0.714	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1742362	rs1398132	106705516	106.705516	0.607	A	A	A	A	A	A	B	B	A	A
2	SNP_A- 1654768	rs826690	108705477	108.705477	0.429	B	B	A	A	A	A	A	A	A	A
2	SNP_A- 1709888	rs1469529	109207139	109.207139	0.583	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1671489	rs3961919	112959552	112.959552	0.298	B	B	A	A	A	A	A	A	A	A

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
2	SNP_A- 1720080	rs2166965	114191141	114.191141	0.679	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1712138	rs1346762	114988791	114.988791	0.72	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1752188	rs9284719	118395025	118.395025	0.595	B	B	A	A	A	A	A	A	A	A
2	SNP_A- 1685413	rs1370380	120731125	120.731125	0.286	B	B	A	A	A	A	B	B	A	A
2	SNP_A- 1721631	rs4848174	122659698	122.659698	0.655	A	A	A	A	B	B	B	B	A	A
2	SNP_A- 1707304	rs1215318	125809045	125.809045	0.536	A	A	B	B	B	B	B	B	B	B
2	SNP_A- 1673583	rs548032	127461866	127.461866	0.631	A	A	A	A	A	A	A	A	A	A
2	SNP_A- 1671177	rs2124432	128900396	128.900396	0.61	B	B	A	A	A	A	A	A	A	A
2	SNP_A- 1676259	rs10496731	135431360	135.43136	0.488	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1689435	rs10496750	137176540	137.17654	0.667	B	B	B	A	B	B	A	A	B	B
2	SNP_A- 1695208	rs10490739	137712397	137.712397	0.287	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1651715	rs3884566	139082237	139.082237	0.357	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1665733	rs3922799	139592638	139.592638	0.476	B	B	B	B	B	B	B	B	A	A
2	SNP_A- 1713885	rs838042	140153918	140.153918	0.262	A	A	B	A	B	B	B	B	B	B
2	SNP_A- 1663529	rs1518441	140908218	140.908218	0.286	A	A	B	B	B	B	B	B	B	B
2	SNP_A- 1643152	rs10496859	141502410	141.50241	0.536	B	B	A	A	A	A	A	A	B	B
2	SNP_A- 1689866	rs355562	142245134	142.245134	0.321	B	B	B	B	B	B	B	B	B	B
2	SNP_A- 1688373	rs7560400	143121832	143.121832	0.75	A	A	B	B	B	B	B	B	A	A
2	SNP_A- 1725903	rs1437717	146329325	146.329325	0.571	B	B	B	B	B	B	B	B	A	A
2	SNP_A- 1729119	rs1528842	148291308	148.291308	0.75	B	B	B	B	B	B	A	A	A	A
2	SNP_A- 1716616	rs6734792	151450390	151.45039	0.738	A	A	A	A	A	A	B	B	A	A
2	SNP_A- 1645341	rs9287956	151979514	151.979514	0.464	B	B	A	A	A	A	B	B	B	B

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
2	SNP_A-1711079	rs1370502	153235438	153.235438	0.667	B	B	B	B	B	B	A	A	A	A
2	SNP_A-1751360	rs10497129	153977886	153.977886	0.31	A	A	A	A	A	A	B	B	B	B
2	SNP_A-1682179	rs1469155	155088509	155.088509	0.726	A	A	A	A	A	A	B	B	A	A
2	SNP_A-1729675	rs6750583	159423695	159.423695	0.738	B	B	A	B	A	A	A	A	A	A
2	SNP_A-1710753	rs997163	161593412	161.593412	0.366	A	A	B	B	B	B	A	A	B	B
2	SNP_A-1657420	rs1227921	162517707	162.517707	0.512	B	B	A	B	A	A	A	A	B	B
2	SNP_A-1681353	rs1446471	164812395	164.812395	0.345	B	B	A	A	B	A	A	A	B	B
2	SNP_A-1755647	rs10497261	166152395	166.152395	0.702	A	A	A	A	A	A	A	A	B	A
2	SNP_A-1656096	rs9287874	167411538	167.411538	0.738	A	A	A	A	A	A	A	A	B	A
2	SNP_A-1673653	rs2278785	168822282	168.822282	0.381	B	B	B	B	B	B	A	A	B	B
2	SNP_A-1702574	rs830995	169955143	169.955143	0.702	A	A	A	A	A	A	A	A	A	A
2	SNP_A-1645337	rs961313	170759024	170.759024	0.274	B	B	B	B	B	B	A	A	B	B
2	SNP_A-1687817	rs731693	171622741	171.622741	0.667	A	A	A	A	A	A	A	A	B	B
2	SNP_A-1749036	rs4095835	172330518	172.330518	0.429	B	B	B	B	B	B	B	B	B	A
2	SNP_A-1683223	rs7575189	173840675	173.840675	0.512	B	B	A	B	A	A	A	A	B	B
2	SNP_A-1743510	rs2119137	174843221	174.843221	0.333	A	A	A	A	B	A	A	A	B	B
2	SNP_A-1673703	rs1993385	175563974	175.563974	0.476	A	A	A	B	A	A	A	A	A	A
2	SNP_A-1730586	rs9287989	176543248	176.543248	0.643	B	B	A	A	A	A	A	A	A	A
2	SNP_A-1676261	rs6722762	177140660	177.14066	0.345	A	A	B	B	B	B	A	A	A	A
2	SNP_A-1668972	rs10497467	177733918	177.733918	0.75	A	A	A	B	A	A	A	A	A	A
2	SNP_A-1643400	rs2008999	179796838	179.796838	0.643	A	A	B	B	B	B	A	A	A	A
2	SNP_A-1721647	rs259845	180560120	180.56012	0.75	A	A	A	A	A	A	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-6	pC-7	pC-8
2	SNP_A- 1705890	rs1110998	217169458	217.169458	0.429	B	B	A	A	A	A	B	B
2	SNP_A- 1743410	rs6719545	218277340	218.27734	0.286	B	A	B	B	B	B	B	A
2	SNP_A- 1728154	rs1344645	219363524	219.363524	0.405	A	A	B	B	B	B	A	A
2	SNP_A- 1726837	rs715345	220649461	220.649461	0.274	A	A	A	A	A	A	B	B
2	SNP_A- 1721280	rs1356399	221348562	221.348562	0.702	A	A	A	A	A	A	B	A
2	SNP_A- 1655920	rs1430234	222049201	222.049201	0.274	B	B	B	B	B	B	B	B
2	SNP_A- 1711521	rs4673013	222802583	222.802583	0.619	B	A	A	A	A	A	A	A
2	SNP_A- 1695224	rs1961637	223730613	223.730613	0.452	A	A	A	A	A	A	B	B
2	SNP_A- 1713318	rs10498158	224777152	224.777152	0.417	A	A	B	B	B	B	B	B
2	SNP_A- 1702406	rs10498171	225622115	225.622115	0.524	B	A	A	A	A	A	B	A
2	SNP_A- 1643000	rs1835533	226193946	226.193946	0.738	A	A	A	A	A	A	A	A
2	SNP_A- 1739924	rs1522804	226814661	226.814661	0.548	A	A	A	A	A	A	B	B
2	SNP_A- 1683533	rs1950134	227888457	227.888457	0.714	A	A	A	A	A	A	A	A
2	SNP_A- 1663421	rs1524023	228615089	228.615089	0.75	A	A	A	A	A	A	A	A
2	SNP_A- 1707748	rs6759815	229797926	229.797926	0.571	B	B	A	A	A	A	B	B
2	SNP_A- 1661533	rs4973304	230936568	230.936568	0.298	B	B	B	B	B	B	A	A
2	SNP_A- 1727506	rs10498257	231818543	231.818543	0.702	B	A	A	A	A	A	B	A
2	SNP_A- 1728658	rs3791711	233258388	233.258388	0.524	B	A	B	B	B	B	B	A
2	SNP_A- 1747120	rs1880747	235240125	235.240125	0.512	B	A	A	A	A	A	B	A
2	SNP_A- 1738177	rs103718	239180488	239.180488	0.441	A	A	A	A	A	A	B	B
3	SNP_A- 1675236	rs1516342	147906	0.147906	0.262	A	A	B	B	B	B	A	A
3	SNP_A- 1754907	rs10510204	981912	0.981912	0.405	A	A	A	A	A	A	A	A

[illegible]

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

[illegible]

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
3	SNP_A-1642486	rs9309840	80029943	80.029943	0.588	B	B	B	B	B	B	B	A	B	B
3	SNP_A-1685115	rs2639611	81623522	81.623522	0.274	B	B	B	B	B	B	B	B	A	A
3	SNP_A-1642250	rs9309888	82418655	82.418655	0.262	B	A	B	B	B	B	B	B	A	A
3	SNP_A-1732971	rs10511085	85614577	85.614577	0.619	B	A	B	A	B	A	A	A	A	A
3	SNP_A-1731608	rs1509783	87634505	87.634505	0.476	B	B	B	B	B	B	A	A	B	B
3	SNP_A-1721601	rs9310061	88146455	88.146455	0.631	A	A	B	B	B	A	A	A	A	A
3	SNP_A-1715294	rs724972	89664098	89.664098	0.607	A	A	A	A	A	A	A	A	A	A
3	SNP_A-1648583	rs10511152	96638708	96.638708	0.381	B	B	A	A	A	A	A	A	B	A
3	SNP_A-1701406	rs3856571	99031739	99.031739	0.298	B	A	B	B	B	B	B	B	B	B
3	SNP_A-1643841	rs10511169	100116062	100.116062	0.691	A	A	A	A	A	A	A	A	B	A
3	SNP_A-1697988	rs2700633	100643241	100.643241	0.643	A	A	A	A	A	A	A	A	B	A
3	SNP_A-1740468	rs10511183	102046105	102.046105	0.738	A	A	A	A	A	A	A	A	A	A
3	SNP_A-1746982	rs974059	103277828	103.277828	0.25	B	B	B	B	B	B	A	A	B	A
3	SNP_A-1687227	rs1391423	103923668	103.923668	0.732	A	A	A	A	A	A	A	A	A	A
3	SNP_A-1677819	rs10511221	105099054	105.099054	0.726	B	A	A	A	A	A	A	A	A	A
3	SNP_A-1663937	rs6783422	106031580	106.03158	0.393	A	A	A	A	A	A	B	B	A	A
3	SNP_A-1674588	rs10511243	106653352	106.653352	0.667	A	A	A	A	A	A	B	B	A	A
3	SNP_A-1652015	rs2222039	108202685	108.202685	0.691	B	A	A	A	A	A	A	A	A	A
3	SNP_A-1722407	rs1525873	111232702	111.232702	0.702	B	A	B	B	B	B	A	A	A	A
3	SNP_A-1674512	rs1512514	111766406	111.766406	0.488	B	A	A	A	A	A	A	A	A	A
3	SNP_A-1747616	rs1797626	114308943	114.308943	0.702	A	A	B	B	A	A	A	A	A	A
3	SNP_A-1668954	rs1553209	116705663	116.705663	0.476	B	A	A	A	A	A	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
3	SNP_A-1674292	rs7621196	117804184	117.804184	0.321	B	B	A	A	A	A	B	A	A	A
3	SNP_A-1643903	rs1218621	118459636	118.459636	0.31	A	A	B	B	B	B	B	B	B	B
3	SNP_A-1728638	rs950649	121567065	121.567065	0.691	B	B	A	A	A	A	A	A	A	A
3	SNP_A-1730195	rs2126140	122627958	122.627958	0.5	B	B	B	A	B	B	B	B	A	A
3	SNP_A-1741126	rs10511409	123610479	123.610479	0.738	B	B	A	A	A	A	B	B	B	B
3	SNP_A-1739520	rs1373606	125496637	125.496637	0.342	A	A	B	B	B	B	A	A	A	A
3	SNP_A-1727336	rs1374804	127391196	127.391196	0.524	A	B	B	A	B	B	B	B	A	A
3	SNP_A-1683659	rs2718880	132343455	132.343455	0.75	A	A	A	A	A	A	A	A	A	A
3	SNP_A-1747192	rs1553975	132999274	132.999274	0.369	B	B	A	A	A	A	A	A	B	B
3	SNP_A-1744702	rs2310229	133541978	133.541978	0.691	A	A	A	A	A	A	A	A	A	A
3	SNP_A-1730051	rs711923	136539253	136.539253	0.744	A	A	A	A	A	A	A	A	A	A
3	SNP_A-1654278	rs838623	144671624	144.671624	0.619	A	A	A	A	A	A	A	A	B	A
3	SNP_A-1730514	rs4610179	146387799	146.387799	0.726	B	B	A	A	A	A	A	A	A	A
3	SNP_A-1700733	rs4592991	147111601	147.111601	0.393	B	B	B	B	B	B	A	A	B	B
3	SNP_A-1744174	rs7645488	149410366	149.410366	0.31	B	B	B	B	B	B	B	B	B	B
3	SNP_A-1718574	rs2130319	150976344	150.976344	0.333	A	B	B	B	B	B	A	A	B	B
3	SNP_A-1718772	rs7648424	151906089	151.906089	0.488	B	B	B	B	B	B	A	B	B	B
3	SNP_A-1663723	rs10513399	152600180	152.60018	0.488	B	B	B	B	B	B	B	B	B	B
3	SNP_A-1746211	rs2418925	155234610	155.23461	0.524	A	A	B	B	A	B	B	B	B	B
3	SNP_A-1658251	rs6772323	157710345	157.710345	0.667	A	A	A	A	A	A	A	A	A	A
3	SNP_A-1736960	rs4679851	160261035	160.261035	0.274	A	B	B	B	B	B	B	B	B	B
3	SNP_A-1716368	rs10513549	161237209	161.237209	0.25	B	B	A	A	A	A	B	A	A	A

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

[illegible]

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-6	pC-6 donor	pC-7	pC-7 donor
4	SNP_A-1708293	rs10517094	44153139	44.153139	0.31	B	B	B	B	B	B	B	B	B
4	SNP_A-1672145	rs10517121	44712712	44.712712	0.583	A	A	A	A	A	A	A	B	A
4	SNP_A-1742914	rs1552419	45366813	45.366813	0.583	A	A	A	A	A	A	B	A	A
4	SNP_A-1741538	rs279842	46181884	46.181884	0.439	B	B	B	B	B	B	B	A	A
4	SNP_A-1726797	rs3934674	46854066	46.854066	0.305	B	B	B	B	B	B	B	B	B
4	SNP_A-1734487	rs6447614	47908885	47.908885	0.549	A	A	A	A	A	A	A	B	A
4	SNP_A-1659623	rs6850277	54268853	54.268853	0.667	B	B	A	A	A	A	A	B	A
4	SNP_A-1724073	rs2726610	55528245	55.528245	0.548	B	B	B	B	B	B	B	A	A
4	SNP_A-1643184	rs4580704	56167635	56.167635	0.643	A	A	A	A	A	A	A	A	A
4	SNP_A-1647321	rs10517400	58338522	58.338522	0.679	A	A	B	B	A	A	A	B	B
4	SNP_A-1685901	rs10517453	60065841	60.065841	0.679	A	A	B	B	B	B	B	B	B
4	SNP_A-1660836	rs2129274	61712878	61.712878	0.613	B	B	B	B	B	B	B	B	A
4	SNP_A-1712860	rs2345043	62476674	62.476674	0.619	A	A	A	A	A	A	B	B	B
4	SNP_A-1706808	rs2199219	63012534	63.012534	0.321	A	A	A	A	A	A	B	B	A
4	SNP_A-1657186	rs7674285	65578799	65.578799	0.536	B	B	B	B	B	B	A	A	A
4	SNP_A-1701798	rs1450036	67486005	67.486005	0.619	A	A	A	A	B	B	A	A	A
4	SNP_A-1734479	rs2736466	70507268	70.507268	0.679	A	A	A	A	A	A	A	A	A
4	SNP_A-1645045	rs3775745	71293834	71.293834	0.536	B	B	A	A	A	A	A	A	A
4	SNP_A-1741102	rs7678694	75663264	75.663264	0.476	B	B	A	A	A	A	B	B	A
4	SNP_A-1670999	rs925454	77604654	77.604654	0.595	A	A	A	A	B	B	A	A	B
4	SNP_A-1738063	rs2703134	78171011	78.171011	0.691	A	A	A	A	A	A	A	A	A
4	SNP_A-1654306	rs10518188	79483184	79.483184	0.405	A	A	B	B	B	B	B	A	B

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
4	SNP_A-1661108	rs2119421	80807501	80.807501	0.714	A	A	A	A	A	A	A	A	B	B
4	SNP_A-1703940	rs9307787	83047673	83.047673	0.75	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1650367	rs6813014	84235884	84.235884	0.548	B	B	A	A	B	B	B	B	A	A
4	SNP_A-1752998	rs10516708	85194717	85.194717	0.643	A	A	A	A	A	A	A	A	B	B
4	SNP_A-1669642	rs10516739	86522131	86.522131	0.655	B	B	B	B	A	B	A	A	B	B
4	SNP_A-1725569	rs10516760	87083328	87.083328	0.25	B	B	B	B	B	B	A	A	A	A
4	SNP_A-1732366	rs4693803	88425710	88.42571	0.5	A	A	A	A	B	B	A	A	B	B
4	SNP_A-1657663	rs10516796	89213912	89.213912	0.634	A	A	A	A	A	A	B	B	B	B
4	SNP_A-1718322	rs1903002	90098072	90.098072	0.464	B	B	A	A	B	A	A	A	A	A
4	SNP_A-1659867	rs7693500	90643667	90.643667	0.691	A	A	A	A	A	A	A	A	B	B
4	SNP_A-1705800	rs4694023	91613152	91.613152	0.393	B	B	B	B	B	B	A	A	B	B
4	SNP_A-1757446	rs7696847	92155216	92.155216	0.714	A	A	B	B	A	B	A	B	B	B
4	SNP_A-1749382	rs6827937	94157783	94.157783	0.452	B	B	B	B	B	B	A	B	B	B
4	SNP_A-1727842	rs10516919	94713877	94.713877	0.667	B	B	A	A	A	A	A	A	A	A
4	SNP_A-1745861	rs1048627	95944765	95.944765	0.595	A	A	A	A	B	B	A	A	A	A
4	SNP_A-1683945	rs1384869	96613355	96.613355	0.274	B	B	A	A	A	A	B	B	B	B
4	SNP_A-1756011	rs6853079	99800789	99.800789	0.286	B	B	B	B	B	B	B	B	A	A
4	SNP_A-1703546	rs1230164	100343201	100.343201	0.274	B	B	B	B	A	B	B	B	B	B
4	SNP_A-1740940	rs238486	103377982	103.377982	0.595	A	A	A	A	B	B	A	A	B	B
4	SNP_A-1684917	rs227284	103964838	103.964838	0.655	A	A	A	A	B	B	B	B	B	B
4	SNP_A-1753948	rs445761	104804695	104.804695	0.679	B	B	A	A	A	A	A	A	A	A
4	SNP_A-1747884	rs2866685	105649408	105.649408	0.5	B	B	A	A	B	B	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
4	SNP_A-1720092	rs1873361	106282703	106.282703	0.345	B	B	A	A	A	A	B	B	B	B
4	SNP_A-1721929	rs715706	106873632	106.873632	0.286	B	B	B	B	B	B	B	B	A	A
4	SNP_A-1662125	rs1468221	108745388	108.745388	0.31	A	A	B	B	B	B	A	A	B	B
4	SNP_A-1642856	rs7654940	110143969	110.143969	0.524	B	B	B	B	A	B	B	B	B	B
4	SNP_A-1686749	rs6841595	113711446	113.711446	0.317	B	B	B	B	B	B	B	B	A	A
4	SNP_A-1736814	rs10516593	114436416	114.436416	0.524	B	B	B	B	A	A	A	A	A	A
4	SNP_A-1732667	rs998359	116228635	116.228635	0.441	B	B	B	B	B	B	B	B	A	A
4	SNP_A-1671469	rs292910	117406405	117.406405	0.607	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1696003	rs2125710	118964366	118.964366	0.25	B	B	B	B	B	B	B	B	A	A
4	SNP_A-1695754	rs10518293	119688966	119.688966	0.691	A	A	B	B	B	B	A	A	A	A
4	SNP_A-1745189	rs10518336	120880537	120.880537	0.536	A	A	B	B	A	A	B	B	A	A
4	SNP_A-1648947	rs2036696	121573324	121.573324	0.667	A	A	B	B	B	B	B	B	A	A
4	SNP_A-1702984	rs998327	122441717	122.441717	0.726	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1733111	rs4833836	123858274	123.858274	0.381	B	B	B	B	B	B	A	A	B	B
4	SNP_A-1643743	rs444646	124370464	124.370464	0.548	A	A	A	A	A	A	B	B	A	A
4	SNP_A-1746251	rs10518307	125084153	125.084153	0.262	B	B	B	B	B	B	B	B	B	B
4	SNP_A-1648121	rs7682791	125875709	125.875709	0.631	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1699868	rs953211	126708654	126.708654	0.488	B	B	A	A	A	A	B	B	A	A
4	SNP_A-1706772	rs4834083	127331109	127.331109	0.726	A	A	B	B	A	A	A	A	A	A
4	SNP_A-1653649	rs318510	130173248	130.173248	0.571	A	A	B	B	B	B	A	A	A	A
4	SNP_A-1655974	rs2969001	131140397	131.140397	0.643	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1694056	rs6846560	131988611	131.988611	0.357	B	B	B	B	B	B	A	A	B	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
4	SNP_A-1719820	rs10518609	133609659	133.609659	0.658	A	A	B	B	B	B	A	A	A	A
4	SNP_A-1721507	rs9307688	134441091	134.441091	0.726	B	B	A	A	A	A	A	A	B	A
4	SNP_A-1716218	rs9307703	135374277	135.374277	0.321	B	B	B	B	B	B	A	A	B	B
4	SNP_A-1719154	rs6535037	135968531	135.968531	0.691	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1718316	rs10519369	137048788	137.048788	0.619	B	B	A	B	B	B	B	B	A	B
4	SNP_A-1643751	rs7692053	138020209	138.020209	0.631	A	A	B	B	B	B	A	A	A	A
4	SNP_A-1712218	rs1376088	139852726	139.852726	0.357	B	B	B	B	B	B	A	A	B	B
4	SNP_A-1688437	rs10519540	141950175	141.950175	0.429	A	A	B	B	B	B	A	A	A	A
4	SNP_A-1669152	rs2062597	143153292	143.153292	0.61	A	A	A	A	A	A	B	B	A	A
4	SNP_A-1651007	rs331963	144031456	144.031456	0.369	A	A	B	B	B	B	A	A	B	B
4	SNP_A-1705078	rs789351	146225975	146.225975	0.679	B	B	A	A	A	A	A	A	A	A
4	SNP_A-1700284	rs10519824	148107681	148.107681	0.658	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1655082	rs6810951	149441717	149.441717	0.333	B	B	B	B	B	B	B	B	B	B
4	SNP_A-1650743	rs10489053	150276232	150.276232	0.643	A	A	A	A	A	A	A	A	A	A
4	SNP_A-1695870	rs991529	151852936	151.852936	0.488	B	B	B	B	B	B	A	A	A	A
4	SNP_A-1750768	rs361101	153131731	153.131731	0.631	B	B	B	B	A	B	A	A	B	B
4	SNP_A-1694614	rs7662116	154375569	154.375569	0.691	A	A	A	A	A	A	B	A	A	A
4	SNP_A-1651497	rs1125228	155126657	155.126657	0.738	A	A	B	B	B	B	B	B	B	B
4	SNP_A-1732214	rs6536240	158751762	158.751762	0.381	A	A	B	B	B	B	A	A	B	A
4	SNP_A-1721547	rs7678486	159498426	159.498426	0.25	B	B	B	B	B	B	B	B	A	A
4	SNP_A-1695472	rs7665879	160305968	160.305968	0.31	A	A	B	B	B	B	A	A	B	A
4	SNP_A-1653797	rs6856295	160845965	160.845965	0.595	B	B	B	B	A	B	B	B	A	A

[illegible]

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
5	SNP_A-1689409	rs10512651	1816661	1.816661	0.405	B	B	A	A	B	A	A	A	A	A
5	SNP_A-1642488	rs1445862	3675257	3.675257	0.25	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1651781	rs272190	5103830	5.10383	0.25	A	A	A	A	A	A	A	A	B	B
5	SNP_A-1663379	rs2560294	5619114	5.619114	0.726	A	A	A	A	A	A	A	B	B	B
5	SNP_A-1643560	rs10512858	6486915	6.486915	0.613	B	B	A	A	A	A	A	A	A	A
5	SNP_A-1651637	rs4629562	7847326	7.847326	0.619	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1693207	rs9313236	8348429	8.348429	0.25	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1744546	rs12515692	9883408	9.883408	0.357	A	A	B	B	B	B	B	B	A	A
5	SNP_A-1721268	rs2937513	11007551	11.007551	0.619	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1702624	rs173671	12217918	12.217918	0.476	A	A	A	B	A	A	A	A	A	A
5	SNP_A-1695478	rs1476154	13000353	13.000353	0.691	B	B	A	A	A	A	A	A	A	A
5	SNP_A-1757294	rs3734108	13806984	13.806984	0.56	A	A	A	B	A	A	A	A	A	A
5	SNP_A-1696687	rs2938832	15817866	15.817866	0.25	A	A	B	B	B	B	A	A	A	A
5	SNP_A-1713461	rs585991	17246633	17.246633	0.274	B	B	A	A	A	A	B	B	B	B
5	SNP_A-1661473	rs1394215	18359538	18.359538	0.548	B	B	A	A	A	A	A	B	B	A
5	SNP_A-1646961	rs2942296	19421031	19.421031	0.429	B	B	B	A	B	B	B	B	A	A
5	SNP_A-1698916	rs248202	21159137	21.159137	0.274	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1757332	rs7705523	23659025	23.659025	0.714	A	A	A	B	A	A	A	A	A	A
5	SNP_A-1672683	rs1995599	24552793	24.552793	0.548	A	A	A	B	A	A	B	B	A	A
5	SNP_A-1660984	rs9293241	26606178	26.606178	0.56	B	B	A	A	A	A	A	B	B	B
5	SNP_A-1704664	rs921469	29989233	29.989233	0.583	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1644843	rs1921111	30906615	30.906615	0.405	B	B	B	B	B	B	A	A	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
5	SNP_A-1678791	rs893551	33493407	33.493407	0.607	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1724049	rs716302	35846025	35.846025	0.357	A	A	A	A	A	A	A	A	B	B
5	SNP_A-1703432	rs159751	37035755	37.035755	0.464	A	A	B	B	B	B	B	B	A	A
5	SNP_A-1645375	rs4072686	38003109	38.003109	0.405	A	A	B	B	B	B	B	B	B	A
5	SNP_A-1719252	rs675502	39878266	39.878266	0.679	A	A	B	B	A	A	A	A	A	A
5	SNP_A-1685613	rs1697938	40890439	40.890439	0.441	A	A	A	A	A	A	B	B	A	A
5	SNP_A-1731232	rs276278	42016012	42.016012	0.298	B	B	B	B	B	B	B	B	B	A
5	SNP_A-1694450	rs1072746	43646445	43.646445	0.441	A	A	B	B	B	B	B	A	A	A
5	SNP_A-1675759	rs2404958	50098792	50.098792	0.619	A	A	A	A	B	A	A	A	A	A
5	SNP_A-1723309	rs9283709	51510492	51.510492	0.595	B	A	B	B	A	A	A	A	B	B
5	SNP_A-1728968	rs10512988	52085030	52.08503	0.357	B	A	A	A	A	A	B	A	A	A
5	SNP_A-1746984	rs9292039	53454075	53.454075	0.268	B	B	B	B	B	B	A	A	B	A
5	SNP_A-1697874	rs6450270	54287290	54.28729	0.714	A	A	A	A	A	A	B	A	A	A
5	SNP_A-1684501	rs889310	56000924	56.000924	0.476	B	B	A	A	A	A	B	A	A	A
5	SNP_A-1673657	rs2539731	57109292	57.109292	0.475	B	B	B	B	B	B	A	A	B	B
5	SNP_A-1716782	rs9292159	57677129	57.677129	0.31	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1724117	rs9292180	58192447	58.192447	0.25	B	B	A	A	A	A	B	B	A	A
5	SNP_A-1755537	rs10514860	58859777	58.859777	0.726	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1653871	rs6859376	59471964	59.471964	0.56	A	A	B	B	B	B	A	A	B	B
5	SNP_A-1653455	rs159375	60469024	60.469024	0.691	A	A	A	A	A	A	B	B	B	A
5	SNP_A-1682537	rs356598	63380121	63.380121	0.631	B	B	A	A	A	A	B	B	B	B
5	SNP_A-1755307	rs7704890	66151331	66.151331	0.357	A	A	B	B	B	B	B	B	A	A

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
5	SNP_A-1671457	rs6858907	67817289	67.817289	0.417	B	B	A	B	A	A	B	B	B	B
5	SNP_A-1654744	rs1600073	74472493	74.472493	0.61	B	B	A	B	A	A	A	A	A	A
5	SNP_A-1653531	rs10514059	75460983	75.460983	0.658	A	A	A	A	A	A	A	A	B	B
5	SNP_A-1720510	rs2972341	76504599	76.504599	0.536	B	B	A	A	A	A	B	B	A	B
5	SNP_A-1682839	rs949645	78478278	78.478278	0.564	A	A	B	B	B	B	B	B	A	B
5	SNP_A-1747624	rs264986	79206180	79.20618	0.31	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1730614	rs964102	80843469	80.843469	0.679	A	A	A	A	A	A	A	A	B	B
5	SNP_A-1732246	rs10514249	82540612	82.540612	0.56	A	A	A	A	A	A	B	A	B	B
5	SNP_A-1729977	rs4639197	83381853	83.381853	0.25	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1742238	rs323744	86861304	86.861304	0.5	B	B	A	A	A	A	B	A	A	A
5	SNP_A-1751644	rs819344	89093506	89.093506	0.463	A	A	B	B	A	B	B	B	B	B
5	SNP_A-1690642	rs2935499	89626568	89.626568	0.548	A	A	B	B	B	B	A	B	B	B
5	SNP_A-1744488	rs52308	90817903	90.817903	0.512	B	B	A	A	A	A	B	B	A	A
5	SNP_A-1670907	rs248339	95229134	95.229134	0.643	A	A	B	B	B	B	B	B	B	B
5	SNP_A-1729028	rs31248	96040439	96.040439	0.275	B	B	B	B	A	B	A	B	B	B
5	SNP_A-1657092	rs10515273	97821155	97.821155	0.75	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1643346	rs2887526	98552712	98.552712	0.667	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1722905	rs2369754	99184261	99.184261	0.488	A	A	B	B	A	B	A	B	B	B
5	SNP_A-1664073	rs1477625	101358141	101.358141	0.271	B	B	B	B	B	B	B	B	B	B
5	SNP_A-1742802	rs9327861	101895776	101.895776	0.655	B	B	A	A	A	A	B	A	A	A
5	SNP_A-1745283	rs39984	102625191	102.625191	0.31	A	A	B	B	B	B	A	A	B	B
5	SNP_A-1734843	rs10515355	103975436	103.975436	0.738	A	A	A	A	A	A	B	B	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
5	SNP_A-1730932	rs4957531	106511277	106.511277	0.463	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1757418	rs245243	109258634	109.258634	0.714	A	A	A	A	B	A	A	A	A	A
5	SNP_A-1646761	rs10491424	110481705	110.481705	0.56	B	B	A	A	B	A	A	A	A	A
5	SNP_A-1691719	rs1213404	111130917	111.130917	0.35	B	B	B	B	B	B	B	A	B	B
5	SNP_A-1747768	rs971517	112050154	112.050154	0.476	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1726679	rs10519378	113555966	113.555966	0.738	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1738592	rs2546480	114841054	114.841054	0.452	A	A	B	B	B	B	B	B	A	A
5	SNP_A-1708792	rs2662458	115402242	115.402242	0.655	B	B	B	B	B	B	A	A	B	B
5	SNP_A-1720512	rs1027292	116078486	116.078486	0.548	B	B	A	A	A	A	A	A	A	A
5	SNP_A-1701708	rs1504978	118638459	118.638459	0.655	B	B	B	B	A	B	A	A	A	A
5	SNP_A-1689317	rs10519615	119189176	119.189176	0.643	B	B	B	B	B	B	A	A	A	A
5	SNP_A-1751260	rs6897147	119692229	119.692229	0.691	A	A	A	A	A	A	B	B	A	A
5	SNP_A-1654688	rs161011	123703275	123.703275	0.286	A	A	B	B	B	B	B	B	B	B
5	SNP_A-1699578	rs7716491	124265772	124.265772	0.738	B	B	A	A	A	A	A	B	B	B
5	SNP_A-1703238	rs1826263	124839517	124.839517	0.571	B	B	A	A	A	A	A	A	A	A
5	SNP_A-1715428	rs964185	125631547	125.631547	0.345	A	A	B	B	B	B	B	B	B	B
5	SNP_A-1751090	rs1345663	126678081	126.678081	0.31	B	B	A	A	A	A	A	A	A	A
5	SNP_A-1694738	rs9327460	127338947	127.338947	0.524	A	A	A	A	A	A	A	B	B	B
5	SNP_A-1658519	rs1181962	128414700	128.4147	0.333	B	B	A	A	A	A	A	A	B	B
5	SNP_A-1677377	rs25810	129015788	129.015788	0.595	A	A	A	A	A	A	A	A	A	A
5	SNP_A-1673843	rs10520083	129967905	129.967905	0.345	A	A	B	B	B	B	B	B	B	B
5	SNP_A-1705560	rs9327673	133230970	133.23097	0.286	B	B	B	B	B	B	A	A	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
5	SNP_A-1647073	rs411005	160517741	160.517741	0.476	A B	A B	A A	A A	A A	A A	B B	B B	A A	A A
5	SNP_A-1724235	rs2170901	161840216	161.840216	0.429	B B	B B	A B	A B	A B	A B	B B	B B	A A	A A
5	SNP_A-1754048	rs300238	162682948	162.682948	0.452	A B	A B	A B	A B	A B	A B	A A	A A	A B	A B
5	SNP_A-1745987	rs158295	163217790	163.21779	0.25	B B	B B	B B	B B	B B	B B	A A	A B	B B	B B
5	SNP_A-1720394	rs6869856	166017651	166.017651	0.412	A A	A A	A A	A A	A A	A A	A A	A A	A A	A A
5	SNP_A-1687531	rs1911557	169681232	169.681232	0.25	B B	B B	B B	B B	B B	B B	A B	A B	A B	A B
5	SNP_A-1749300	rs10516089	171083836	171.083836	0.726	A B	A B	A A	A A	A A	A A	A B	A B	A A	A A
5	SNP_A-1665975	rs1909706	173644330	173.64433	0.707	A A	A A	A A	A A	A A	A A	A A	A A	A A	A A
5	SNP_A-1724885	rs965017	174509108	174.509108	0.548	A B	A B	A B	A B	B B	A B	A A	A A	A A	A A
5	SNP_A-1644515	rs1071882	178068646	178.068646	0.702	A A	A A	A B	A B	A A	A B	A A	A A	A A	A A
5	SNP_A-1748220	rs2892344	180297919	180.297919	0.536	A B	A B	B B	B B	B B	B B	B B	B B	A B	A B
6	SNP_A-1732501	rs3765437	508013	0.508013	0.536	A A	A A	B B	B B	B B	B B	B B	B B	A A	A A
6	SNP_A-1728682	rs238073	1192930	1.19293	0.381	A A	A A	B B	B B	B B	B B	A A	A A	A B	A B
6	SNP_A-1747718	rs6919059	1729095	1.729095	0.691	A A	A B	A A	A A	A A	A A	A B	A B	A A	A A
6	SNP_A-1723553	rs2326366	3923256	3.923256	0.417	B B	A B	A A	A B	A A	A B	B B	B B	A B	A B
6	SNP_A-1747058	rs10484314	5593086	5.593086	0.333	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
6	SNP_A-1673883	rs3851514	6219569	6.219569	0.75	B B	B B	B B	A B	B B	A B	A B	A B	A A	A A
6	SNP_A-1737825	rs267202	7799235	7.799235	0.619	A B	A B	A A	A B	A A	A B	A A	A A	A A	A A
6	SNP_A-1680945	rs1543731	8355978	8.355978	0.346	A A	A A	A A	A B	A A	A B	B B	B B	B B	B B
6	SNP_A-1702006	rs9296701	9687981	9.687981	0.536	A B	A B	B B	B B	B B	B B	B B	B B	A B	A B
6	SNP_A-1715186	rs4512212	10379387	10.379387	0.464	B B	B B	A A	A B	A A	A B	B B	B B	B B	B B
6	SNP_A-1680453	rs2182335	11324963	11.324963	0.714	A A	A A	A A	A B	A A	A B	B B	B B	A A	A A

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Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
6	SNP_A-1658085	rs10484664	51124482	51.124482	0.256	B	B	B	B	B	B	B	B	B	A
6	SNP_A-1723157	rs913098	51750772	51.750772	0.667	A	A	A	A	A	A	A	A	A	A
6	SNP_A-1726221	rs509946	52411949	52.411949	0.369	B	B	A	B	A	B	B	B	B	B
6	SNP_A-1717116	rs10484785	53457958	53.457958	0.476	B	A	B	B	B	B	A	A	B	B
6	SNP_A-1717814	rs1393779	54808762	54.808762	0.464	A	A	A	A	A	A	B	B	B	B
6	SNP_A-1693069	rs1925179	56129171	56.129171	0.655	A	A	A	A	A	A	A	A	A	A
6	SNP_A-1664153	rs6934928	58422082	58.422082	0.714	B	A	A	A	A	A	B	A	A	A
6	SNP_A-1682123	rs565795	62597708	62.597708	0.61	A	A	A	A	A	A	B	B	A	A
6	SNP_A-1692597	rs9293849	63255396	63.255396	0.333	B	B	B	A	B	A	A	A	B	A
6	SNP_A-1729072	rs9294630	65677619	65.677619	0.702	A	A	A	A	A	A	A	A	A	A
6	SNP_A-1685655	rs2502270	67886666	67.886666	0.488	A	A	A	A	A	A	B	B	A	A
6	SNP_A-1744006	rs4707479	68787830	68.78783	0.286	A	A	B	B	B	B	B	B	B	A
6	SNP_A-1683273	rs579588	69639537	69.639537	0.714	A	A	B	A	B	B	B	B	B	B
6	SNP_A-1659091	rs591809	72270133	72.270133	0.524	B	B	B	B	B	B	B	B	A	A
6	SNP_A-1660794	rs959369	74620278	74.620278	0.607	A	A	A	A	A	A	A	A	A	A
6	SNP_A-1656648	rs1575856	76774483	76.774483	0.262	B	B	B	B	B	B	B	B	B	A
6	SNP_A-1675424	rs1457947	77533004	77.533004	0.619	A	A	A	A	A	A	B	B	A	A
6	SNP_A-1657250	rs236225	79172654	79.172654	0.744	A	A	A	A	A	A	A	A	A	A
6	SNP_A-1646741	rs239500	80761863	80.761863	0.595	B	B	A	A	A	A	B	B	B	B
6	SNP_A-1733643	rs310387	81832380	81.83238	0.56	A	A	A	A	A	A	A	A	B	A
6	SNP_A-1684117	rs2323435	82365338	82.365338	0.417	B	B	B	B	B	B	B	B	B	B
6	SNP_A-1749278	rs958568	83211843	83.211843	0.417	B	B	B	B	B	B	A	A	B	A

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

[illegible]

[illegible]

[illegible]

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
7	SNP_A-1656052	rs7785008	10921568	10.921568	0.452	A B	A B	B B	B B	B B	B B	A A	A A	A B	A B
7	SNP_A-1678735	rs10270630	11629477	11.629477	0.738	B B	B B	A B	A B	B B	B B	A A	A A	A B	A B
7	SNP_A-1672885	rs1036667	12197823	12.197823	0.488	B B	B B	A B	A B	A A	A B	A A	A A	A A	A A
7	SNP_A-1707354	rs2214867	13507965	13.507965	0.417	A A	A A	A A	A A	A A	A A	B B	B B	A B	A B
7	SNP_A-1724539	rs7793372	14320689	14.320689	0.619	B B	B B	B B	B B	B B	B B	A A	A A	A B	A B
7	SNP_A-1756798	rs1527203	15931001	15.931001	0.643	A A	A A	A B	A B	A B	A B	A A	A A	A A	A A
7	SNP_A-1755023	rs706057	16577230	16.57723	0.56	A B	A B	A B	A B	A B	A B	A B	A B	A B	A B
7	SNP_A-1647845	rs4721619	17291814	17.291814	0.667	A B	A B	A A	A A	A A	A A	A B	A B	A A	A A
7	SNP_A-1693824	rs2731551	18050825	18.050825	0.25	B B	B B	A B	A B	A B	A B	B B	B B	B B	B B
7	SNP_A-1724213	rs10486334	18974842	18.974842	0.726	B B	B B	A B	A B	A B	A B	B B	B B	A A	A A
7	SNP_A-1716746	rs2248634	21065118	21.065118	0.262	B B	B B	B B	B B	B B	B B	A B	A B	B B	B B
7	SNP_A-1706218	rs7781044	21636203	21.636203	0.61	A A	A A	A A	A A	A A	A A	A B	A B	A B	A B
7	SNP_A-1718088	rs2286497	22701238	22.701238	0.305	B B	B B	A B	A B	A B	A B	A B	A B	A B	A B
7	SNP_A-1755947	rs2521642	24200036	24.200036	0.31	B B	B B	B B	B B	B B	B B	A B	A B	B B	B B
7	SNP_A-1751950	rs4275130	26366016	26.366016	0.75	A B	A B	A A	A A	A A	A A	A A	A A	A A	A A
7	SNP_A-1725907	rs6953785	27237607	27.237607	0.536	A B	A B	A B	B B	A B	A B	A B	A B	A A	A A
7	SNP_A-1729503	rs4498447	28177012	28.177012	0.524	B B	B B	A B	B B	A B	A B	B B	B B	A B	A B
7	SNP_A-1663287	rs1859681	28699408	28.699408	0.275	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
7	SNP_A-1728544	rs1476991	29293282	29.293282	0.571	A A	A A	A A	A A	A A	A A	A A	A A	A B	A B
7	SNP_A-1718026	rs997349	29955684	29.955684	0.357	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
7	SNP_A-1695134	rs10487729	31345524	31.345524	0.726	A A	A A	A A	A A	A A	A A	A B	A B	A B	A B
7	SNP_A-1694740	rs215675	32156237	32.156237	0.286	A A	A B	B B	B B	B B	B B	B B	B B	A B	A B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
7	SNP_A-1717858	rs10254116	33010729	33.010729	0.631	B	A	A	A	A	A	A	A	A	A
7	SNP_A-1678175	rs10486619	33600838	33.600838	0.262	B	B	B	B	B	B	B	B	A	A
7	SNP_A-1749566	rs741202	35093154	35.093154	0.262	B	B	B	B	A	A	B	B	A	A
7	SNP_A-1731924	rs4720228	36725169	36.725169	0.476	B	A	B	B	B	B	B	B	B	B
7	SNP_A-1671783	rs2893552	37928803	37.928803	0.679	A	A	A	A	A	A	B	B	A	A
7	SNP_A-1730217	rs4723791	38613746	38.613746	0.56	B	A	A	A	A	A	A	A	A	A
7	SNP_A-1669882	rs10486802	39497008	39.497008	0.571	A	A	B	B	B	B	A	A	A	A
7	SNP_A-1721388	rs7807596	40599281	40.599281	0.417	A	A	B	B	A	A	B	B	A	A
7	SNP_A-1750290	rs384469	41099793	41.099793	0.702	A	A	A	A	A	A	B	B	A	A
7	SNP_A-1695614	rs721273	42867596	42.867596	0.702	A	A	B	B	B	B	A	A	A	A
7	SNP_A-1736506	rs2330918	43444472	43.444472	0.75	A	B	A	A	A	A	A	A	A	A
7	SNP_A-1732094	rs10253161	46769632	46.769632	0.714	A	A	A	A	A	A	A	A	B	A
7	SNP_A-1710294	rs7357251	47841498	47.841498	0.417	A	A	A	A	A	A	B	B	B	B
7	SNP_A-1669906	rs3923511	48463293	48.463293	0.688	A	A	A	A	A	A	A	B	B	B
7	SNP_A-1748806	rs716719	50102978	50.102978	0.262	A	A	B	B	B	B	B	B	B	B
7	SNP_A-1646085	rs2159809	52287324	52.287324	0.39	A	A	B	B	B	B	B	B	B	B
7	SNP_A-1655668	rs6955211	63316490	63.31649	0.464	B	A	A	A	A	A	A	A	B	B
7	SNP_A-1695272	rs9638255	67214110	67.21411	0.655	A	A	A	A	A	A	A	A	A	A
7	SNP_A-1673105	rs1699443	68224124	68.224124	0.583	A	A	A	A	A	A	A	A	B	A
7	SNP_A-1667673	rs10499812	69098641	69.098641	0.333	A	B	B	B	B	B	B	B	B	B
7	SNP_A-1757146	rs6976144	77019455	77.019455	0.5	A	A	B	B	B	B	B	B	A	A
7	SNP_A-1741890	rs10485887	77712706	77.712706	0.548	A	A	A	B	A	B	B	B	A	B

[illegible]

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-6	pC-6 donor	pC-7	pC-7 donor
7	SNP_A-1740412	rs10487331	110945463	110.945463	0.726	A	A	A	A	A	A	B	A	A
7	SNP_A-1745955	rs2529588	111697006	111.697006	0.726	A	A	A	A	A	A	A	A	A
7	SNP_A-1724315	rs1548395	112947523	112.947523	0.298	B	B	B	B	B	B	B	A	A
7	SNP_A-1719538	rs6973150	114297804	114.297804	0.45	B	B	A	A	A	A	B	B	B
7	SNP_A-1736164	rs10500054	115247129	115.247129	0.5	B	B	B	B	B	B	A	A	B
7	SNP_A-1733815	rs7783832	116468422	116.468422	0.298	B	B	B	B	B	B	B	B	B
7	SNP_A-1676935	rs10487392	117466579	117.466579	0.488	B	B	A	A	A	A	A	A	A
7	SNP_A-1647647	rs10488301	119761267	119.761267	0.262	A	A	B	B	B	B	A	A	B
7	SNP_A-1655036	rs1206486	121146345	121.146345	0.441	B	B	B	B	B	B	A	A	B
7	SNP_A-1643783	rs10487974	122442567	122.442567	0.381	A	A	A	A	A	A	B	B	B
7	SNP_A-1690238	rs6948425	123386447	123.386447	0.476	A	A	A	A	A	A	A	A	B
7	SNP_A-1745008	rs723444	124253175	124.253175	0.417	B	B	A	A	A	A	B	B	B
7	SNP_A-1675675	rs2107098	124969695	124.969695	0.488	B	B	A	A	A	A	B	A	B
7	SNP_A-1678693	rs2299447	125743520	125.74352	0.738	A	A	A	A	A	A	A	A	A
7	SNP_A-1670675	rs6467115	126530478	126.530478	0.643	A	A	A	A	A	A	A	A	B
7	SNP_A-1708033	rs10487505	127454114	127.454114	0.464	B	B	A	A	A	A	B	B	B
7	SNP_A-1656498	rs10488628	127961843	127.961843	0.405	A	A	B	B	B	B	A	A	A
7	SNP_A-1742598	rs7803075	130199321	130.199321	0.726	A	A	B	B	B	B	B	A	A
7	SNP_A-1695048	rs1790998	133595635	133.595635	0.476	A	A	A	A	A	A	B	B	B
7	SNP_A-1721434	rs2551778	134556904	134.556904	0.548	A	A	A	A	A	A	A	A	A
7	SNP_A-1669022	rs10253975	135674764	135.674764	0.662	B	B	A	A	A	A	A	A	A
7	SNP_A-1715624	rs2253729	139396073	139.396073	0.583	A	A	B	B	B	B	A	A	B

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-6	pC-6 donor	pC-7	pC-7 donor
7	SNP_A- 1652925	rs1527304	141162389	141.162389	0.571	A A	A A	B B	B B	B B	A A	A A	A A	A B
7	SNP_A- 1715016	rs6949653	143162918	143.162918	0.691	A A	A B	A B	A B	A B	A A	A A	A A	A A
7	SNP_A- 1666637	rs4725680	144870787	144.870787	0.369	A A	A B	B B	B B	B B	A A	A A	A A	A A
7	SNP_A- 1681703	rs10487936	145527849	145.527849	0.732	A A	A A	A A	A A	A A	A A	A A	B B	A B
7	SNP_A- 1680321	rs10278315	146403556	146.403556	0.726	A A	A A	A A	A A	A A	A A	A A	A A	A A
7	SNP_A- 1720798	rs1177946	147495250	147.49525	0.643	A A	A A	A A	A A	A A	A A	A A	B B	B B
7	SNP_A- 1713513	rs1403222	149691561	149.691561	0.536	A B	A B	A A	A A	A A	B B	B B	A A	A B
7	SNP_A- 1736364	rs306293	154243700	154.2437	0.643	A A	A A	B B	B B	B B	A A	A A	B B	A B
7	SNP_A- 1691199	rs2301916	156473603	156.473603	0.369	A B	A B	A B	A B	A B	B B	B B	A B	A B
8	SNP_A- 1659972	rs747351	228574	0.228574	0.369	A B	A B	A B	A B	A A	A B	A B	A B	A B
8	SNP_A- 1725579	rs4876153	2291741	2.291741	0.691	B B	B B	A A	A A	A A	A A	A A	A A	A B
8	SNP_A- 1651465	rs9314492	3332437	3.332437	0.476	A A	A A	B B	B B	B B	B B	B B	B B	A B
8	SNP_A- 1695486	rs10503246	4117771	4.117771	0.714	A B	A B	A A	A A	A A	B B	A B	B B	A B
8	SNP_A- 1650643	rs4146469	5253259	5.253259	0.441	A B	A B	A B	A B	A B	B B	B B	B B	A B
8	SNP_A- 1714359	rs6559072	5839489	5.839489	0.679	A B	A B	A A	A A	A A	B B	B B	A A	A A
8	SNP_A- 1660050	rs3020252	6450411	6.450411	0.634	A B	A B	B B	B B	B B	A A	A A	B B	A B
8	SNP_A- 1757262	rs2409113	8849712	8.849712	0.72	A B	A B	A A	A A	A A	A A	A A	A A	A A
8	SNP_A- 1680667	rs1588198	9929939	9.929939	0.655	A B	A B	A B	A B	A B	A A	A B	A A	A A
8	SNP_A- 1679891	rs2278335	10740863	10.740863	0.702	A B	A B	A A	A A	A A	A A	A A	A A	A B
8	SNP_A- 1715348	rs10503478	13876453	13.876453	0.607	A A	A A	B B	B B	B B	A A	B B	B B	A B
8	SNP_A- 1659353	rs2410193	14445035	14.445035	0.738	A A	A A	A A	A A	A A	B A	B B	A A	A B
8	SNP_A- 1756484	rs351572	16065839	16.065839	0.595	A A	A A	A A	A A	A A	A A	A A	B A	A B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
8	SNP_A- 1750990	rs7003503	17226143	17.226143	0.25	B	B	A	A	A	A	B	B	B	A
8	SNP_A- 1688509	rs7006702	19316813	19.316813	0.333	A	A	A	B	A	A	B	B	B	A
8	SNP_A- 1747706	rs2083637	19909455	19.909455	0.738	A	A	A	B	A	A	A	A	A	A
8	SNP_A- 1646595	rs2306518	22526253	22.526253	0.357	B	A	B	B	B	B	B	B	A	A
8	SNP_A- 1699334	rs10503733	23589963	23.589963	0.714	A	A	A	A	A	A	A	A	A	A
8	SNP_A- 1752532	rs2976457	24923988	24.923988	0.548	B	B	A	A	A	A	A	B	B	B
8	SNP_A- 1746191	rs10503776	25765786	25.765786	0.671	B	B	A	A	A	A	B	B	A	A
8	SNP_A- 1742962	rs10503872	30556573	30.556573	0.476	A	A	B	A	A	A	A	A	B	B
8	SNP_A- 1710298	rs10503907	32291552	32.291552	0.607	A	A	A	B	B	A	A	A	A	A
8	SNP_A- 1646333	rs1551652	34443033	34.443033	0.662	A	A	B	A	A	A	B	B	A	A
8	SNP_A- 1679337	rs10503970	34985910	34.98591	0.262	B	B	B	A	A	A	B	B	B	B
8	SNP_A- 1701068	rs581187	37119893	37.119893	0.286	B	B	A	A	A	A	B	B	B	A
8	SNP_A- 1747018	rs3935233	39307991	39.307991	0.31	A	A	B	B	B	B	B	B	B	B
8	SNP_A- 1730295	rs9298596	40431722	40.431722	0.333	A	A	B	A	A	A	B	B	B	B
8	SNP_A- 1664173	rs341817	50186153	50.186153	0.56	A	A	A	B	B	A	A	B	B	A
8	SNP_A- 1712754	rs318913	51075845	51.075845	0.262	B	B	B	B	B	B	B	B	B	B
8	SNP_A- 1716236	rs10504120	52554998	52.554998	0.726	A	A	A	A	A	A	A	A	A	A
8	SNP_A- 1645251	rs2249236	53110767	53.110767	0.286	A	A	A	B	A	A	A	A	B	B
8	SNP_A- 1674928	rs360956	54063839	54.063839	0.61	B	B	B	A	A	A	A	A	B	B
8	SNP_A- 1661925	rs7824078	55966296	55.966296	0.631	A	A	B	A	A	A	A	A	A	A
8	SNP_A- 1734483	rs2670052	57666163	57.666163	0.583	A	A	A	B	A	A	A	A	A	A
8	SNP_A- 1649879	rs9297980	58641477	58.641477	0.476	A	A	A	B	A	A	A	A	A	A

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Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
8	SNP_A-1679699	rs2245797	95329376	95.329376	0.31	B	B	B	B	B	B	A	A	A	A
8	SNP_A-1738642	rs962451	101400186	101.400186	0.583	A	A	A	A	A	A	A	A	B	B
8	SNP_A-1677965	rs4495397	103476369	103.476369	0.268	B	B	A	A	A	A	B	B	B	B
8	SNP_A-1718730	rs543736	104082125	104.082125	0.619	A	A	B	B	B	B	A	A	A	A
8	SNP_A-1724051	rs10505064	105831730	105.83173	0.345	A	A	B	B	B	B	B	A	B	B
8	SNP_A-1691919	rs2930485	107881851	107.881851	0.607	B	B	B	B	B	B	A	B	B	B
8	SNP_A-1652191	rs10505107	108392560	108.39256	0.619	A	A	A	A	A	A	A	A	A	A
8	SNP_A-1756952	rs1353298	108959098	108.959098	0.321	B	B	B	B	B	B	B	B	A	A
8	SNP_A-1695466	rs5772	110167808	110.167808	0.571	A	A	A	B	A	A	A	A	A	A
8	SNP_A-1747370	rs10505135	111120579	111.120579	0.345	A	A	B	B	B	B	A	B	B	B
8	SNP_A-1745327	rs10505156	112369457	112.369457	0.25	A	A	B	B	B	B	B	B	B	B
8	SNP_A-1681911	rs10505180	113392265	113.392265	0.726	B	B	A	A	A	A	A	A	A	A
8	SNP_A-1694542	rs2125552	113984509	113.984509	0.274	B	B	B	B	B	B	B	B	B	B
8	SNP_A-1713409	rs9297496	114629527	114.629527	0.321	B	B	B	B	B	B	B	B	A	A
8	SNP_A-1725803	rs7828185	116438576	116.438576	0.286	B	B	B	B	B	B	B	B	B	B
8	SNP_A-1698988	rs10505328	119219639	119.219639	0.441	A	A	B	B	B	B	B	B	B	B
8	SNP_A-1753414	rs3924784	121618858	121.618858	0.667	A	A	A	A	A	A	B	A	A	A
8	SNP_A-1735413	rs17478	122793072	122.793072	0.595	A	A	A	A	A	A	B	A	A	A
8	SNP_A-1655430	rs6470143	124219594	124.219594	0.345	B	B	B	B	B	B	B	B	A	A
8	SNP_A-1754805	rs3909562	124803864	124.803864	0.405	A	A	A	A	A	A	B	B	A	A
8	SNP_A-1696789	rs2382993	125770106	125.770106	0.345	B	A	B	B	B	B	B	A	B	B
8	SNP_A-1686811	rs897153	126747483	126.747483	0.643	B	A	A	B	A	A	A	A	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
8	SNP_A- 1753008	rs2091933	127485749	127.485749	0.679	A A	A B	B B	B B	B B	B B	A A	A A	A B	A B
8	SNP_A- 1651085	rs10505486	128074016	128.074016	0.441	B B	B B	B B	B B	B B	B B	B B	A B	A B	A B
8	SNP_A- 1682761	rs4123791	129288419	129.288419	0.417	B B	B B	A A	A A	A A	A A	A A	A A	A A	A A
8	SNP_A- 1692841	rs9297775	129805894	129.805894	0.333	B B	A B	B B	B B	B B	B B	B B	B B	B B	B B
8	SNP_A- 1653731	rs10505545	130646449	130.646449	0.538	A A	A A	A B	A B	A B	A B	B B	B B	B B	B B
8	SNP_A- 1655374	rs7460225	131408555	131.408555	0.464	A A	A B	A B	A B	A B	A B	A A	A B	A A	A A
8	SNP_A- 1672735	rs7008202	132143592	132.143592	0.357	B B	A B	A A	A A	A A	A A	B A	B B	A B	A B
8	SNP_A- 1725115	rs4736424	133782292	133.782292	0.31	B B	B B	B B	B B	B B	B B	A A	A B	B B	B B
8	SNP_A- 1647079	rs10505607	134527931	134.527931	0.441	A A	A B	B B	B B	B B	B B	B B	B B	A B	A B
8	SNP_A- 1700220	rs4909801	135948341	135.948341	0.702	A A	A B	B B	B B	B B	B B	A A	A B	A A	A A
8	SNP_A- 1675316	rs4909582	137288153	137.288153	0.488	A A	A A	B B	A B	A B	A B	B B	B B	A A	A A
8	SNP_A- 1661056	rs9324439	138086052	138.086052	0.452	B B	A B	B B	B B	B B	B B	B B	B B	A B	A B
8	SNP_A- 1689603	rs1325053	139156386	139.156386	0.732	A A	A A	A A	B B	B B	B B	B B	B B	A A	A A
8	SNP_A- 1710354	rs2468705	140618265	140.618265	0.75	A B	A B	B B	A B	A B	A B	A A	A A	A A	A A
9	SNP_A- 1643050	rs10491691	336963	0.336963	0.655	B B	B B	A A	A A	A A	A A	A B	A B	B B	B B
9	SNP_A- 1704718	rs2370220	907667	0.907667	0.726	A A	A A	B B	B B	B B	B B	A A	A A	A A	A A
9	SNP_A- 1681445	rs7040916	2645520	2.64552	0.726	B B	B B	A A	A A	A A	A A	A A	A A	A A	A A
9	SNP_A- 1734535	rs1358908	3162093	3.162093	0.524	A A	A A	B B	B B	B B	B B	B B	B B	A A	A A
9	SNP_A- 1685961	rs1455177	3782613	3.782613	0.488	B B	B B	B B	B B	B B	B B	A B	A B	A B	A B
9	SNP_A- 1642494	rs10491650	5193054	5.193054	0.354	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
9	SNP_A- 1696419	rs1407473	7989681	7.989681	0.31	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
9	SNP_A- 1709516	rs1433548	8927116	8.927116	0.31	A B	A B	A B	A B	A B	A B	B B	B B	B B	B B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
9	SNP_A-1682679	rs1613507	9791755	9.791755	0.563	A B	A B	A A	A A	A A	A A	B B	B B	A A	A A
9	SNP_A-1673445	rs10511545	10341048	10.341048	0.726	A A	A A	A A	A A	A A	A A	A A	A A	A A	A A
9	SNP_A-1679185	rs4740473	11080005	11.080005	0.369	A B	A B	A A	A A	A A	A A	B B	B B	B B	B B
9	SNP_A-1744452	rs1825739	11777410	11.77741	0.429	B B	B B	B B	B B	B B	B B	A B	A B	A A	A B
9	SNP_A-1714556	rs1086377	12824688	12.824688	0.702	A A	A A	B B	B B	B B	B B	A B	A B	A A	A A
9	SNP_A-1672461	rs7038474	13355816	13.355816	0.702	A B	A B	A A	A A	A A	A A	B B	B B	B B	A B
9	SNP_A-1704214	rs10511587	13970584	13.970584	0.738	A B	A B	A A	A A	A A	A A	A B	A B	A A	A A
9	SNP_A-1714243	rs4615688	14495861	14.495861	0.714	A A	A A	A A	A A	A A	A A	A A	A A	A A	A A
9	SNP_A-1741448	rs10511603	15006475	15.006475	0.536	B B	B B	B B	B B	B B	B B	A B	A B	A A	A A
9	SNP_A-1742240	rs1001265	17618726	17.618726	0.726	B B	B B	A A	A A	A A	A A	A A	A A	A A	A A
9	SNP_A-1675206	rs7862683	18257947	18.257947	0.427	B B	B B	A A	A A	B B	B B	B B	B B	B B	B B
9	SNP_A-1706426	rs7859334	20660966	20.660966	0.56	A A	A A	B B	B B	A B	A B	A B	A B	B B	A B
9	SNP_A-1669996	rs871024	21793880	21.79388	0.441	A A	A A	A A	A A	A A	A A	A B	A B	B B	A B
9	SNP_A-1662201	rs10511705	22537789	22.537789	0.512	B B	B B	B B	B B	A B	A B	A B	A B	B B	A B
9	SNP_A-1673761	rs9298846	23216243	23.216243	0.655	A B	A B	A A	A A	A A	A A	A A	A A	A A	A B
9	SNP_A-1752066	rs10511761	25602704	25.602704	0.441	B B	B B	B B	B B	B B	B B	A A	A A	A A	A A
9	SNP_A-1690106	rs4978049	26131011	26.131011	0.381	A B	A B	B B	B B	B B	B B	B B	B B	B B	B B
9	SNP_A-1700687	rs983863	26681668	26.681668	0.345	B B	B B	B B	B B	A B	A B	A A	A A	A A	A A
9	SNP_A-1690672	rs1452357	28090846	28.090846	0.707	B B	B B	B B	B B	A B	A B	A A	A A	A A	A A
9	SNP_A-1693514	rs824257	28765262	28.765262	0.655	A A	A A	A A	A A	A A	A A	A A	A A	B B	B B
9	SNP_A-1665553	rs10511842	30009704	30.009704	0.25	A A	A B	B B	B B	A B	A B	B B	B B	A A	A B
9	SNP_A-1724125	rs10511886	31826555	31.826555	0.607	B B	A B	B B	B B	A B	A B	A B	A B	B B	B B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
9	SNP_A-1648177	rs20583	33016572	33.016572	0.452	A	A	B	B	B	B	A	A	A	A
9	SNP_A-1717742	rs6476493	35884737	35.884737	0.691	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1671263	rs4880042	36940301	36.940301	0.393	A	A	B	B	B	B	B	B	B	B
9	SNP_A-1681599	rs2181139	38364977	38.364977	0.25	B	A	A	A	A	A	A	A	B	A
9	SNP_A-1666811	rs4111409	40345280	40.34528	0.262	B	B	B	B	B	B	B	B	B	B
9	SNP_A-1727790	rs7864775	69030853	69.030853	0.548	B	B	B	B	B	B	B	B	A	A
9	SNP_A-1699350	rs10511972	69672094	69.672094	0.619	B	B	A	A	A	A	B	B	B	B
9	SNP_A-1753754	rs10511984	70399849	70.399849	0.75	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1748876	rs10511999	71526051	71.526051	0.595	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1750024	rs1998372	72123726	72.123726	0.369	B	B	B	B	B	A	B	B	B	B
9	SNP_A-1733975	rs2377524	76002013	76.002013	0.321	B	B	B	B	B	B	B	B	B	A
9	SNP_A-1707951	rs10512079	78602073	78.602073	0.25	A	A	A	A	A	A	A	A	B	B
9	SNP_A-1655498	rs1316823	79531349	79.531349	0.643	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1721234	rs1572147	80160841	80.160841	0.634	A	A	B	A	B	B	A	A	B	A
9	SNP_A-1757764	rs7873639	80780459	80.780459	0.286	B	B	B	B	B	B	A	A	A	A
9	SNP_A-1685995	rs2774635	82184146	82.184146	0.286	B	B	B	B	B	B	B	B	A	B
9	SNP_A-1698246	rs1436932	83903397	83.903397	0.476	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1743644	rs7030902	85064645	85.064645	0.548	A	A	B	B	B	B	B	B	A	B
9	SNP_A-1642838	rs1475524	87362117	87.362117	0.357	B	B	B	A	B	B	A	B	A	A
9	SNP_A-1683979	rs4744114	91732136	91.732136	0.452	B	B	B	A	B	B	B	B	A	A
9	SNP_A-1645449	rs1547201	95896039	95.896039	0.548	A	A	B	B	B	B	A	A	A	A
9	SNP_A-1751508	rs1924001	102134812	102.134812	0.643	B	B	A	A	A	A	A	A	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
9	SNP_A-1724479	rs1463983	105506339	105.506339	0.429	B	B	A	A	A	A	B	B	A	A
9	SNP_A-1653563	rs2418076	110092906	110.092906	0.298	B	B	A	A	A	A	B	B	B	B
9	SNP_A-1744924	rs1813202	111767658	111.767658	0.286	A	A	B	B	B	B	A	A	B	B
9	SNP_A-1731818	rs10513222	113757379	113.757379	0.321	B	B	A	B	A	A	A	A	B	B
9	SNP_A-1733479	rs10513267	115067920	115.06792	0.75	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1643236	rs4112759	117313823	117.313823	0.75	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1750306	rs7849366	118191918	118.191918	0.286	A	A	A	B	A	A	A	A	B	B
9	SNP_A-1686447	rs10514837	118919482	118.919482	0.321	B	B	B	B	B	B	B	B	B	B
9	SNP_A-1656426	rs10491529	120012279	120.012279	0.25	B	B	B	B	B	B	B	B	B	B
9	SNP_A-1677789	rs306796	121206889	121.206889	0.631	A	A	A	A	A	A	A	A	A	A
9	SNP_A-1705544	rs7043602	126285054	126.285054	0.738	A	A	A	A	A	A	B	B	A	A
9	SNP_A-1653355	rs883335	129165519	129.165519	0.595	B	B	A	A	A	A	A	A	B	B
9	SNP_A-1699424	rs2269337	130602238	130.602238	0.742	B	B	A	A	A	A	A	A	A	A
9	SNP_A-1747024	rs2809243	132799854	132.799854	0.298	B	B	A	A	A	A	B	B	A	A
10	SNP_A-1659685	rs1392827	1234414	1.234414	0.667	A	A	B	B	B	B	B	B	A	A
10	SNP_A-1753764	rs4880915	1747289	1.747289	0.293	B	B	B	B	B	B	B	B	B	B
10	SNP_A-1727231	rs9329289	2532389	2.532389	0.405	A	A	B	B	B	B	B	B	B	B
10	SNP_A-1732637	rs2388557	3181527	3.181527	0.321	B	B	B	B	B	B	A	A	B	B
10	SNP_A-1679829	rs1679440	4468715	4.468715	0.286	B	B	B	B	B	B	B	B	B	B
10	SNP_A-1713889	rs946785	7041660	7.04166	0.595	A	A	B	B	B	B	B	B	B	B
10	SNP_A-1717612	rs4385796	8539643	8.539643	0.286	B	B	B	B	B	B	B	B	A	A
10	SNP_A-1740604	rs1762757	9449776	9.449776	0.726	A	A	A	A	A	A	B	B	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
0	1686911	rs10508380	10003736	10.003736	0.738	A	A	B	B	A	B	B	B	A	A
1	SNP_A-					B	B	A	A	B	A	A	A	B	B
0	1739848	rs1041044	10644387	10.644387	0.5	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
0	1721418	rs4750093	11829643	11.829643	0.429	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
0	1739768	rs1108131	12537753	12.537753	0.75	B	B	B	B	A	B	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
0	1737160	rs564166	13110955	13.110955	0.738	B	B	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	A	A	B	A	A	A	A	A
0	1678303	rs10508465	13725194	13.725194	0.429	A	A	B	B	B	B	B	B	A	A
1	SNP_A-					B	B	B	B	B	B	A	A	A	A
0	1669628	rs10508473	14241057	14.241057	0.417	B	B	B	B	B	B	B	B	A	A
1	SNP_A-					B	B	B	B	B	B	B	B	B	A
0	1714770	rs1361588	16119457	16.119457	0.298	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	B	B
0	1700268	rs10490962	17240369	17.240369	0.56	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	B	A	B	B	B	B
0	1744374	rs10508555	18316688	18.316688	0.441	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	A	A
0	1748644	rs984292	19028813	19.028813	0.393	B	B	B	B	A	B	B	B	A	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
0	1686549	rs2358348	19533421	19.533421	0.643	A	A	B	B	B	B	A	A	A	A
1	SNP_A-					B	B	A	A	B	A	B	B	B	B
0	1678189	rs788977	21229153	21.229153	0.262	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
0	1672001	rs1417374	23168481	23.168481	0.298	B	B	A	A	A	A	A	A	A	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
0	1726471	rs2150651	24829491	24.829491	0.321	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
0	1751938	rs10508686	25367068	25.367068	0.714	A	A	B	B	A	B	A	A	A	A
1	SNP_A-					A	A	A	A	B	A	A	A	A	A
0	1713661	rs4747530	25876455	25.876455	0.56	B	B	B	B	B	B	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	B	B
0	1706402	rs10508717	26712334	26.712334	0.524	A	A	B	B	A	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
0	1713649	rs1970631	28271741	28.271741	0.452	A	A	B	B	B	B	A	A	A	B
1	SNP_A-					B	B	A	A	B	A	B	B	B	A
0	1707064	rs703041	29265782	29.265782	0.25	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	B	A	B	A	B	B
0	1755663	rs2776644	30294654	30.294654	0.488	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	A	A	B	B	A	A	A	A	A
0	1679427	rs2490527	32711123	32.711123	0.631	B	B	B	B	B	B	A	B	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

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1	SNP_A- 0 1678169	rs2269101	33546185	33.546185	0.286	A A	A B	A B	A A	A A	A B	A B	A B	B B	A B
1	SNP_A- 0 1674978	rs224750	34271036	34.271036	0.619	A A	A A	A A	A A	A A	A A	B A	A B	A B	A A
1	SNP_A- 0 1722205	rs1032408	43808849	43.808849	0.738	A A	A A	B B	B B	B B	B B	A A	A A	A A	A A
1	SNP_A- 0 1700828	rs1583421	45099157	45.099157	0.583	B B	A B	A A	A A	A A	A A	A A	A A	A A	A A
1	SNP_A- 0 1718604	rs10508908	49643864	49.643864	0.5	B B	B B	A A	B B	B B	B B	A A	B A	B B	A B
1	SNP_A- 0 1741518	rs10508929	51841987	51.841987	0.423	A A	A B	A A	B B	B B	B B	A B	B B	A B	A A
1	SNP_A- 0 1674358	rs2339628	52548976	52.548976	0.679	A A	A B	B B	B B	B B	B B	B B	B B	A B	A B
1	SNP_A- 0 1665161	rs1937666	53326630	53.32663	0.464	A B	A B	A A	B B	B B	B B	A A	A B	B B	B B
1	SNP_A- 0 1648887	rs10508976	54302305	54.302305	0.56	B B	B B	B B	A A	A B	A B	A B	A B	B B	B B
1	SNP_A- 0 1660432	rs422296	54965065	54.965065	0.714	A A	A A	B B	A A	A B	B B	A A	A A	A B	A B
1	SNP_A- 0 1642640	rs6481257	58608558	58.608558	0.274	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
1	SNP_A- 0 1697033	rs10509093	60193775	60.193775	0.452	A A	A A	B B	B B	B B	B B	A A	A A	A A	A A
1	SNP_A- 0 1723683	rs4245585	61596196	61.596196	0.286	B B	B B	B B	A A	A B	B B	B B	B B	B B	B B
1	SNP_A- 0 1653973	rs10509139	62150158	62.150158	0.691	A B	A B	A A	A A	A A	A A	A A	A A	A A	A A
1	SNP_A- 0 1713014	rs2787720	63018471	63.018471	0.488	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
1	SNP_A- 0 1667099	rs1255484	65108003	65.108003	0.488	B B	B B	B B	B B	B B	B B	B B	B B	A A	A A
1	SNP_A- 0 1658163	rs7073489	67452445	67.452445	0.274	A B	A B	B B	B B	B B	B B	B B	B B	B B	B B
1	SNP_A- 0 1642112	rs4746654	68476694	68.476694	0.441	B B	B B	B B	B B	B B	B B	B B	B B	A A	A A
1	SNP_A- 0 1720304	rs7918860	70340702	70.340702	0.583	B B	B B	A A	B B	A B	B B	A A	A A	A B	A B
1	SNP_A- 0 1729287	rs10509321	71655739	71.655739	0.298	A B	A B	A A	A A	A A	A A	B A	B B	A B	A B
1	SNP_A- 0 1707688	rs10509334	73110058	73.110058	0.427	B B	B B	B B	B B	B B	B B	A B	A B	A A	A A
1	SNP_A- 0 1654508	rs1865636	77473753	77.473753	0.5	A A	A A	B B	A A	A B	A B	B B	B B	B B	B B

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1	SNP_A-					A	A	A	A	A	A	A	A	A	A
0	1697249	rs10509384	78693188	78.693188	0.726	B	B	A	A	A	A	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
0	1679101	rs1344967	79197624	79.197624	0.262	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	B	A	A	A	A	A	A
0	1748530	rs10509397	79905374	79.905374	0.476	B	B	A	B	B	B	B	B	A	A
1	SNP_A-					A	A	A	B	A	A	A	A	A	A
0	1736610	rs7914988	80540330	80.54033	0.441	B	B	A	B	B	B	A	A	B	B
1	SNP_A-					A	A	B	A	A	A	A	A	A	A
0	1665139	rs342372	84579316	84.579316	0.536	B	B	B	A	B	B	A	A	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	A	A
0	1715818	rs2067731	86973180	86.97318	0.381	B	B	B	A	B	B	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
0	1689101	rs2949392	87497414	87.497414	0.5	A	A	B	A	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
0	1657815	rs391683	90510663	90.510663	0.679	B	B	B	A	B	B	B	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	B	B
0	1706118	rs303212	91151335	91.151335	0.298	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
0	1703070	rs747334	92734724	92.734724	0.476	A	A	B	B	B	B	B	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
0	1717632	rs716361	93308518	93.308518	0.321	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
0	1713435	rs2490739	94587885	94.587885	0.631	A	A	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
0	1642080	rs3781270	95520148	95.520148	0.607	A	A	A	A	A	A	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
0	1680183	rs10509692	97226588	97.226588	0.583	B	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
0	1705694	rs10509700	97884521	97.884521	0.5	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
0	1753314	rs793515	98978459	98.978459	0.345	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
0	1742188	rs10509754	103711687	103.711687	0.262	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
0	1716744	rs2451500	106622867	106.622867	0.707	A	A	A	A	A	A	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
0	1684935	rs10509832	109070424	109.070424	0.667	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	B	B	B	B
0	1676403	rs4113	111223756	111.223756	0.369	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
0	1726183	rs7099088	114343455	114.343455	0.631	B	B	B	B	B	B	B	B	A	A
1	SNP_A-					B	B	B	B	B	B	B	B	A	A
0	1732939	rs10509976	115170888	115.170888	0.286	B	B	B	B	B	B	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-6	pC-6 donor	pC-7	pC-7 donor
1 0	SNP_A- 1675599	rs2420070	116671318	116.671318	0.548	A B	A B	B B	B B	B B	B B	B B	B B	B B
1 0	SNP_A- 1700278	rs4447088	117536799	117.536799	0.274	B B	B B	B B	B B	B B	B B	A B	A B	A B
1 0	SNP_A- 1660760	rs880977	118409221	118.409221	0.452	A B	A B	A A	A A	A A	A A	A B	A B	A B
1 0	SNP_A- 1747698	rs2619111	118956986	118.956986	0.702	A A	A A	A B	A B	A B	A B	A A	A A	A A
1 0	SNP_A- 1682085	rs10490913	120144426	120.144426	0.537	A B	A B	B B	B B	B B	B B	A B	A B	A B
1 0	SNP_A- 1731688	rs1980030	120960017	120.960017	0.393	A B	A B	B B	B B	B B	B B	A B	A B	B B
1 0	SNP_A- 1641760	rs1326654	122305416	122.305416	0.405	A B	A B	B B	B B	B B	B B	B B	B B	B B
1 0	SNP_A- 1741090	rs2420995	123842994	123.842994	0.393	B B	B B	B B	B B	B B	B B	A B	A B	A B
1 0	SNP_A- 1751948	rs845101	125180422	125.180422	0.631	A B	A B	A A	A A	A A	A A	A A	A A	A A
1 0	SNP_A- 1711689	rs1278305	127801415	127.801415	0.524	B B	B B	B B	B B	B B	B B	A B	A B	B B
1 0	SNP_A- 1715610	rs10510154	128412532	128.412532	0.738	A A	A A	A A	A A	A A	A A	A A	A A	A A
1 0	SNP_A- 1706112	rs2251104	130003906	130.003906	0.333	A A	A A	B B	B B	B B	B B	A B	A B	A B
1 0	SNP_A- 1712012	rs1886380	130596834	130.596834	0.702	A A	A A	A B	B B	A A	B A	A A	A A	B B
1 0	SNP_A- 1652639	rs4077516	133237947	133.237947	0.369	A A	A B	B B	B B	B B	B B	B B	B B	A B
1 1	SNP_A- 1727870	rs2499935	5066470	5.06647	0.417	B B	B B	A A	A B	B B	A B	B B	B B	B B
1 1	SNP_A- 1656094	rs2001778	5575584	5.575584	0.452	B B	B B	B A	B B	B B	B B	B B	B B	A B
1 1	SNP_A- 1680969	rs10500667	6284499	6.284499	0.274	B B	B B	A A	A B	B B	A B	B B	B B	B B
1 1	SNP_A- 1656388	rs2595456	6841339	6.841339	0.524	B B	B B	B B	B B	B B	B B	B B	A B	A B
1 1	SNP_A- 1649885	rs3884596	7488751	7.488751	0.571	A B	A B	B B	B B	B B	B B	A A	A B	A B
1 1	SNP_A- 1663461	rs3993279	10627568	10.627568	0.321	B B	B B	A B	A B	A A	A B	B B	B B	B B
1 1	SNP_A- 1723239	rs10500740	11167698	11.167698	0.274	A B	A B	B B	B B	B B	B B	A B	A B	A B
1 1	SNP_A- 1712474	rs1344613	12408280	12.40828	0.31	A B	A B	B B	B B	B B	B B	A B	A B	B B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
1	1705810	rs1894131	15104916	15.104916	0.441	A	B	A	A	A	A	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
1	1674594	rs2190454	17490211	17.490211	0.333	A	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	A	A
1	1701156	rs211102	18003069	18.003069	0.25	B	B	B	B	A	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
1	1685951	rs894556	19822510	19.82251	0.56	B	B	B	B	B	B	A	A	B	B
1	SNP_A-					B	A	A	A	A	A	A	A	A	A
1	1685201	rs10500886	20976742	20.976742	0.607	B	B	A	A	A	A	A	A	A	A
1	SNP_A-					B	B	A	A	A	A	B	B	A	A
1	1668135	rs6483807	21873219	21.873219	0.5	B	B	A	B	B	B	B	B	A	A
1	SNP_A-					B	A	B	B	B	B	A	A	A	A
1	1713403	rs10500927	22398998	22.398998	0.262	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	A	A	A	A	A	A	A
1	1697826	rs1600958	23180524	23.180524	0.388	B	B	B	B	B	B	A	A	A	A
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
1	1753516	rs975980	24515539	24.515539	0.441	A	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
1	1652525	rs10501011	25497059	25.497059	0.417	A	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
1	1665219	rs980562	30413393	30.413393	0.726	A	B	A	B	B	B	B	B	A	A
1	SNP_A-					B	B	B	A	A	A	B	B	B	B
1	1720570	rs1848394	30965654	30.965654	0.619	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	A	A
1	1749112	rs10488689	31659092	31.659092	0.286	B	B	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
1	1701102	rs1033717	33023147	33.023147	0.342	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	A	A	A	A	A	A	A
1	1752850	rs2136509	34753380	34.75338	0.537	B	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
1	1691121	rs10501163	36830990	36.83099	0.286	A	A	A	A	A	A	A	A	B	B
1	SNP_A-					B	A	A	A	A	A	A	A	B	B
1	1725595	rs992118	40016469	40.016469	0.286	B	B	A	B	B	B	A	B	B	B
1	SNP_A-					A	A	A	A	A	A	B	A	B	A
1	1667717	rs7102885	40922404	40.922404	0.655	A	A	A	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	A	A	A	A	A	A	A
1	1717738	rs1531932	41781058	41.781058	0.643	A	A	B	B	A	B	A	A	A	A
1	SNP_A-					A	A	B	B	B	B	B	A	B	B
1	1709380	rs692726	50396846	50.396846	0.321	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	B	B	A	A	A	A	A
1	1752494	rs629948	55113024	55.113024	0.643	A	A	A	B	B	B	A	A	A	A
1	SNP_A-					A	A	B	A	A	A	B	A	B	B
1	1697650	rs1080800	56067666	56.067666	0.381	A	B	B	A	A	B	B	B	B	B

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-1658985	rs540505	56621831	56.621831	0.536	A	A	B	B	B	B	B	A	B	A
1	SNP_A-1749414	rs612688	57333672	57.333672	0.25	B	B	B	B	B	B	A	A	B	B
1	SNP_A-1698180	rs10501369	57870148	57.870148	0.512	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1729269	rs1941030	59982334	59.982334	0.56	B	B	A	B	B	A	A	A	A	A
1	SNP_A-1656934	rs528736	65461684	65.461684	0.393	B	A	A	B	B	A	A	A	B	B
1	SNP_A-1738462	rs624765	69826722	69.826722	0.714	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1645461	rs527529	74298448	74.298448	0.573	A	A	B	B	B	B	A	A	A	A
1	SNP_A-1711405	rs1793483	76653115	76.653115	0.583	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1739334	rs3819256	77379509	77.379509	0.571	B	B	A	B	A	A	B	B	A	A
1	SNP_A-1712184	rs7128417	77883622	77.883622	0.25	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1734963	rs483089	78543310	78.54331	0.655	A	A	A	B	A	A	A	A	A	A
1	SNP_A-1695384	rs1569168	79525377	79.525377	0.441	A	A	A	A	A	A	A	A	B	A
1	SNP_A-1695760	rs10501496	80598450	80.59845	0.298	B	B	A	A	A	A	B	B	A	B
1	SNP_A-1679629	rs666649	81460553	81.460553	0.56	A	A	A	B	A	A	A	A	B	A
1	SNP_A-1674894	rs2000922	82720260	82.72026	0.619	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1645839	rs7924334	83853909	83.853909	0.714	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1654894	rs10501586	84433725	84.433725	0.726	A	A	A	A	A	A	B	B	A	B
1	SNP_A-1756404	rs10501612	85594787	85.594787	0.342	B	B	B	B	B	B	A	A	B	B
1	SNP_A-1722491	rs503952	86520236	86.520236	0.268	A	A	B	B	B	B	B	B	A	A
1	SNP_A-1740548	rs10501723	89922680	89.92268	0.5	B	B	B	A	B	B	A	A	A	B
1	SNP_A-1741388	rs1528760	90459676	90.459676	0.738	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1755135	rs10501759	91082163	91.082163	0.537	B	B	B	B	B	B	A	A	A	A

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-1656446	rs554735	91994827	91.994827	0.524	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1720756	rs2605592	92842667	92.842667	0.702	B	B	A	A	A	A	B	B	B	B
1	SNP_A-1672903	rs609493	93708735	93.708735	0.286	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1659851	rs12627	94442268	94.442268	0.607	B	B	B	B	B	B	A	A	B	B
1	SNP_A-1649021	rs1940201	95387950	95.38795	0.31	A	A	A	A	A	A	B	B	A	A
1	SNP_A-1706350	rs10501859	95973889	95.973889	0.298	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1670058	rs1939713	99567868	99.567868	0.631	A	A	A	A	A	A	B	A	A	A
1	SNP_A-1712712	rs667504	100221671	100.221671	0.738	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1729283	rs313403	102697742	102.697742	0.524	A	A	B	B	B	B	A	A	A	A
1	SNP_A-1643334	rs260818	103425315	103.425315	0.417	B	B	B	B	B	B	B	B	A	A
1	SNP_A-1690312	rs10502051	104808805	104.808805	0.286	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1746850	rs10502080	106341710	106.34171	0.346	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1718590	rs2640757	107936868	107.936868	0.31	A	A	B	B	B	B	B	B	B	B
1	SNP_A-1739572	rs2298501	109571744	109.571744	0.56	A	A	B	B	B	B	B	B	B	B
1	SNP_A-1742110	rs170486	110202174	110.202174	0.452	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1720008	rs10502152	111296905	111.296905	0.321	B	B	B	B	B	B	A	A	B	B
1	SNP_A-1658493	rs7118530	113395335	113.395335	0.357	A	A	B	B	B	B	A	A	A	A
1	SNP_A-1689389	rs2247060	114257194	114.257194	0.536	B	B	B	B	B	B	B	B	B	B
1	SNP_A-1652091	rs572619	115738853	115.738853	0.619	A	A	B	B	B	B	A	A	A	A
1	SNP_A-1737192	rs660443	116265903	116.265903	0.362	A	A	A	A	A	A	A	A	A	A
1	SNP_A-1643985	rs1219410	121294459	121.294459	0.691	B	B	A	A	A	A	A	A	B	B
1	SNP_A-1728568	rs872414	122170647	122.170647	0.452	A	A	A	A	A	A	B	A	B	B

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					B	B	A	A	A	A	B	B	B	B
1	1696469	rs2078158	122950070	122.95007	0.333	B	B	A	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
1	1748196	rs1940751	127447038	127.447038	0.683	A	A	A	A	A	A	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
1	1741458	rs1368850	130433518	130.433518	0.598	A	B	A	B	B	B	B	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
1	1732434	rs748807	131232636	131.232636	0.452	A	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1644365	rs7973282	1095178	1.095178	0.738	A	A	A	A	A	A	A	B	A	A
1	SNP_A-					B	B	B	B	B	B	A	A	B	B
2	1716332	rs215994	2587421	2.587421	0.274	B	B	B	B	B	B	A	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	B	B	B
2	1708039	rs4625554	4286565	4.286565	0.298	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1727428	rs1861584	5578079	5.578079	0.702	A	A	B	B	B	B	A	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1708085	rs4883241	9384549	9.384549	0.369	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					B	A	B	B	B	B	B	B	B	B
2	1709352	rs560444	9940542	9.940542	0.321	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	B	B
2	1667917	rs1009954	11789366	11.789366	0.333	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
2	1749536	rs10505774	13327672	13.327672	0.714	A	B	A	A	A	A	B	B	A	A
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
2	1696855	rs10492150	14935164	14.935164	0.333	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1680095	rs4366546	18267461	18.267461	0.75	A	A	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	B	A
2	1714486	rs10505845	19976927	19.976927	0.714	A	A	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	B	A
2	1729086	rs4131935	20632200	20.6322	0.738	B	B	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	A	B	A	A	A	A	A	A
2	1673313	rs2417981	21483114	21.483114	0.5	B	B	B	B	B	B	A	A	A	A
1	SNP_A-					A	A	A	B	A	A	A	A	A	A
2	1645425	rs3884510	24249990	24.24999	0.512	A	A	B	B	B	B	B	B	A	A
1	SNP_A-					B	A	B	B	B	B	B	B	B	B
2	1672243	rs10505945	24803300	24.8033	0.381	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	A	A	A	A	A	A	A	B	A
2	1692085	rs10505972	25379461	25.379461	0.393	B	B	B	A	B	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	A	A
2	1674778	rs9300175	27617467	27.617467	0.417	B	B	B	B	B	B	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1649795	rs148898	29606383	29.606383	0.691	A	A	A	A	A	A	A	B	A	A

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					B	A	B	B	B	B	B	B	B	B
2	1658781	rs10506065	30342307	30.342307	0.417	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	B	B	A	A	A	A	A
2	1722521	rs7979386	30966129	30.966129	0.464	A	B	A	B	B	B	A	B	A	A
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1705996	rs2593998	32333520	32.33352	0.714	A	A	A	A	A	A	A	B	A	B
1	SNP_A-					A	A	A	A	A	A	B	A	B	A
2	1644085	rs1905428	33450742	33.450742	0.512	A	A	A	A	A	A	B	B	B	B
1	SNP_A-					A	A	B	A	A	A	B	A	B	A
2	1711331	rs2389276	33989158	33.989158	0.595	A	B	B	A	A	B	B	B	B	B
1	SNP_A-					B	A	A	B	B	A	A	A	A	A
2	1692149	rs10506124	37305503	37.305503	0.571	B	B	A	B	B	B	A	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	B	A
2	1720482	rs7969928	39561348	39.561348	0.393	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
2	1659791	rs7309345	40585255	40.585255	0.75	B	B	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	A	B	A	A	B	A	A	A
2	1754513	rs1369610	41755818	41.755818	0.369	A	B	A	B	B	B	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1693494	rs1506678	43535759	43.535759	0.631	A	B	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	B	B	B	B	A	A	B	B
2	1702318	rs7310869	44951653	44.951653	0.536	A	B	B	B	B	B	A	A	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
2	1748898	rs10506292	49031020	49.03102	0.381	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1733843	rs7968810	52445260	52.44526	0.738	A	A	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	B	A	A	A	B	B	B	A
2	1712318	rs10506393	56672989	56.672989	0.691	A	B	B	A	A	B	B	B	B	B
1	SNP_A-					A	A	A	B	B	A	A	A	A	A
2	1657234	rs3913094	57197682	57.197682	0.655	A	A	A	B	B	B	A	A	A	B
1	SNP_A-					A	A	A	A	A	A	B	A	A	A
2	1662747	rs10506408	58834234	58.834234	0.512	A	B	A	A	A	A	B	B	A	B
1	SNP_A-					B	A	A	B	B	A	A	A	B	B
2	1688045	rs7308021	61145687	61.145687	0.571	B	B	A	B	B	B	A	A	B	B
1	SNP_A-					B	B	B	A	A	A	A	A	A	A
2	1749010	rs513203	62226007	62.226007	0.56	B	B	B	A	A	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
2	1730271	rs1596727	63609374	63.609374	0.583	A	A	A	A	A	A	B	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
2	1716970	rs8756	64646019	64.646019	0.595	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
2	1721334	rs10506514	65583191	65.583191	0.298	B	B	B	B	B	B	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1646303	rs7313431	66378203	66.378203	0.631	A	A	A	A	A	A	A	A	A	A

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					A	A	B	A	A	A	A	A	B	B
2	1695666	rs710779	68249633	68.249633	0.476	B	B	B	A	A	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	A	A	B	B
2	1700862	rs2567134	69233806	69.233806	0.31	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	A	A	A	B	B	B	B
2	1757570	rs7960254	70109323	70.109323	0.405	B	B	B	A	A	B	B	B	B	B
1	SNP_A-					B	B	B	A	A	A	A	A	B	B
2	1676631	rs10506645	70671767	70.671767	0.31	B	B	B	A	A	B	B	B	B	B
1	SNP_A-					A	A	B	A	A	A	A	A	B	B
2	1743470	rs7964705	72103027	72.103027	0.31	A	A	B	A	A	B	B	B	B	B
1	SNP_A-					B	B	A	B	B	A	A	A	A	A
2	1660536	rs1396226	73586112	73.586112	0.429	B	B	A	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	A	A	A	A	A	A	A
2	1662713	rs1275643	74439702	74.439702	0.393	B	B	B	A	A	B	B	B	A	A
1	SNP_A-					B	B	B	B	B	B	B	B	A	A
2	1667227	rs310877	75889008	75.889008	0.274	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1732426	rs7315131	76389953	76.389953	0.381	B	B	A	A	A	A	A	B	A	A
1	SNP_A-					B	B	B	A	A	A	A	A	A	A
2	1667491	rs1796135	77491016	77.491016	0.524	B	B	B	A	A	B	A	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
2	1643877	rs1244908	79104469	79.104469	0.631	A	A	B	B	B	B	A	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
2	1737202	rs10506839	79948071	79.948071	0.31	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	B	B	A	A	A	A	A
2	1700433	rs10506846	80609736	80.609736	0.655	A	A	A	B	B	B	A	B	B	B
1	SNP_A-					A	A	B	A	A	A	A	A	A	A
2	1738317	rs892540	81919943	81.919943	0.667	B	B	B	A	A	B	A	A	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
2	1688895	rs7960510	82715458	82.715458	0.274	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
2	1675076	rs839159	85096176	85.096176	0.726	B	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
2	1663055	rs2635067	85762474	85.762474	0.571	B	B	B	A	A	B	A	A	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
2	1727255	rs1019206	87893500	87.8935	0.333	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	A	A	A	A
2	1657981	rs2731240	89061896	89.061896	0.31	B	B	B	B	B	B	A	B	A	A
1	SNP_A-					B	B	B	B	B	B	A	A	B	B
2	1696519	rs924328	91753976	91.753976	0.31	B	B	B	B	B	B	A	A	B	B
1	SNP_A-					B	B	A	A	A	A	B	A	A	A
2	1747554	rs4761590	93076279	93.076279	0.655	B	B	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	B	B
2	1701918	rs759572	95985503	95.985503	0.524	B	B	B	A	B	B	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1734475	rs1394380	97055132	97.055132	0.75	A	A	A	A	A	A	B	B	A	A
1	SNP_A-					A	A	A	B	A	A	A	A	A	A
2	1690482	rs10492276	97699500	97.6995	0.691	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
2	1704900	rs1718312	101743655	101.743655	0.393	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
2	1698694	rs10507166	102367680	102.36768	0.369	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
2	1731482	rs7954946	103966503	103.966503	0.333	B	B	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
2	1689283	rs10507197	104564170	104.56417	0.583	A	A	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	B	B
2	1723539	rs1444581	105816718	105.816718	0.488	B	B	A	A	A	A	A	A	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	A	A
2	1676727	rs715447	107449185	107.449185	0.464	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1742456	rs10507234	108519202	108.519202	0.714	B	B	A	A	A	A	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1655216	rs4767550	116413870	116.41387	0.595	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					B	A	A	A	A	A	B	B	B	B
2	1673501	rs1726392	117061645	117.061645	0.321	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1748666	rs3858710	118701913	118.701913	0.573	A	B	A	A	A	A	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
2	1708029	rs1558062	124778387	124.778387	0.524	A	B	B	B	B	B	A	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	A	A	A
2	1716508	rs345676	126581103	126.581103	0.643	A	B	B	B	B	B	B	B	A	A
1	SNP_A-					B	A	B	B	B	B	A	A	B	B
2	1664795	rs1983314	129393207	129.393207	0.333	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	A	A	A
3	1652867	rs7985257	18787997	18.787997	0.524	B	B	A	A	A	A	B	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
3	1686943	rs535233	20445317	20.445317	0.321	B	B	B	B	B	B	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	B	A	A	A
3	1745741	rs2862901	23933239	23.933239	0.571	B	B	A	A	A	A	B	B	A	A
1	SNP_A-					B	B	A	A	A	A	B	B	A	A
3	1642868	rs10507349	25679528	25.679528	0.274	B	B	A	A	A	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
3	1702806	rs1161470	28322644	28.322644	0.31	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
3	1664657	rs213611	30348913	30.348913	0.705	A	A	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	A	A	A	A
3	1658585	rs206079	31818618	31.818618	0.417	B	B	B	B	B	B	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1 3	SNP_A- 1685897	rs4941700	32383381	32.383381	0.262	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
1 3	SNP_A- 1664201	rs1538001	33683068	33.683068	0.274	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
1 3	SNP_A- 1742432	rs6563348	35588714	35.588714	0.397	A A	A A	B B	B B	B B	B B	A B	A B	B B	B B
1 3	SNP_A- 1709846	rs2224655	36217500	36.2175	0.298	B B	B B	B B	B B	B B	B B	A B	A B	A A	A A
1 3	SNP_A- 1719156	rs1359214	36774982	36.774982	0.452	A B	A B	A A	A A	A A	A A	A B	A B	A B	A B
1 3	SNP_A- 1699940	rs10507466	37361657	37.361657	0.75	A A	A A	A A	A A	A A	A A	A B	A B	A B	A B
1 3	SNP_A- 1757710	rs2197879	38143188	38.143188	0.286	A B	A B	B B	B B	B B	B B	B B	B B	A A	A A
1 3	SNP_A- 1725889	rs4566029	39136387	39.136387	0.691	A A	A A	A A	A A	A A	A A	A B	A B	A A	A A
1 3	SNP_A- 1648291	rs7322754	40220977	40.220977	0.31	B B	B B	B B	A B	A B	A B	B B	B B	B B	B B
1 3	SNP_A- 1644487	rs1409075	42143450	42.14345	0.5	A B	A B	A B	A B	A B	A B	A A	A A	A A	A A
1 3	SNP_A- 1692131	rs9316020	42892291	42.892291	0.274	B B	B B	A B	A B	A B	A B	B B	B B	B B	B B
1 3	SNP_A- 1683729	rs9285153	43710570	43.71057	0.536	B B	B B	B B	B B	B B	B B	A B	A B	A B	A B
1 3	SNP_A- 1675092	rs10507544	46298746	46.298746	0.286	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B
1 3	SNP_A- 1706220	rs1983805	48609971	48.609971	0.655	A A	A A	A A	A A	A A	A A	B B	A B	A A	A A
1 3	SNP_A- 1656586	rs1359613	49664241	49.664241	0.381	A A	A B	A A	A A	A A	A A	B B	B B	B B	B B
1 3	SNP_A- 1687875	rs9316513	50452286	50.452286	0.643	A A	A B	A A	A A	A A	A A	B B	A B	A A	A A
1 3	SNP_A- 1699260	rs1891948	52537146	52.537146	0.429	B B	B B	A A	A A	A A	A A	A A	A B	B B	B B
1 3	SNP_A- 1670827	rs9316642	53093973	53.093973	0.571	A A	A B	B B	B B	B B	B B	B B	B B	B B	B B
1 3	SNP_A- 1664927	rs1010947	53921670	53.92167	0.702	A A	A B	A A	A A	A A	A A	A A	A A	A A	A A
1 3	SNP_A- 1686045	rs10507599	54585799	54.585799	0.286	A A	A B	B B	B B	B B	B B	B B	B B	B B	B B
1 3	SNP_A- 1686285	rs2253408	55216697	55.216697	0.75	A A	A A	A B	A B	A B	A B	B B	A B	B B	B B
1 3	SNP_A- 1668215	rs959745	56718869	56.718869	0.274	B B	B B	B B	B B	B B	B B	B B	A B	B B	B B

[illegible]

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1 3	SNP_A- 1693530	rs9319022	83601961	83.601961	0.345	B B	B B	A B	A B	A B	A B	A B	A B	A B	A B
1 3	SNP_A- 1706422	rs1331567	84793816	84.793816	0.56	A A	A A	A A	A A	A A	A A	A A	A A	A A	A A
1 3	SNP_A- 1733077	rs995475	87558036	87.558036	0.357	A B	A B	B B	B B	B B	B B	A B	A B	B B	B B
1 3	SNP_A- 1679861	rs1113478	88908389	88.908389	0.417	A A	A A	A B	A A	A B	A B	A B	A B	A B	A B
1 3	SNP_A- 1649205	rs665530	90571947	90.571947	0.726	A A	A A	A A	A A	A A	A A	A B	A B	A A	A A
1 3	SNP_A- 1726887	rs1926489	91465990	91.46599	0.524	A B	A B	A A	A A	A A	A A	A A	A A	A B	A B
1 3	SNP_A- 1714183	rs913005	92275844	92.275844	0.607	A B	A B	B B	B B	B B	B B	A A	A A	A A	A A
1 3	SNP_A- 1701716	rs9301876	92819688	92.819688	0.56	A A	A A	B B	B B	B B	B B	A A	A A	A A	A A
1 3	SNP_A- 1681625	rs1412938	93661657	93.661657	0.726	A A	A A	A A	A A	A A	A A	A A	A A	A A	A A
1 3	SNP_A- 1648409	rs9302001	94261393	94.261393	0.274	A A	A A	B B	B B	B B	B B	A B	A B	B B	B B
1 3	SNP_A- 1741482	rs7324781	95032754	95.032754	0.405	A B	A B	B B	B B	A B	A B	B B	B B	B B	B B
1 3	SNP_A- 1661319	rs4603415	96610639	96.610639	0.631	A B	A B	A A	A A	A A	A A	A B	A B	A A	A B
1 3	SNP_A- 1664929	rs285067	97536416	97.536416	0.691	A A	A B	B B	B B	A B	A B	A A	A A	A A	A A
1 3	SNP_A- 1709292	rs1886553	98448739	98.448739	0.486	B B	B B	A A	A A	A B	A B	A A	A A	B B	B B
1 3	SNP_A- 1749428	rs2760306	99841672	99.841672	0.298	B B	B B	B B	B B	B B	B B	A B	A B	B B	B B
1 3	SNP_A- 1703098	rs10508075	101237184	101.237184	0.464	A A	A B	A A	A A	A B	A B	A B	A B	A A	A A
1 3	SNP_A- 1680317	rs1015795	102023701	102.023701	0.488	A A	A B	B B	B B	B B	B B	A A	A A	B B	B B
1 3	SNP_A- 1704124	rs279927	102539019	102.539019	0.643	A A	A A	A A	A A	A A	A A	A A	A A	A B	A B
1 3	SNP_A- 1752530	rs1033147	103460337	103.460337	0.333	A A	A A	B B	B B	B B	B B	A B	A B	B B	B B
1 3	SNP_A- 1654228	rs9300981	104440279	104.440279	0.286	B B	A B	B B	B B	B B	B B	A B	A B	B B	A B
1 3	SNP_A- 1715354	rs7318881	105459909	105.459909	0.671	B B	B B	A A	A A	A A	A A	B B	B B	B B	B B
1 3	SNP_A- 1645715	rs7327250	106243682	106.243682	0.329	B B	A B	B B	B B	B B	B B	B B	A B	B B	B B

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines																
ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor	
1 3	SNP_A- 1756346	rs1320446	106965333	106.965333	0.679	B B	B B	B B	B B	A B	A B	B B	A B	A A	A A	
1 3	SNP_A- 1732084	rs231604	107524007	107.524007	0.381	A A	A A	B B	B B	B B	B B	B B	B B	B B	B B	
1 3	SNP_A- 1681321	rs4772985	108080882	108.080882	0.25	B B	B B	B B	B B	B B	B B	B B	B B	B B	B B	
1 3	SNP_A- 1648777	rs10492480	108947427	108.947427	0.333	B B	B B	A A	A A	A A	A A	A A	A A	B B	B B	
1 3	SNP_A- 1654860	rs2183850	110513987	110.513987	0.714	B B	B B	A A	A A	A A	A A	B B	B B	A A	A A	
1 4	SNP_A- 1733261	rs1952805	19586195	19.586195	0.345	B B	B B	B B	B B	B B	B B	B B	B B	A B	A B	
1 4	SNP_A- 1702470	rs1923	22511019	22.511019	0.429	B B	A B	A A	A A	A A	A A	A B	A B	A A	A A	
1 4	SNP_A- 1645139	rs4983041	24495978	24.495978	0.595	B B	A B	A B	A A	B B	A B	A A	A A	A B	A B	
1 4	SNP_A- 1676969	rs10483331	26546808	26.546808	0.417	A B	A B	B B	B B	B B	B B	B B	B B	A A	A A	
1 4	SNP_A- 1680111	rs4981658	27234585	27.234585	0.732	A A	A A	A A	A A	A A	A A	B B	B B	A A	A A	
1 4	SNP_A- 1734437	rs2333423	28146939	28.146939	0.381	A B	A B	B B	B B	B B	B B	B B	B B	B B	B B	
1 4	SNP_A- 1669916	rs10483350	28885906	28.885906	0.738	A A	A A	B B	B B	B B	B B	A A	A A	A A	A A	
1 4	SNP_A- 1732697	rs225842	29622687	29.622687	0.441	A B	A B	B B	B B	B B	B B	B B	B B	A B	A B	
1 4	SNP_A- 1656700	rs1278891	31464813	31.464813	0.595	A A	A A	B B	A A	B B	B B	B B	B B	B B	B B	
1 4	SNP_A- 1740154	rs9322929	33377471	33.377471	0.345	A B	A B	A B	B B	A B	A B	B B	B B	B B	B B	
1 4	SNP_A- 1757044	rs799493	34621626	34.621626	0.691	A B	A B	A B	B B	A B	A B	A A	A A	A A	A A	
1 4	SNP_A- 1676887	rs847498	35546428	35.546428	0.607	A A	A A	A A	A A	A A	A A	A A	A A	A A	A A	
1 4	SNP_A- 1665507	rs1950361	36101975	36.101975	0.329	A B	A B	B B	B B	B B	B B	A B	A B	A B	A B	
1 4	SNP_A- 1705178	rs4901596	37659956	37.659956	0.667	A B	A B	A A	A A	A A	A A	A B	A B	B B	B B	
1 4	SNP_A- 1654996	rs6571869	38248210	38.24821	0.679	A A	A A	A B	A B	A B	A B	A B	A B	A A	A A	
1 4	SNP_A- 1708854	rs10483511	39587714	39.587714	0.571	A B	A B	A B	A B	A B	A B	A B	A B	A B	A B	
1 4	SNP_A- 1653001	rs10498360	40670723	40.670723	0.476	A B	A B	B B	B B	B B	B B	B B	B B	A B	A B	

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1 4	SNP_A- 1753660	rs1951874	41387217	41.387217	0.345	A A	A A	A B	A B	A B	A B	B B	B B	A A	A A
1 4	SNP_A- 1653419	rs2010338	45895631	45.895631	0.655	A A	A A	B B	B B	B B	B B	A A	A A	A A	A A
1 4	SNP_A- 1663303	rs10483573	46932227	46.932227	0.357	B B	B B	A A	A A	A A	A A	A A	A A	A B	A B
1 4	SNP_A- 1664801	rs698340	47611853	47.611853	0.585	A B	A B	A A	A A	A A	A A	A A	A A	B B	B B
1 4	SNP_A- 1722201	rs7146291	48172131	48.172131	0.274	B B	B B	B B	B B	B B	B B	B B	B B	A B	A B
1 4	SNP_A- 1650017	rs8006972	48690753	48.690753	0.31	B B	B B	A B	A B	A B	A B	A A	A A	B B	B B
1 4	SNP_A- 1720778	rs10498420	49483793	49.483793	0.476	A B	A B	A B	A B	B B	A B	A B	A B	B B	B B
1 4	SNP_A- 1743320	rs963626	50157439	50.157439	0.691	A A	A A	A A	A A	A A	A A	A B	A B	A A	A A
1 4	SNP_A- 1641756	rs1956574	51163026	51.163026	0.655	A A	A A	A A	A A	A A	A A	A A	A A	B B	B B
1 4	SNP_A- 1669704	rs7151306	52273870	52.27387	0.607	A B	A B	B B	B B	B B	B B	A A	A A	A B	A B
1 4	SNP_A- 1748272	rs877018	52892776	52.892776	0.451	B B	B B	A B	A B	A A	A B	A B	A B	A B	A B
1 4	SNP_A- 1714357	rs1382978	55788938	55.788938	0.536	A A	A A	B B	B B	B B	B B	A A	A B	A A	A A
1 4	SNP_A- 1714205	rs10483679	56503799	56.503799	0.61	B B	A B	A B	A B	A A	A B	A A	A A	B B	B B
1 4	SNP_A- 1654106	rs238376	57129665	57.129665	0.357	A A	A B	B B	B B	B B	B B	A A	A B	A B	A B
1 4	SNP_A- 1690578	rs10498488	58658876	58.658876	0.451	B B	B B	A B	A B	B B	A B	A A	A A	A A	A A
1 4	SNP_A- 1690058	rs9323353	59240800	59.2408	0.619	A A	A A	B B	B B	A A	A B	A A	A A	A A	A A
1 4	SNP_A- 1671347	rs2296274	60986931	60.986931	0.75	B B	A B	A A	A A	A A	A A	A A	A A	A B	B B
1 4	SNP_A- 1755551	rs9285590	61521469	61.521469	0.417	A A	A A	A A	A A	A A	A A	B B	A B	B B	B B
1 4	SNP_A- 1707294	rs1271582	64634456	64.634456	0.441	B B	B B	A A	A A	A A	A A	B B	B B	B B	B B
1 4	SNP_A- 1648725	rs10483805	67325404	67.325404	0.329	B B	A B	A B	A B	A B	A B	B B	B B	A B	A B
1 4	SNP_A- 1699466	rs1956528	67858721	67.858721	0.631	B B	B B	A A	A A	A A	A A	B B	A B	A B	A B
1 4	SNP_A- 1682431	rs749397	69414068	69.414068	0.262	B B	B B	A A	A A	A A	A A	B B	B B	B B	B B

Database S2 Heterozygosity of pHESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
4	1674164	rs2215132	71545542	71.545542	0.262	A	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
4	1672631	rs2803971	72182227	72.182227	0.713	A	A	A	A	A	A	A	A	B	B
1	SNP_A-					A	A	A	A	B	A	A	A	A	A
4	1648423	rs1028258	75447775	75.447775	0.726	A	A	B	B	B	B	A	A	A	A
1	SNP_A-					B	B	B	B	B	B	A	A	B	B
4	1700204	rs7152153	76265708	76.265708	0.286	B	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	A	B	A	A	A	B	B
4	1701478	rs7156671	76991628	76.991628	0.7	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	B	B
4	1706776	rs10483905	78043978	78.043978	0.429	B	B	A	A	A	A	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
4	1667157	rs997842	78614233	78.614233	0.679	A	A	A	A	A	A	A	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
4	1722889	rs2049826	79383063	79.383063	0.345	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	B	A	A	A
4	1645339	rs2372083	81860288	81.860288	0.452	B	B	A	A	A	A	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	B	B
4	1704748	rs2372424	83017248	83.017248	0.438	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
4	1757272	rs8003423	83533541	83.533541	0.643	B	B	B	B	A	B	A	A	A	A
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
4	1644835	rs1530325	84781909	84.781909	0.702	B	B	A	A	A	A	A	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	A	A
4	1680733	rs10498604	86238836	86.238836	0.298	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
4	1702796	rs8018273	86867956	86.867956	0.524	A	A	B	B	B	B	A	A	A	A
1	SNP_A-					B	B	A	A	A	A	A	A	B	B
4	1687761	rs429923	87481126	87.481126	0.405	B	B	A	A	A	A	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
4	1725723	rs1742083	90256423	90.256423	0.321	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
4	1661389	rs10498627	91041872	91.041872	0.583	A	A	B	B	B	B	A	A	B	B
1	SNP_A-					B	B	B	B	B	B	A	A	B	B
4	1705392	rs2148567	93244403	93.244403	0.286	B	B	B	B	B	B	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
4	1734665	rs1456988	97557760	97.55776	0.679	B	B	A	A	A	A	A	A	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
4	1684765	rs200331	98457298	98.457298	0.488	B	B	A	A	A	A	B	B	A	A
1	SNP_A-					B	A	A	A	A	A	A	A	A	A
4	1682935	rs3918051	99023837	99.023837	0.61	B	B	A	A	A	A	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
4	1734911	rs10484072	102695759	102.695759	0.631	A	A	B	B	B	B	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as “pC”) Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
4	1659209	rs1048257	104475429	104.475429	0.667	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					B	A	B	B	B	B	B	B	B	B
5	1669336	rs1405186	21306806	21.306806	0.441	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	B	B
5	1690082	rs2169637	25517776	25.517776	0.262	B	B	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	A	B	A
5	1643639	rs10519635	27330404	27.330404	0.607	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
5	1740804	rs4779462	28026287	28.026287	0.598	B	B	B	B	B	B	A	A	A	A
1	SNP_A-					A	A	A	A	A	A	B	A	A	A
5	1722463	rs2219507	29646927	29.646927	0.691	A	A	A	A	A	A	B	B	A	A
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
5	1730684	rs10519737	30756749	30.756749	0.381	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
5	1648795	rs1343900	31431890	31.43189	0.667	A	A	B	B	B	B	A	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
5	1755583	rs10519956	32849133	32.849133	0.345	B	B	B	B	B	B	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1699406	rs1948650	33827340	33.82734	0.738	A	A	A	A	A	A	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1645977	rs10518868	34381353	34.381353	0.655	A	A	B	B	B	B	B	B	A	A
1	SNP_A-					A	A	B	B	B	B	B	B	A	A
5	1665819	rs471122	41345866	41.345866	0.3	A	A	B	B	B	B	B	B	A	B
1	SNP_A-					B	B	A	A	A	A	B	B	B	B
5	1673073	rs10519044	44169166	44.169166	0.381	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
5	1740676	rs493728	48678247	48.678247	0.441	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	A	B	B	B	B	A	A	B	B
5	1709940	rs1478200	51948279	51.948279	0.357	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	A	A	A	A
5	1720532	rs2553222	52657040	52.65704	0.691	B	B	A	A	A	A	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	B	B	B	A
5	1654466	rs4534776	55408068	55.408068	0.463	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	A	A	A	A
5	1752856	rs1550574	56000660	56.00066	0.536	A	A	B	B	B	B	A	A	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1735597	rs2033721	58609267	58.609267	0.714	A	B	B	B	B	B	A	A	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1642536	rs3935962	59611593	59.611593	0.536	A	B	A	A	A	A	A	A	A	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
5	1726387	rs10519148	60507655	60.507655	0.25	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
5	1750348	rs2652824	61207054	61.207054	0.286	B	B	B	B	B	B	B	B	B	B

Database S2 Heterozygosity of phESC (Abbreviated as "pC") Lines

ch	SNP ID	RS ID (dbSNP)	basepair	basepair (Mb)	Freq A in Caucasian	pC-1	pC-1 donor	pC-3	pC-4	pC-5	pC-5 donor	pC-6	pC-6 donor	pC-7	pC-7 donor
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1741266	rs10518707	65152676	65.152676	0.488	A	B	B	B	B	B	A	A	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	B	B
5	1739192	rs305002	67928959	67.928959	0.595	A	A	A	A	A	A	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
5	1677047	rs2128112	69973340	69.97334	0.262	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	A	A	A	A	A	B	B	A	A
5	1698770	rs3898352	74308825	74.308825	0.631	B	B	B	B	A	B	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1654378	rs1446312	75199244	75.199244	0.738	A	A	A	A	A	A	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	B	B
5	1657306	rs7163689	76352533	76.352533	0.488	A	B	B	B	A	B	B	B	B	B
1	SNP_A-					A	A	A	A	B	A	A	A	A	A
5	1701268	rs1001460	77291934	77.291934	0.56	A	A	B	B	B	B	B	B	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1689635	rs1320323	79128502	79.128502	0.59	A	A	A	A	A	A	A	A	A	A
1	SNP_A-					A	A	B	B	B	B	A	A	B	B
5	1749864	rs1846911	80255705	80.255705	0.329	A	A	B	B	B	B	B	B	B	B
1	SNP_A-					B	A	A	A	A	A	B	B	B	A
5	1714319	rs10520585	83462510	83.46251	0.286	B	B	B	B	A	B	B	B	B	B
1	SNP_A-					B	B	A	A	A	A	B	B	B	A
5	1654264	rs1961601	84030610	84.03061	0.31	B	B	B	B	A	B	B	B	B	B
1	SNP_A-					A	A	A	A	B	A	A	A	A	A
5	1650691	rs1122907	84708371	84.708371	0.691	A	A	B	B	B	B	A	A	A	A
1	SNP_A-					B	A	A	A	A	A	A	A	A	A
5	1665669	rs10520655	85887415	85.887415	0.595	B	B	A	A	A	A	A	A	A	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1694944	rs3817428	87216251	87.216251	0.75	A	A	A	A	A	A	B	B	A	A
1	SNP_A-					A	A	A	A	A	A	B	B	B	B
5	1683397	rs1079537	89675287	89.675287	0.452	B	B	B	B	A	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	A	B	A
5	1752072	rs10520710	90688998	90.688998	0.287	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
5	1731798	rs1989269	91611056	91.611056	0.305	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	A	A	A	A
5	1728656	rs10520754	92760413	92.760413	0.548	A	A	A	A	A	A	A	A	A	A
1	SNP_A-					B	B	B	B	B	B	B	B	B	B
5	1700188	rs4321143	93957372	93.957372	0.262	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	A	A	A	A	B	B	A	A
5	1686439	rs1551466	99344619	99.344619	0.345	B	B	B	B	B	B	B	B	B	B
1	SNP_A-					A	A	B	B	B	B	B	A	A	A
5	1647533	rs352716	100155950	100.15595	0.31	A	A	B	B	B	B	B	B	A	A

The results show heterozygosity of derived phESC lines and displays changes in genotype by comparison with the related donor genotype. Portions of heterozygous segments of the donor genome became

homozygous in phESC. Chromosome-chromosome number; RS ID-RS number in dbSNP database; Base pair-base pair distance as recorded by Affimetrix GeneChip; Freq A in Cauc-the frequency of A allele in Caucasian population.

[0329] In prior research, parthenogenetic activation of mouse oocytes has resulted in homozygous embryonic stem cell lines (Lin et al., Stem Cells (2003) 21:152). In human oocytes, the suppression of the second meiotic division after oocyte parthenogenetic activation and the generation of diploid embryos does not lead to the derivation of wholly homozygous hES cells.

[0330] Based on the HLA-typing results, differentiated cells derived from all phESC lines should be wholly histocompatible with the oocyte donors, making this a method to create cells of therapeutic use (Table 19).

Table 19. HLA-typing for phESC cell lines

	MHC I			MHC II		
	HLA-A	HLA-B	HLA-C	DRB1	DQB1	DQA1
phESC-1	A*01	B*15(63)	Cw*04	DRB1*12	DQB1*06	DQA1*01
	A*02	B*35	Cw*0708	DRB1*13	DQB1*03	DQA1*0505
phESC-1 donor	A*01	B*15(63)	Cw*04	DRB1*12	DQB1*06	DQA1*01
	A*02	B*35	Cw*0708	DRB1*13	DQB1*03	DQA1*0505
phESC-3, 4, 5	A*02	B*52	Cw*03	DRB1*01	DQB1*05	DQA1*0101
	A*03	B*22	Cw*04	DRB1*03	DQB1*02	DQA1*05
phESC-3, 4, 5 donor	A*02	B*52	Cw*03	DRB1*01	DQB1*05	DQA1*0101
	A*03	B*22	Cw*04	DRB1*03	DQB1*02	DQA1*05
phESC-6	A*02	B*07	Cw*04	DRB1*04	DQB1*06	DQA1*01
	A*03	B*27	Cw*07	DRB1*15	DQB1*03	DQA1*03
phESC-6 donor	A*02	B*07	Cw*04	DRB1*04	DQB1*06	DQA1*01
	A*03	B*27	Cw*07	DRB1*15	DQB1*03	DQA1*03
phESC-7	A*01	B*38	Cw*06	DRB1*13	DQB1*06	DQA1*0106
	A*02	B*57	Cw*12	DRB1*14	DQB1*06	DQA1*0103
phESC-7 donor	A*01	B*38	Cw*06	DRB1*13	DQB1*06	DQA1*0106
	A*02	B*57	Cw*12	DRB1*14	DQB1*06	DQA1*0103
NSF	A*25	B*15(62)	Cw*12	DRB1*04	DQB1*06	DQA1*01
	A*32	B*18	Cw*12	DRB1*15	DQB1*03	DQA1*03

[0331] DNA-profiling of the genetic material derived from the human fibroblasts used as feeder cells revealed no contamination of the phESC cell lines with material from the human fibroblasts (Table 19).

[0332] The phESC-1 line remained undifferentiated during ten months of culture, spanning 35 passages. The other cell lines were successfully cultivated over at least 21 passages. The cells from all phESC lines formed cystic embryoid bodies in suspension culture and gave rise to derivatives of all three germ layers: ectoderm, mesoderm, and endoderm, after differentiation in vitro (FIG. 4). Approximately 5% of embryoid bodies from the phESC-1 line gave rise to beating cells five days following plating. The phESC-6 line produced pigmented epithelial-like cells (FIG. 4I, K). Ectoderm differentiation is presented by positive immunocytochemical staining for neuron specific markers neurofilament 68 (FIG. 4A), NCAM (FIG. 4B), beta III-tubulin (FIG. 4C) and the glial cell marker GFAP (FIG. 4D, M). Differentiated cells were positive for mesoderm markers including alpha-actinin (FIG. 4G) and desmin (FIG. 4J), which are muscle specific markers, and the endothelial markers PECAM-1 (FIG. 4E) and VE-Cadherin (FIG. 4F). Endoderm differentiation is presented by positive staining of differentiated derivatives for alpha-fetoprotein. These data demonstrate that phESC can be differentiated into the three germ layers that lead to all cell types of a human body.

[0333] The altered karyotype of phESC-7 may be a reason to exclude it from clinical use. Alterations of genomic imprinting in human embryos can contribute to the development of disorders linked to maternally or paternally expressed genes (Gabriel et al., Proc Natl Acad Sci USA (1998) 95:14857). In order to investigate other characteristics of the phESC lines, and to determine their suitability for use in cell therapy, imprinting analysis was performed.

[0334] Northern blots were made and screened with DNA probes SNRPN, Peg1_2, Peg1_A, H19, and GAPDH (as an internal control) as outlined above. Blotted nucleic acids were obtained from NSF, neonatal skin fibroblasts; hES, human embryonic stem cell line derived from fertilized oocytes; 1, phESC-1; 2, phESC-3, 3, phESC-4, 4, phESC-5; 5, phESC-6; 6 phESC-7. NSF RT-, hES RT-, 1 RT- are negative controls. FIG. 3 shows the results of the imprinting blot.

[0335] The maternal imprinting gene, Peg1_A shows strong binding in all of the cell lines tested. Weaker (relative to Peg1_A), but consistent binding was observed in all of the cell lines for the maternal imprinting gene H19. SNRPN shows binding predominantly in NSF,

hES, phESC-4, and phESC-6. Peg1_2 shows binding predominantly in NSF, hES, phESC-1 (weaker signal), phESC-3, phESC-5, and phESC-6. GAPDH binding confirmed similar loading of RNA in all lanes.

[0336] Cornea formation and histology

[0337] The growing synthetic corneas were cultured by completely immersing the spheres in medium as described. Gross visual inspection of the spheres shows that they are relatively transparent balls of tissue, and grow to over 1 cm in diameter (FIG. 8).

[0338] Upon gross examination, it appears that the spheres are substantially hollow, comprising a wall of approximately 0.5 mm in thickness. Subsequent histological/microscopic examination reveals that the specimens consist of two strips of mainly fibrous tissue, with an occasional fibroblasts. Staining identifies the presence of a basement membrane which is PAS and Trichrome negative, which suggests the presence of Bowman's layer (i.e., the stroma of the cornea). Atop the fibrous tissue layer is a single cell layer which contains nucleoli suggesting epithelium rather than endothelium. Based on this analysis, it was concluded that the tissue specimens are compatible with cornea.

[0339] Although the invention has been described with reference to the above examples, it will be understood that modifications and variations are encompassed within the spirit and scope of the invention. Accordingly, the invention is limited only by the following claims.

References

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5. B.Fischer and B.D. Bavister, Oxygen tension in the oviduct and uterus of rhesus monkeys, hamsters and rabbits. *J Reprod Fertil* (1993) 99:673-679.
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CLAIMS

1. An isolated retinal-stem cell derived synthetic cornea.
2. The isolated cornea of claim 1, wherein the retinal stem cell is differentiated from a parthenogenetically activated human oocyte.
3. The isolated cornea of claim 1, wherein the cornea is terminally differentiated.
4. The isolated cornea of claim 1, wherein the cornea comprises epithelial cells.
5. The isolated cornea of claim 4, wherein the cornea comprises stroma cells.
6. The isolated cornea of claim 1, wherein the cornea has the ability to change light phase velocity.
7. The isolated cornea of claim 1, wherein the cornea has a transverse diameter of about 5 mm to 11.5 mm.
8. The isolated cornea of claim 1, wherein the cornea has a thickness of about 0.5 mm to 0.6 mm in the center and about 0.6 mm to 0.8 mm at the periphery.
9. The isolated cornea of claim 1, wherein the cornea is deposited as ATTC accession No. _____.
10. The isolated cornea of claim 2, wherein the cornea is histocompatible with the oocyte donor.
11. The isolated cornea of claim 2, wherein the cornea comprises homoplasmic mitochondrial DNA (mtDNA).
12. The cornea of claim 10, wherein the cornea is transplantable in humans.
13. A method of producing a synthetic cornea comprising:

a) parthenogenetically activating a human oocyte, wherein activating comprises: i) contacting the oocyte with an ionophore at high O₂ tension and ii) contacting the oocyte with a serine-threonine kinase inhibitor at low O₂ tension;

b) cultivating the activated oocyte of step (a) at low O₂ tension until blastocyst formation;

c) transferring the blastocyst to a layer of feeder cells, and culturing the transferred blastocyst under high O₂ tension;

d) mechanically isolating an inner cell mass (ICM) from trophectoderm of the blastocyst of step (c);

e) culturing the cells of the ICM of step (d) on a layer of human feeder cells under high O₂ tension, wherein retinal stem cells are identified in the culture by human embryonic stem cell markers (hES) and neuron specific markers, and wherein the identified retinal stem cells are subsequently isolated;

f) culturing the isolated stem cells of step (e) in media comprising serum replacement (M/SR), plasmonate, and at least one mitogen that activates the gp130/STAT pathway and/or the MAP kinase pathway on a fibroblast feeder layer treated with a DNA synthesis inhibitor;

g) culturing the mitogen treated cells of step (f) in M/SR comprising plasmonate (M/SRP), without added mitogen, to near confluence, wherein 1/2 volume of the M/SRP is replaced with M/SR periodically until the near confluent cells develop pigmentation and a domed appearance; and

h) transferring the pigmented cells of step (g) in M/SR to a gelatin coated substrate, wherein 1/2 volume of the M/SR is replaced with M/SR periodically until a synthetic cornea develops.

14. The method of claim 13, wherein the cornea develops in the absence of a 3-D scaffold.

15. The method of claim 13, wherein the mitogen is selected from leukemia inhibitory factor (LIF), bFGF, and a combination thereof.

16. The method of claim 13, wherein the DNA synthesis inhibitor is an alkylating agent.

17. The method of claim 16, wherein the DNA synthesis inhibitor is mitomycin C.

18. The method of claim 13, wherein the feeder cells are human.
19. The method of claim 13, wherein the hES markers are selected from the group consisting of SSEA-3, SSEA-4, TRA-1-60, TRA-1-91, OCT-4, and a combination thereof.
20. The method of claim 13, wherein the neuron specific markers are selected from the group consisting of neurofilament 68, NCAM, beta III-tubulin, GFAP, and a combination thereof.
21. A retinal-stem cell derived synthetic cornea obtained by the method of claim 13.
22. A method of treating a subject in need thereof, comprising replacing a cornea of the subject with a synthetic cornea.
23. The method of claim 22, wherein the subject has an injured cornea.
24. The method of claim 22, wherein the subject has a disease which effects the cornea.
25. The method of claim 24, wherein the disease is selected from the group consisting of keratitis, corneal ulcer, corneal abrasion, snow blindness, arc eye, Thygeson's superficial punctate keratopathy, Fuchs' dystrophy, keratoconus, keratpconjunctivitis sicca, corneal infections, and corneal dystrophy.
26. A method of identifying an agent that affects the cornea of an eye comprising:
 - (a) contacting a retinal-stem cell derived synthetic cornea with an agent;
 - and
 - (b) observing a change to the cornea in the presence and absence of the agent, wherein a change to the cornea is indicative of an agent that affects the cornea.
27. The method of claim 26, wherein the agent has a therapeutic effect on the cornea.
28. The method of claim 26, wherein the agent has an adverse effect on the cornea.

29. The method of claim 26, wherein change to the cornea is selected from the group consisting of modulation of gene expression, modulation of protein expression, change in opacity, change in plasticity, change in hardness, change in light phase velocity, and change in shape.

30. The method of claim 28, wherein the agent is an environmental chemical.

31. The method of claim 27, wherein the agent is a drug.

32. The method of claim 31, wherein the drug is a topical drug.

33. A method for replacement of a cornea of an eye with the synthetic cornea according to claim 1, comprising:

- a) surgically excising the cornea from the eye;
- b) inserting the synthetic cornea into the area of the removed cornea; and
- c) allowing the synthetic cornea to interface with tissue underlying the excision to anchor the synthetic cornea to the eye.

34. The method of claim 33, further comprising separating a portion of the outer surface of a cornea thereby forming a corneal flap and a corneal bed, the corneal flap having an anterior surface and a posterior surface, the corneal bed having a shaped anterior surface; implanting the synthetic cornea on the corneal bed, the cornea having an anterior surface and a posterior surface; and replacing the portion of the cornea that was separated.

35. A method of delivering an effective amount of an agent to the eye of a subject comprising:

- a) transforming at least a portion of the cells comprising the synthetic cornea of claim 1 with a nucleic acid vehicle, wherein the vehicle encodes the agent;
- b) identifying a population of cells comprising the synthetic cornea of step (a) which express the agent encoded by the nucleic acid; and
- c) replacing cornea cells of the subject with transformed cells of the synthetic cornea of step (b),

wherein the replaced cells deliver the agent to the eye of the subject.

36. The method of claim 35, wherein the replacing step comprises replacing the cornea of the subject with the synthetic cornea of step (b).

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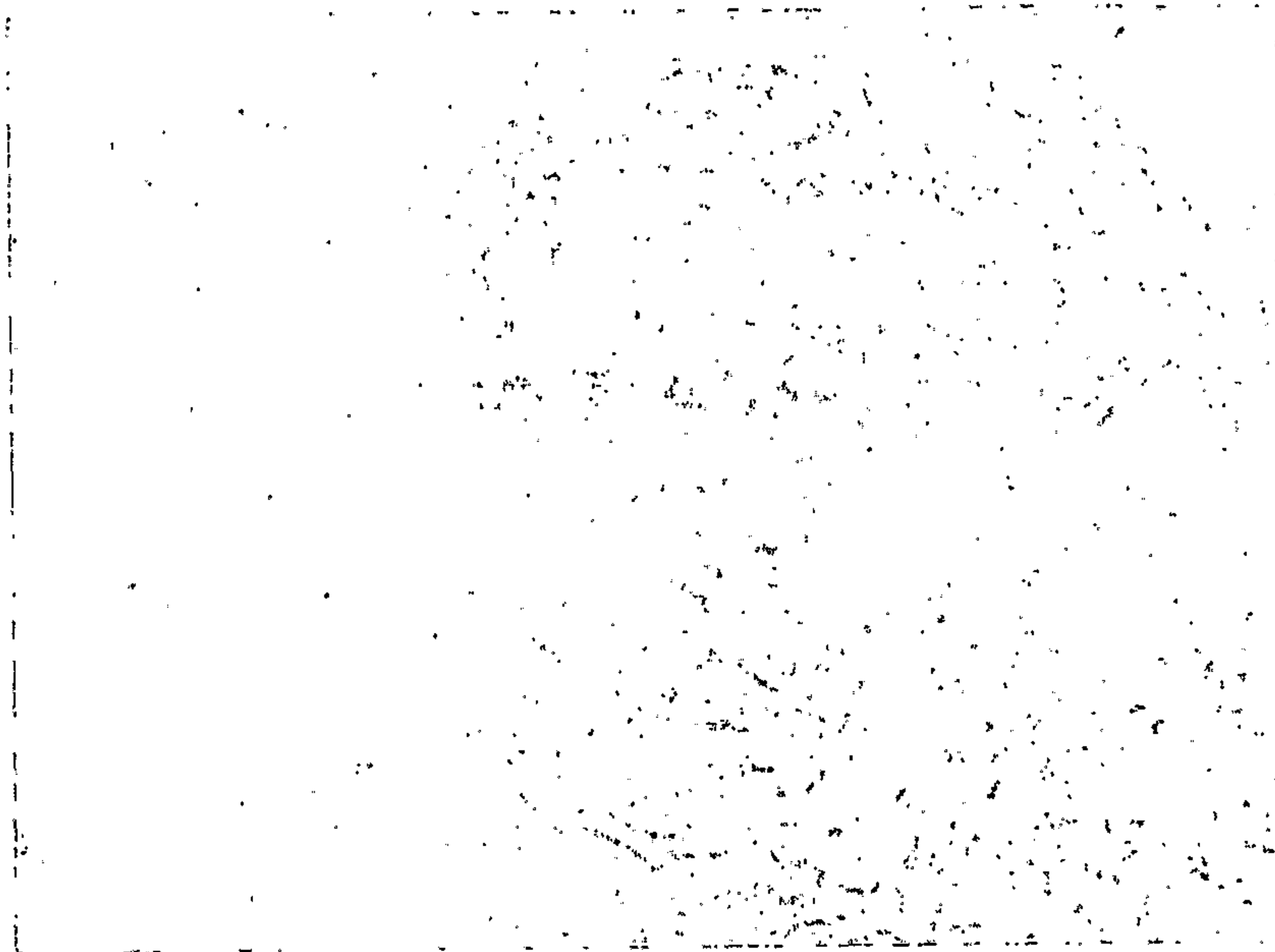


FIG. 1A

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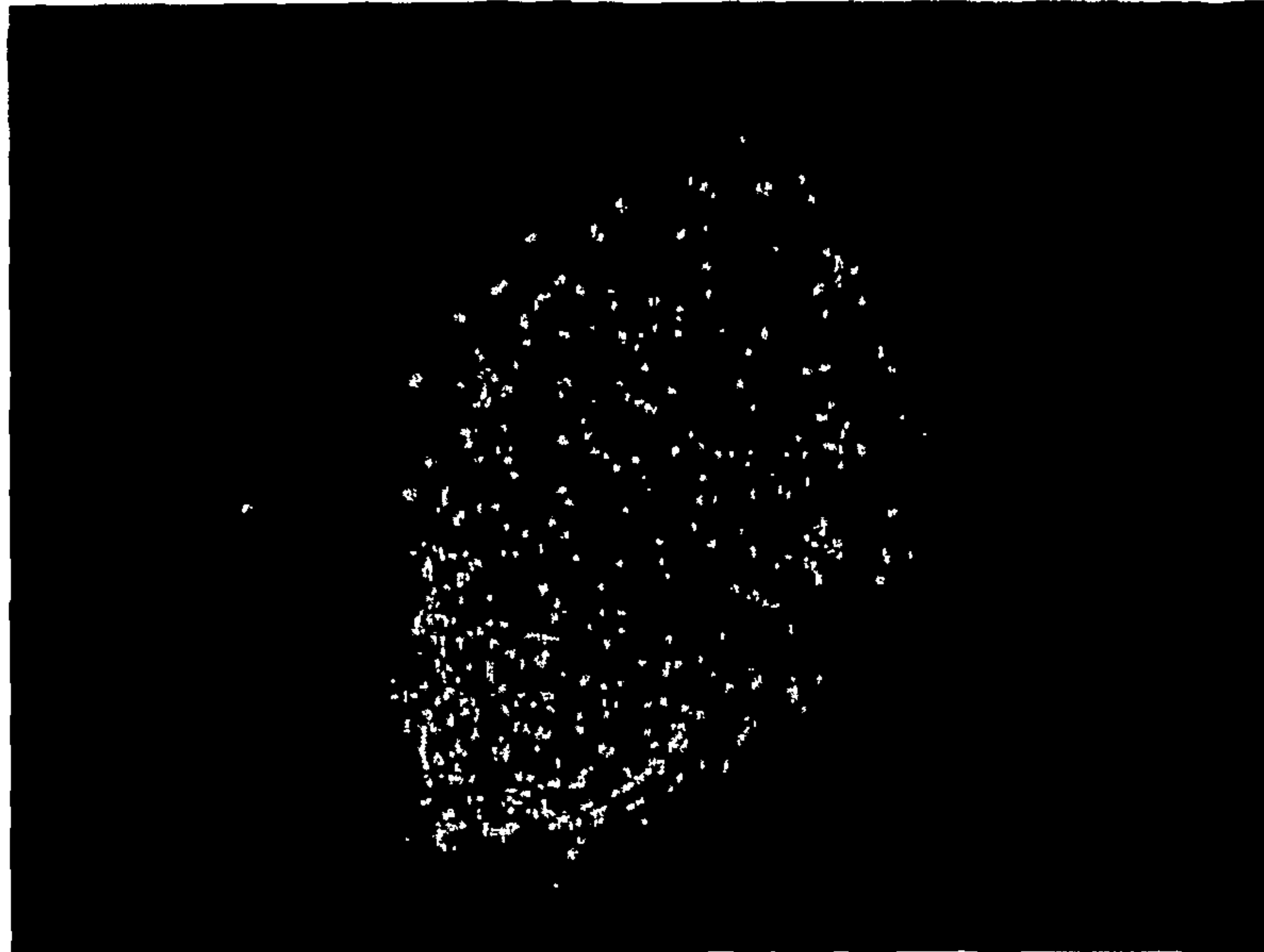


FIG. 1B

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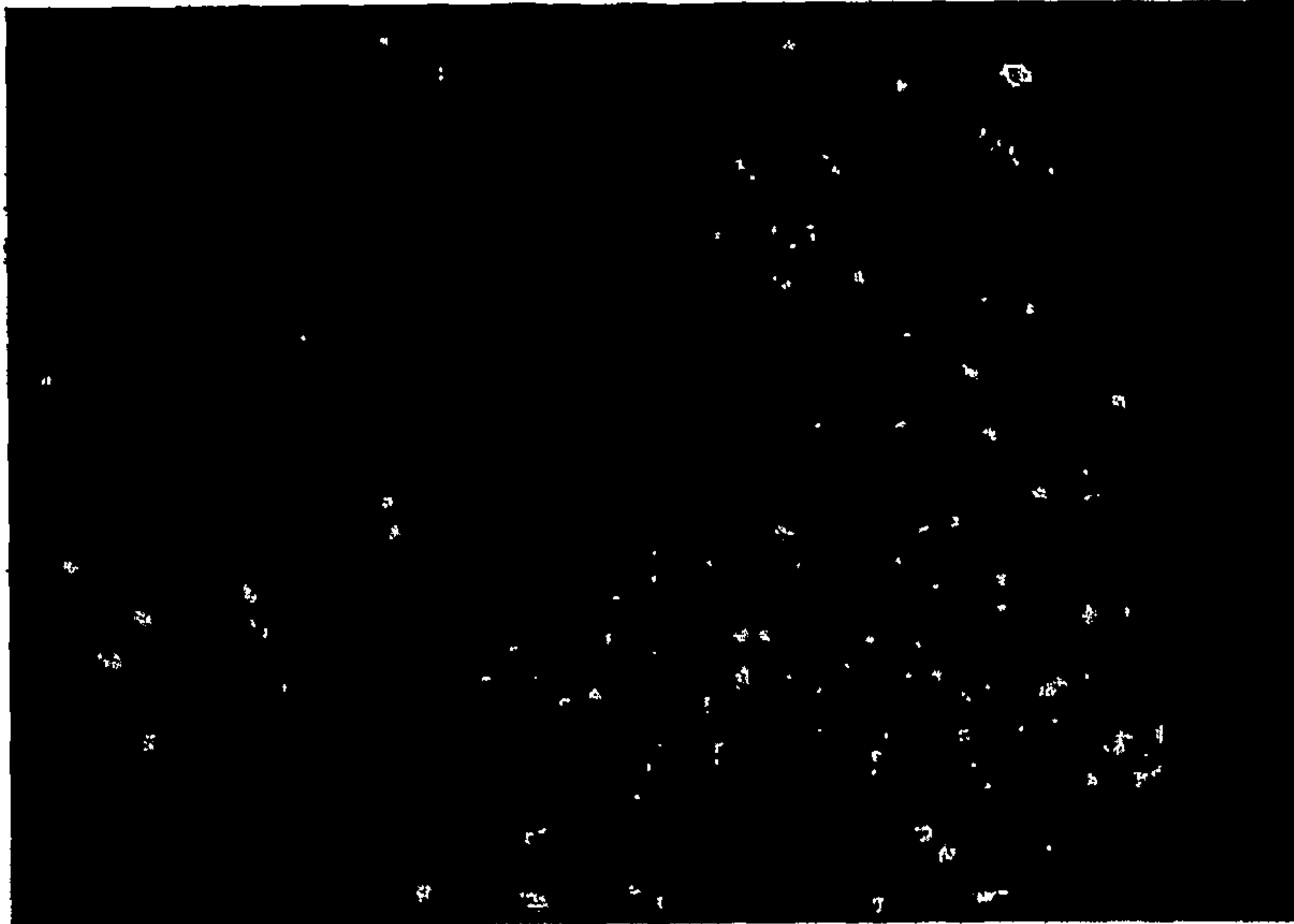


FIG. 1C

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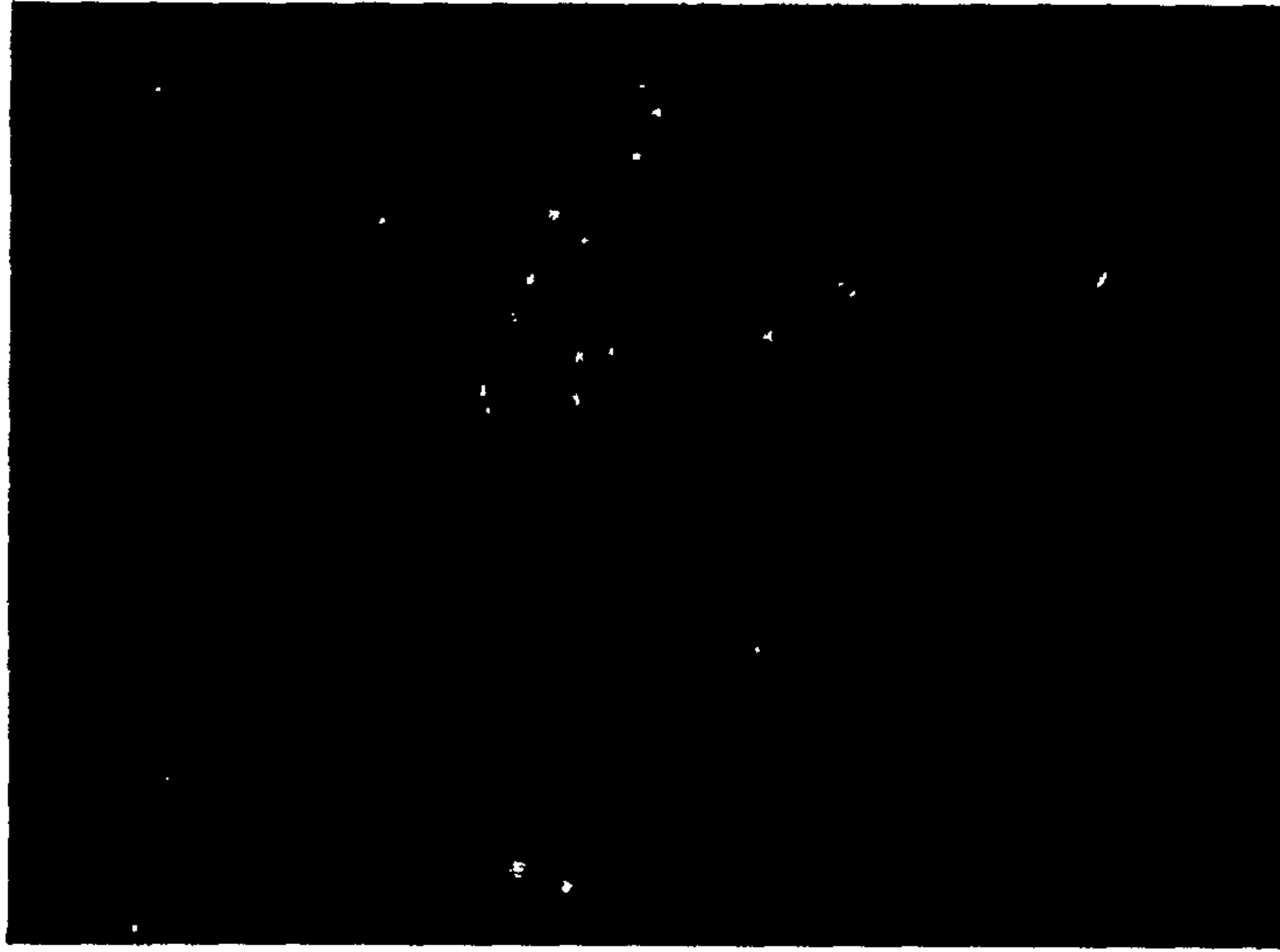


FIG. 1D

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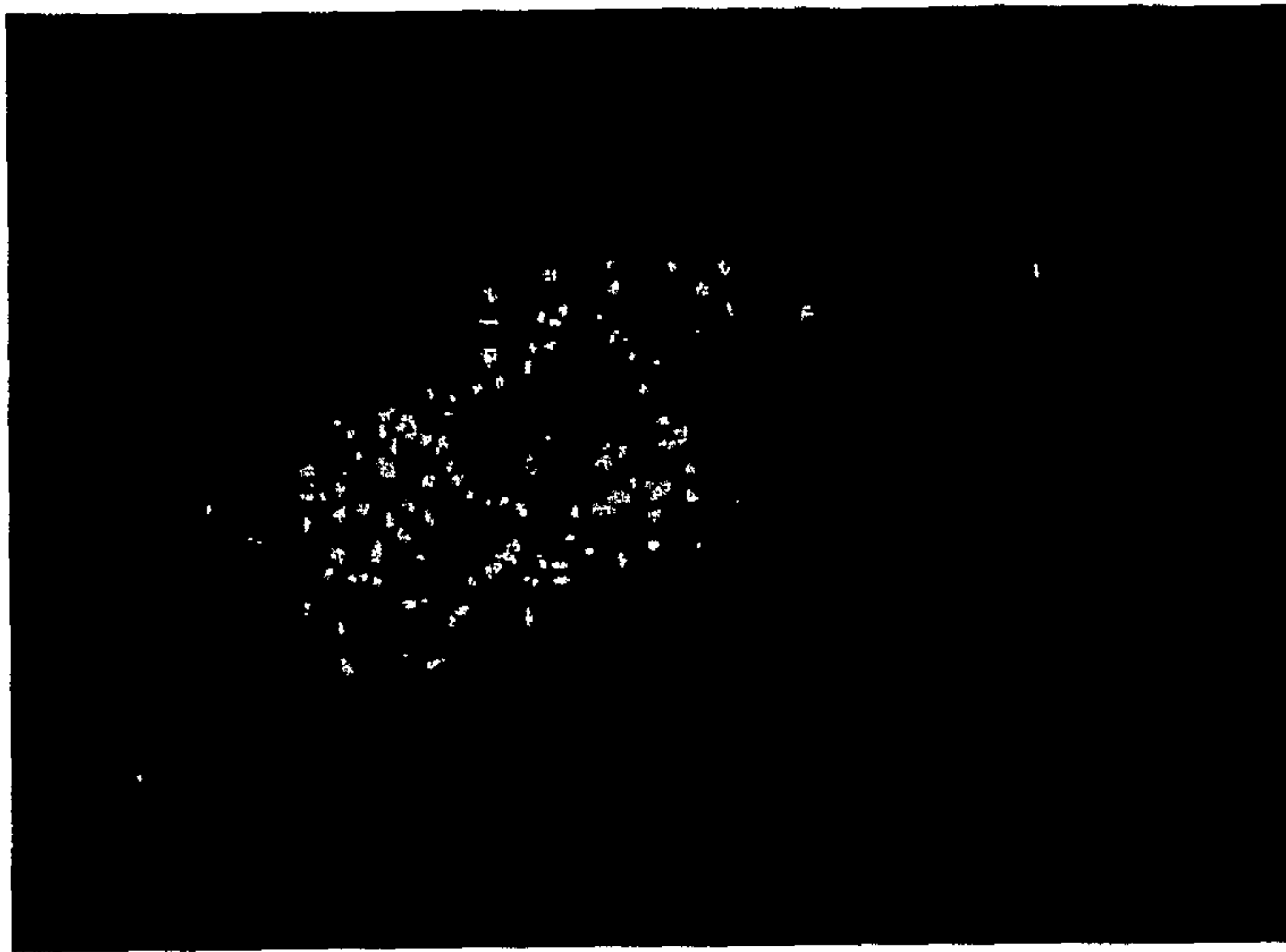


FIG. 1E

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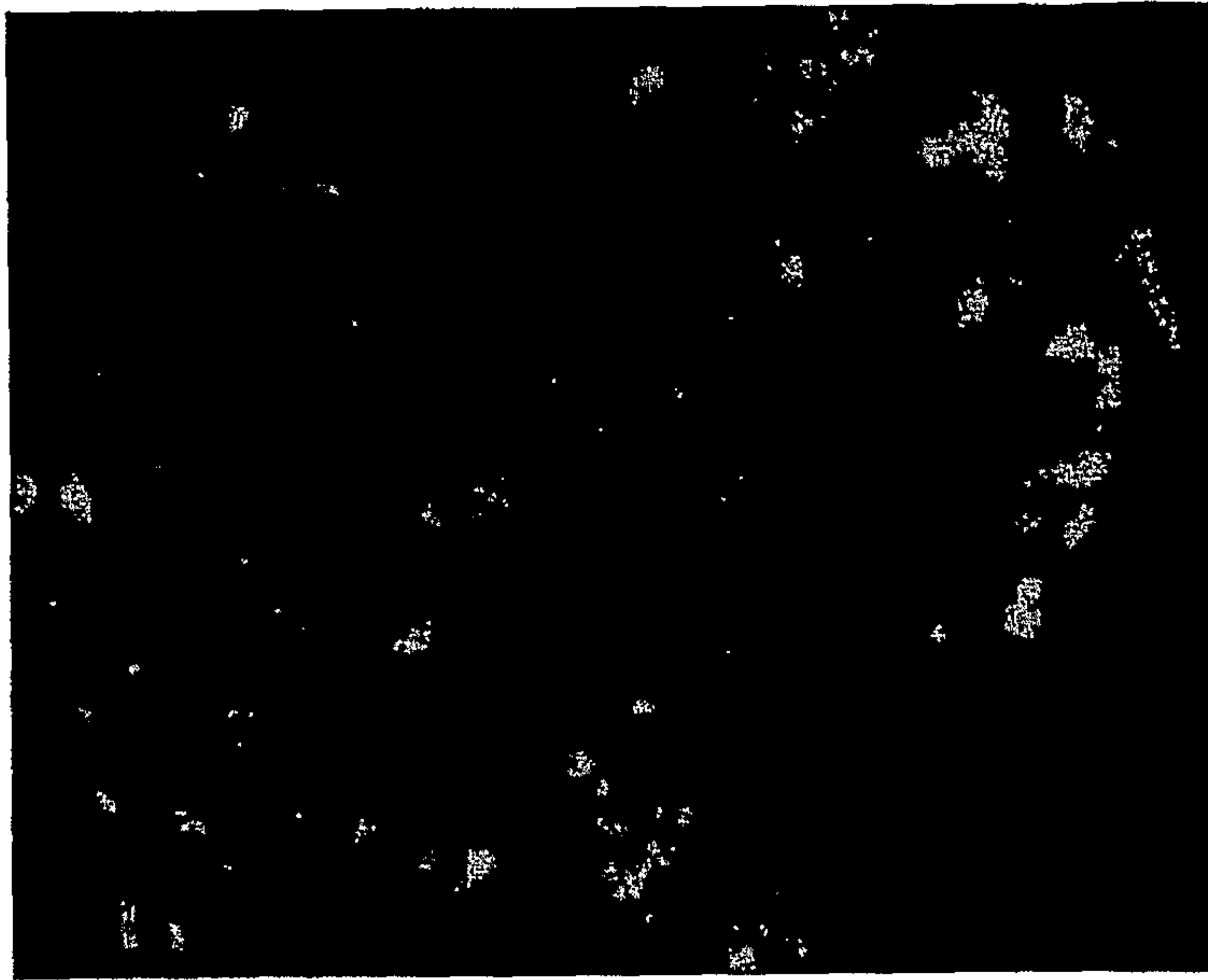


FIG. 1F

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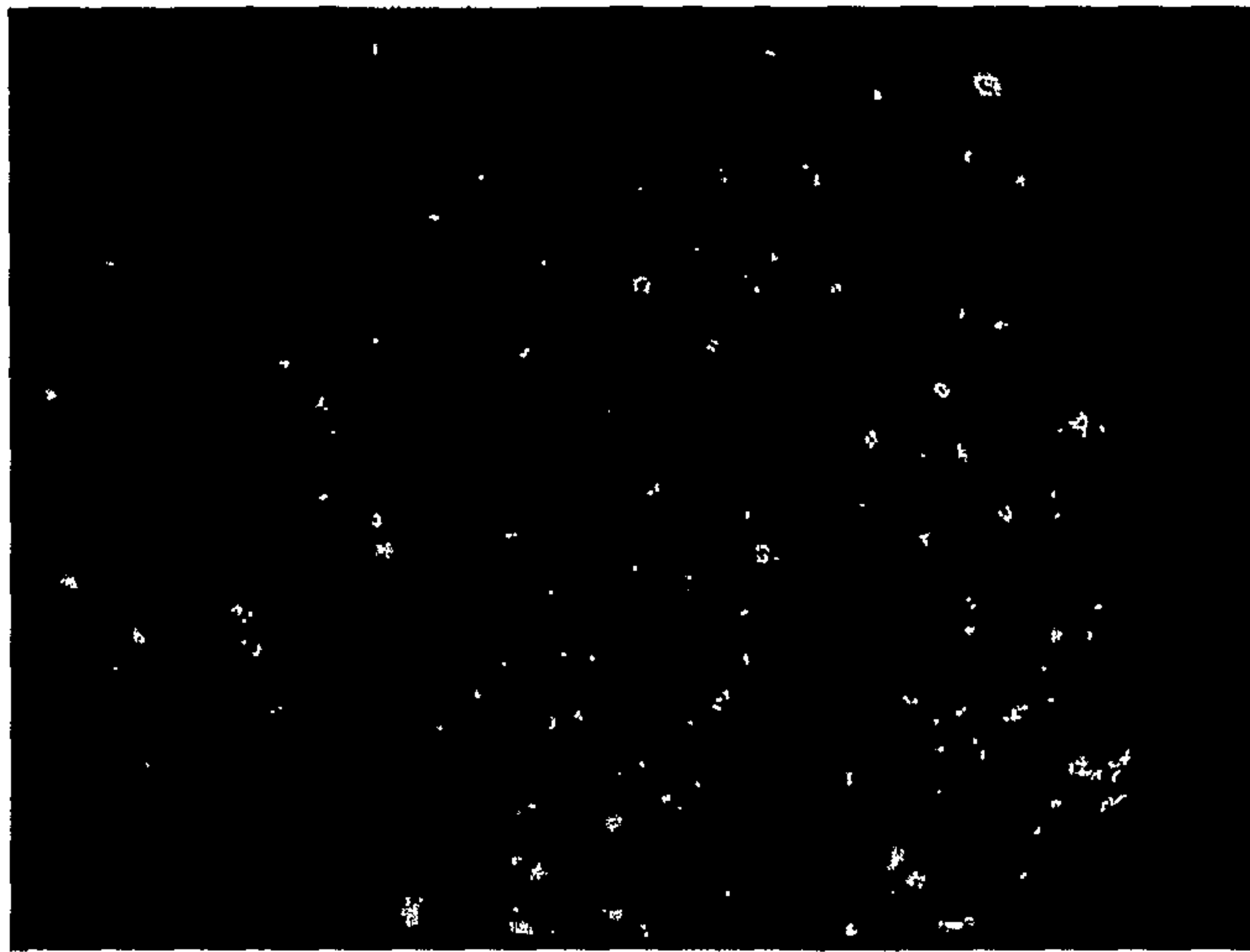


FIG. 1G

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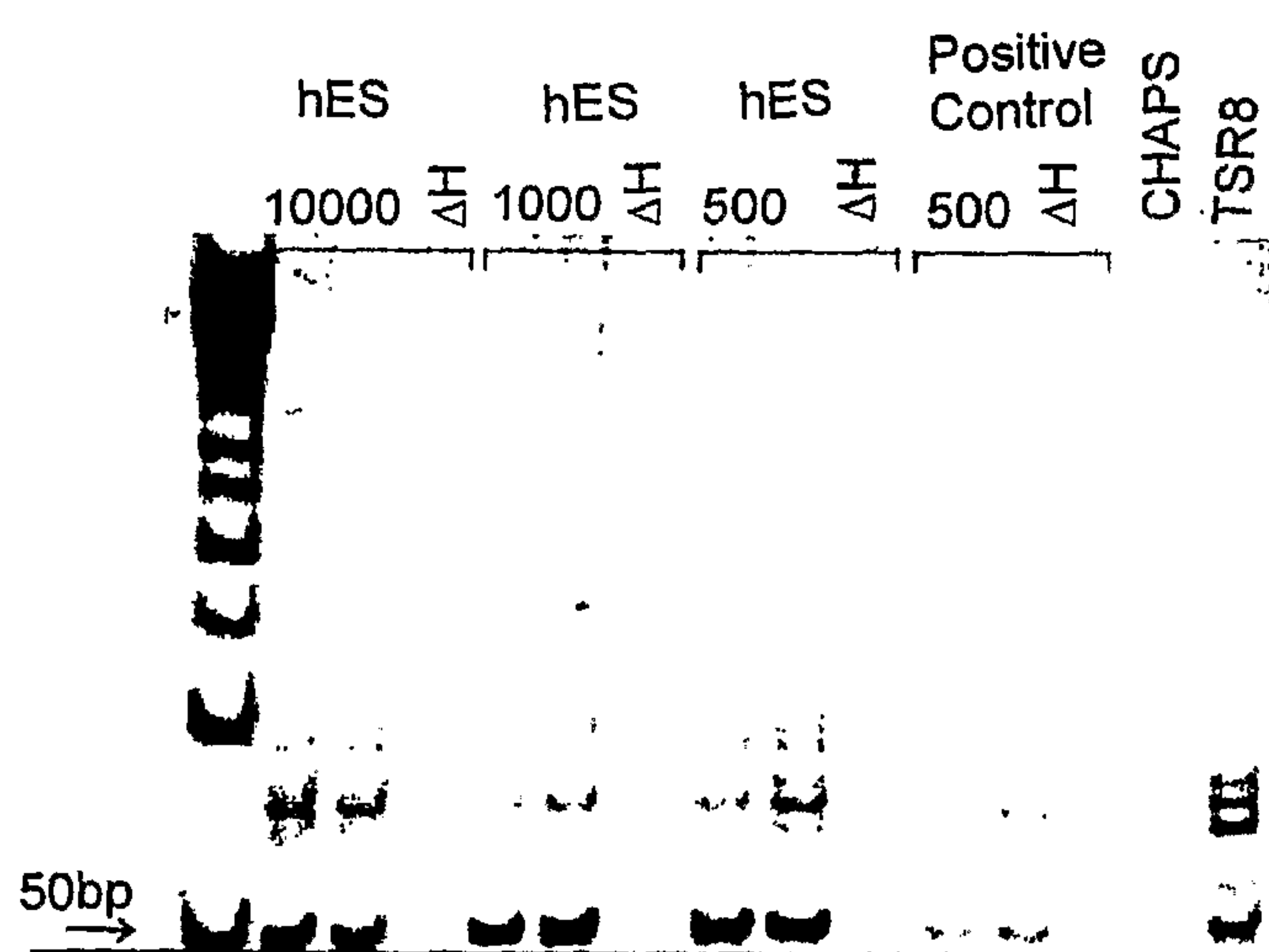


FIG. 2A

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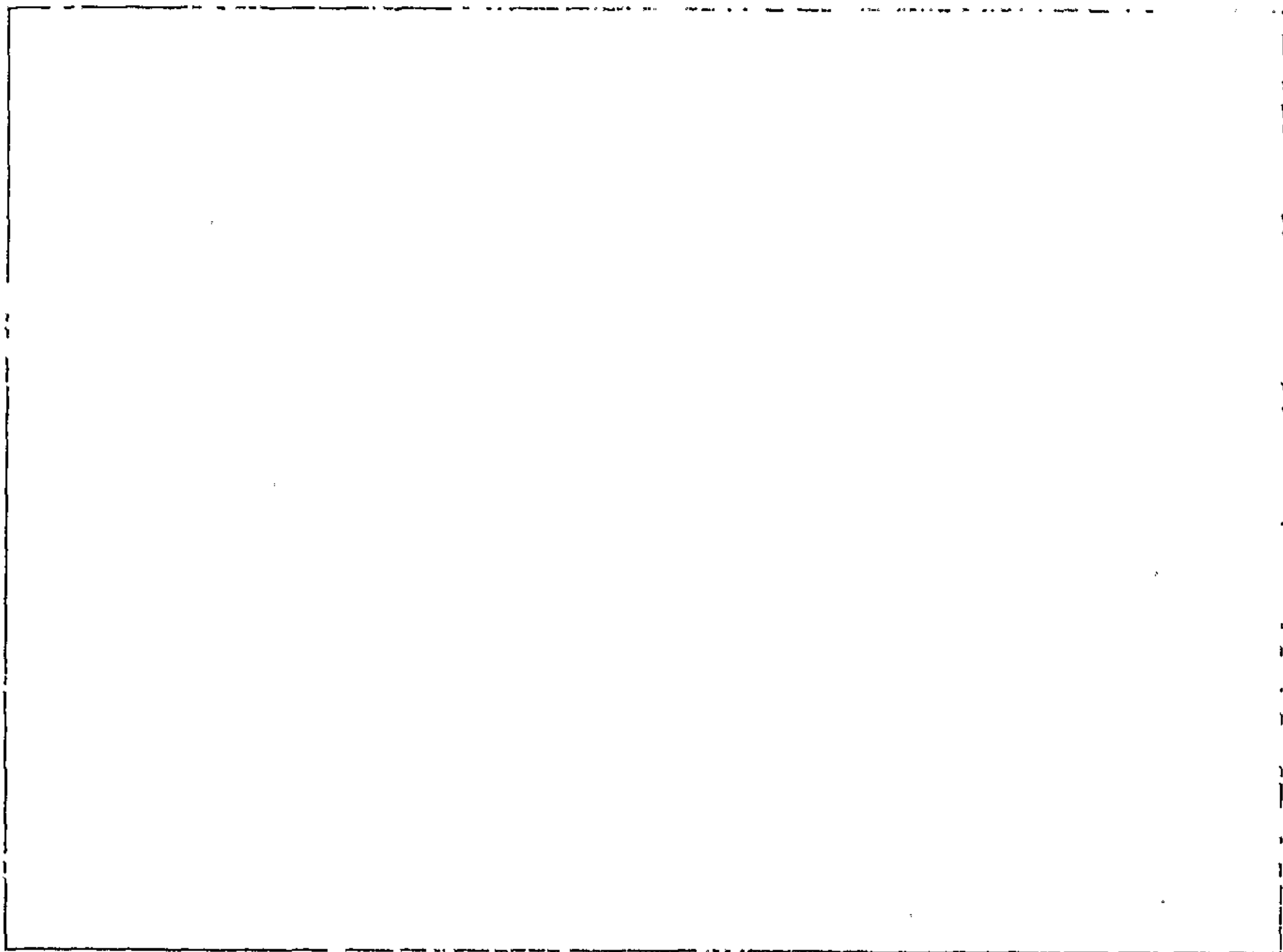


FIG. 2B

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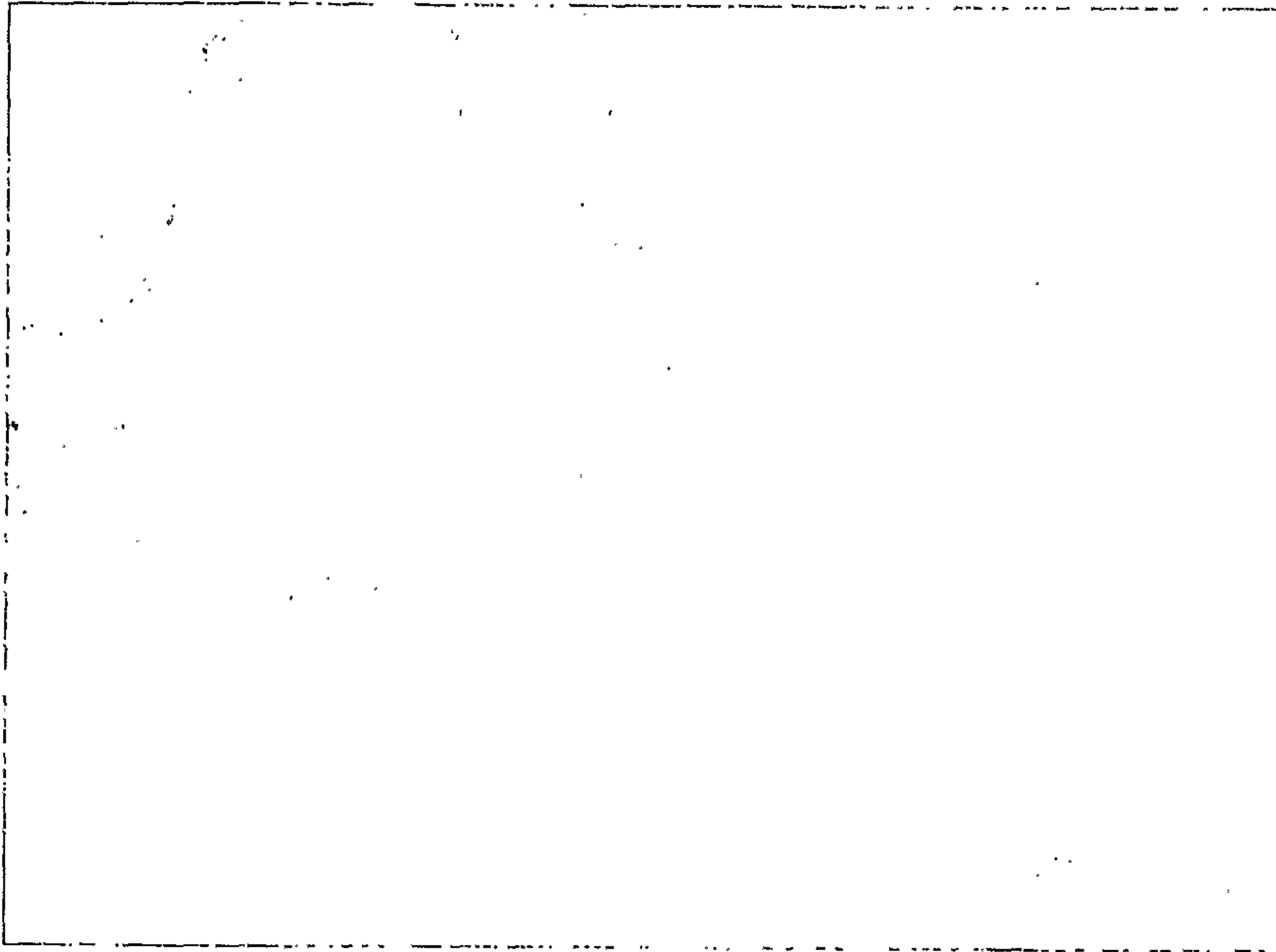
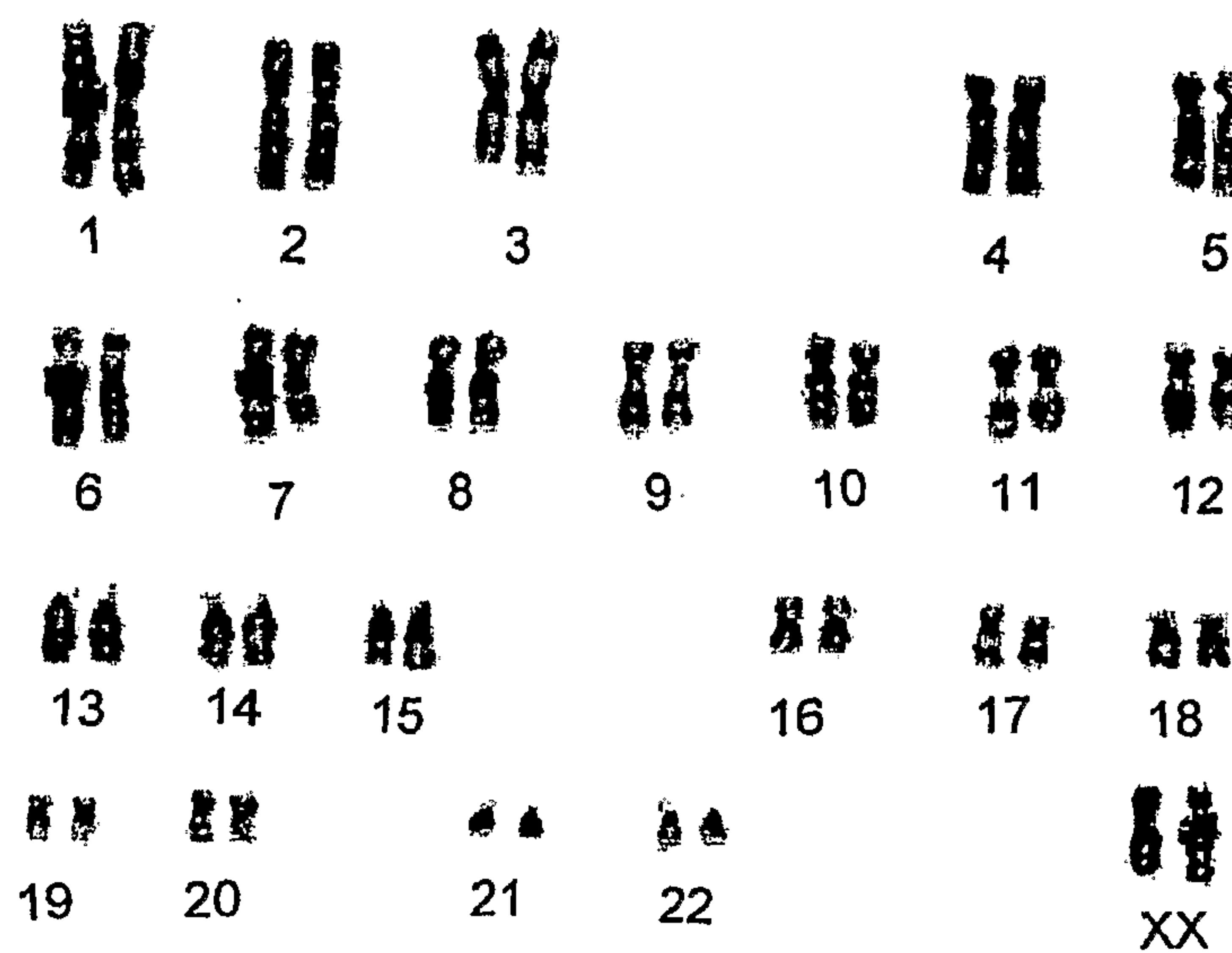


FIG. 2C

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3:ΦX-80

46,XX

FIG. 2D

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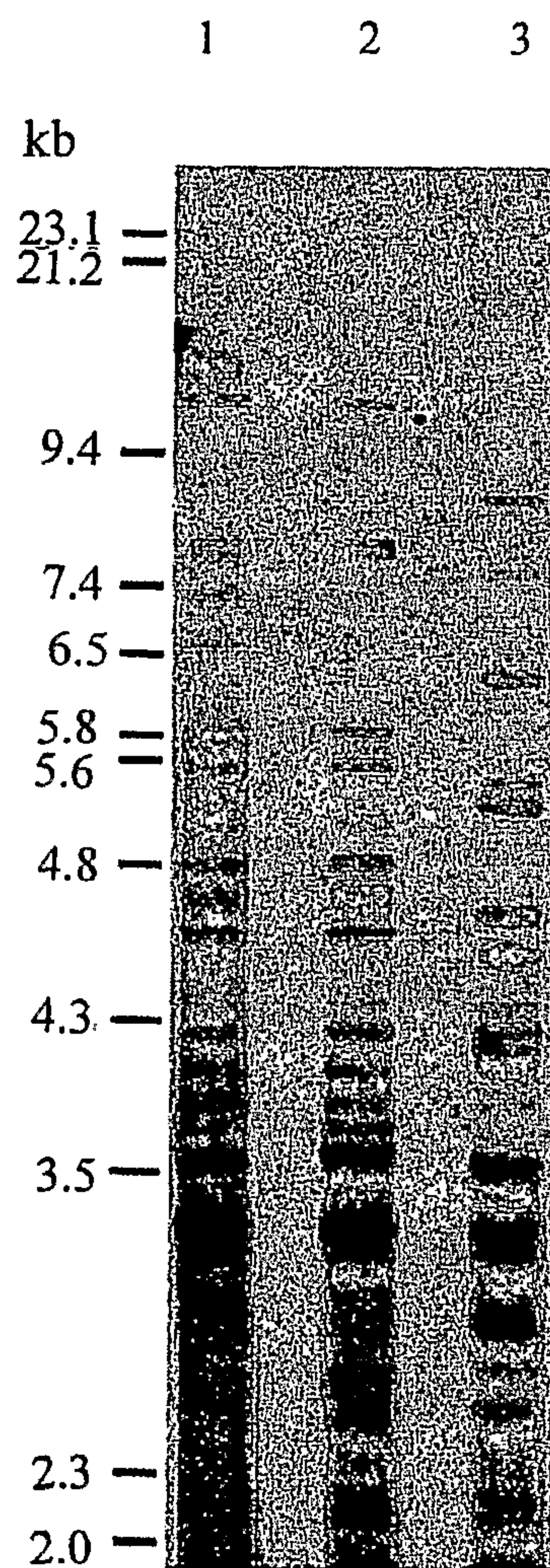
*Hinf*I – (CAC)₅

FIG. 2E

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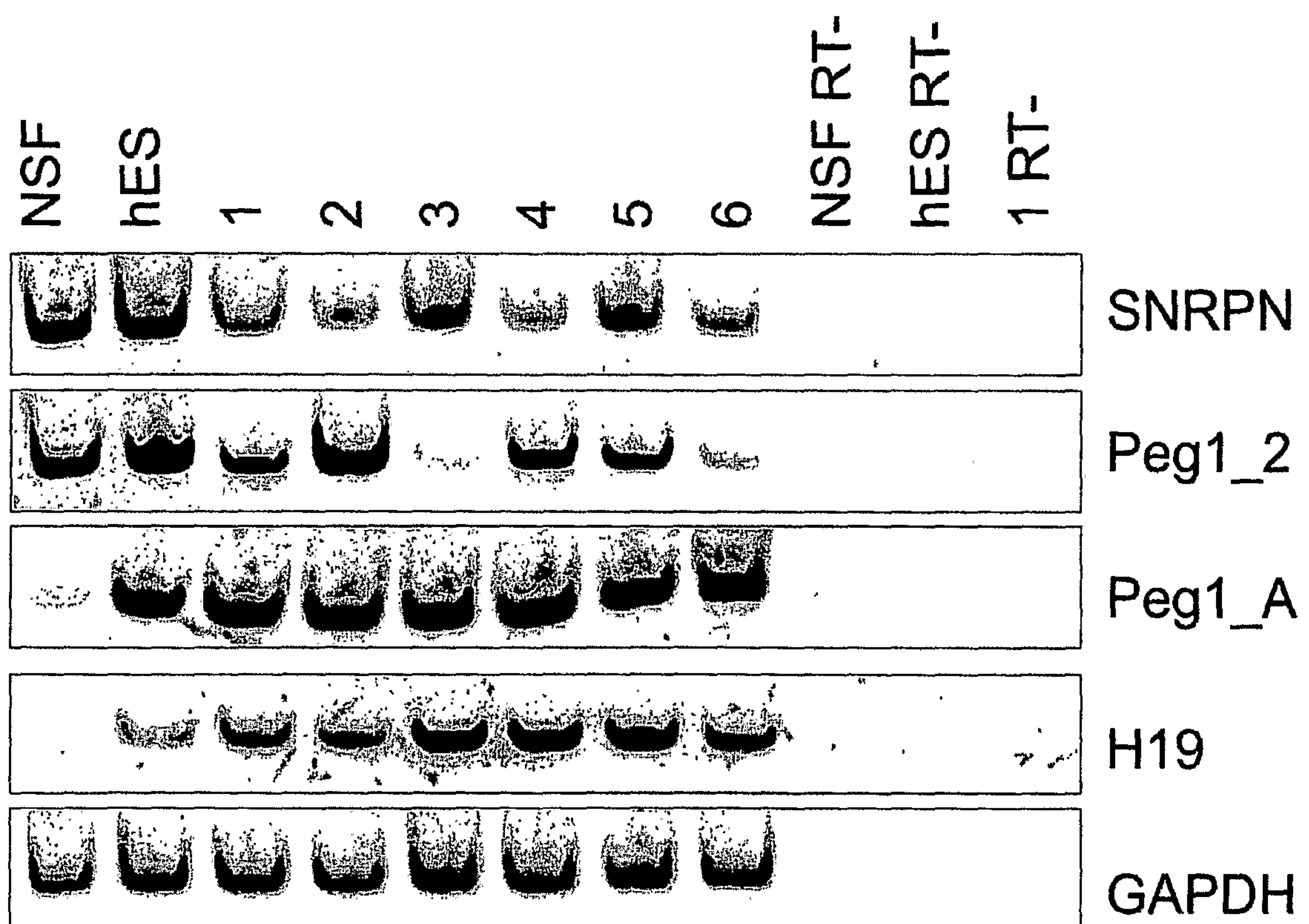


FIG. 3

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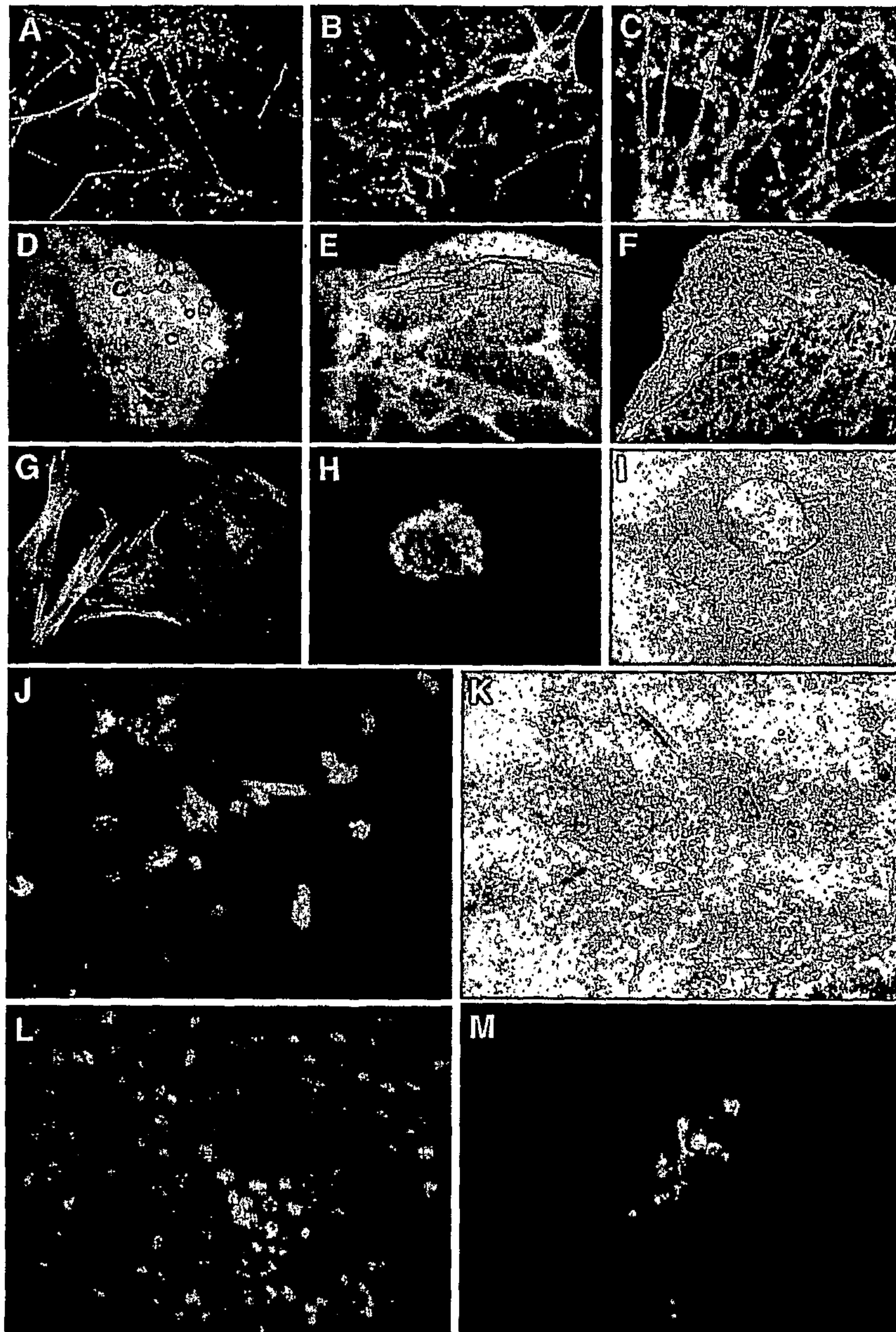


FIG. 4

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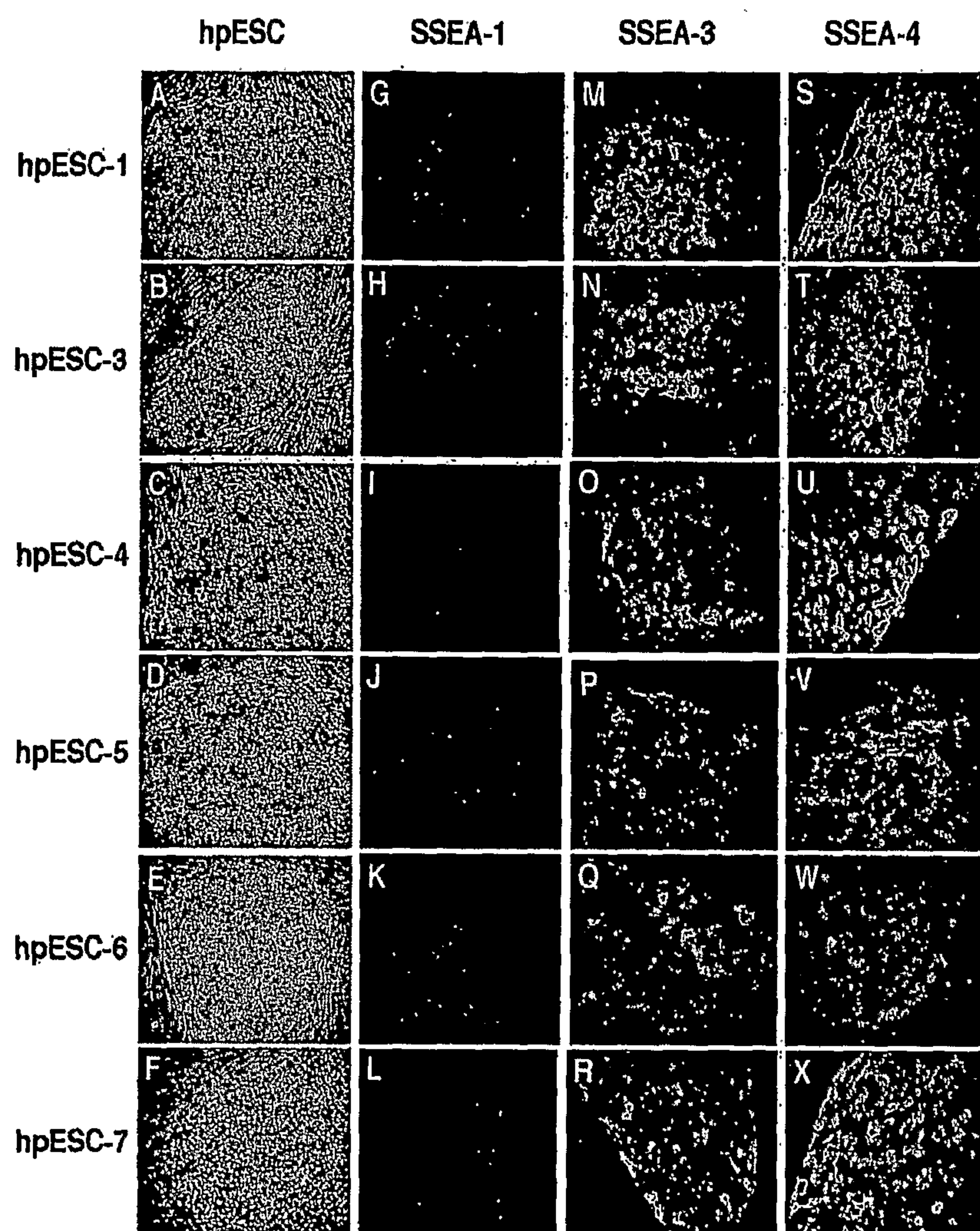


FIG. 5

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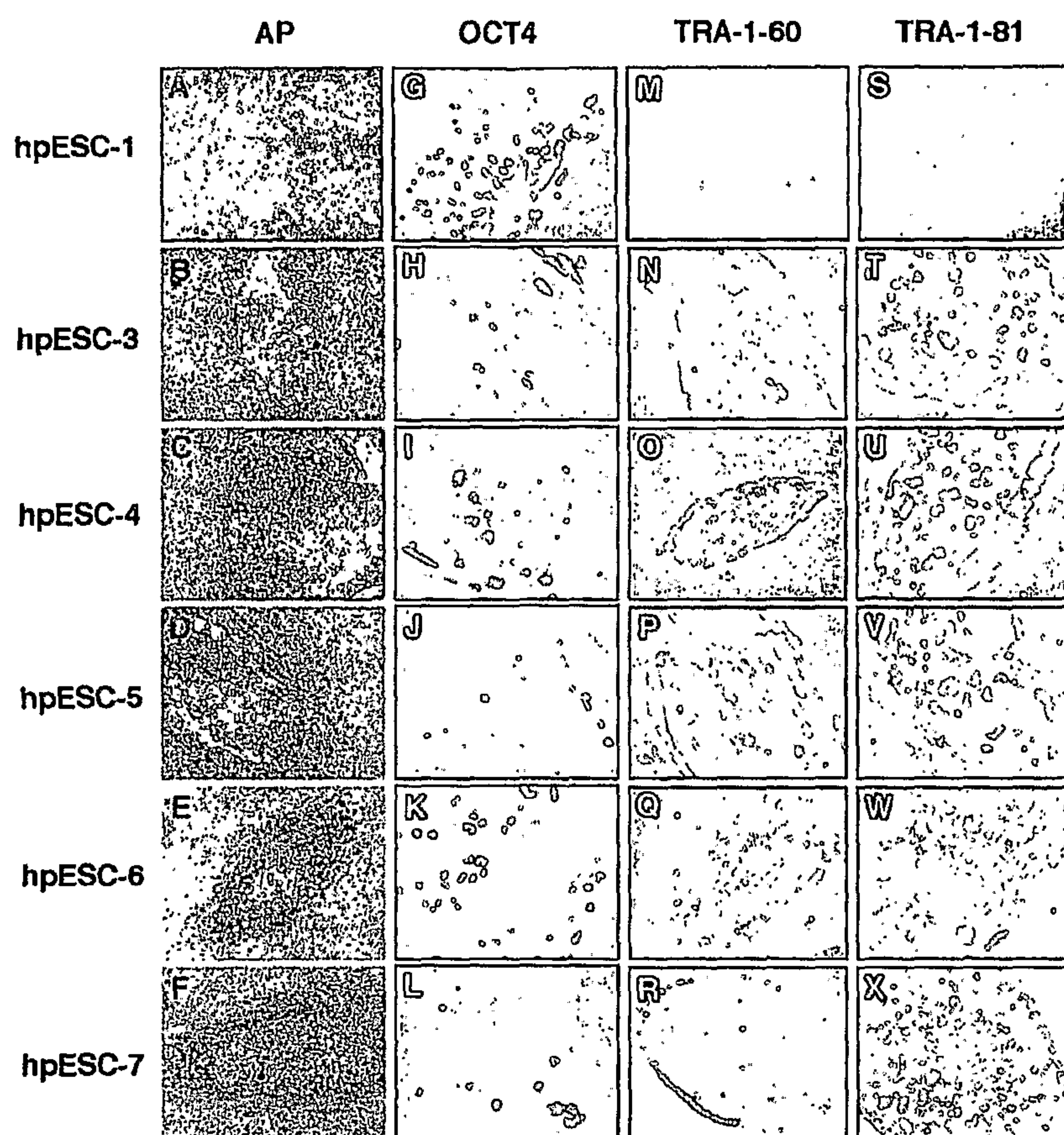


FIG. 5 (cont'd)

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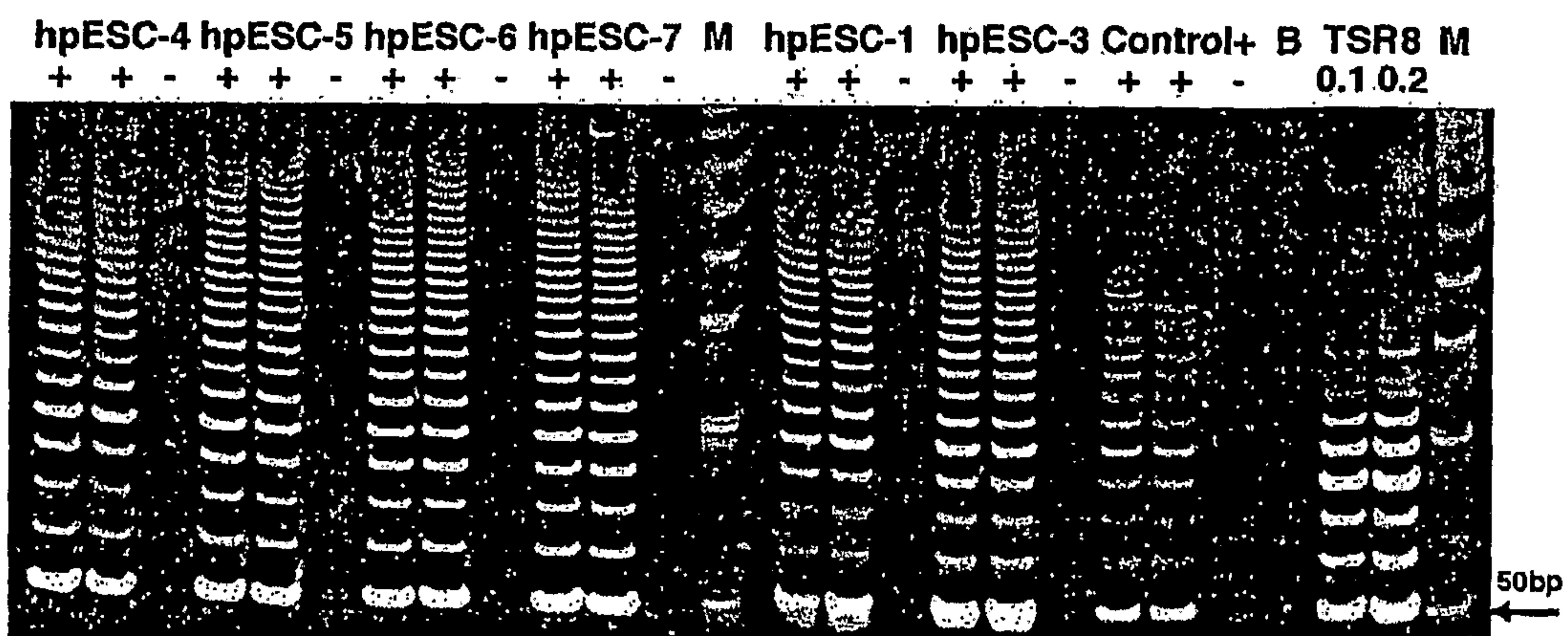


FIG. 6

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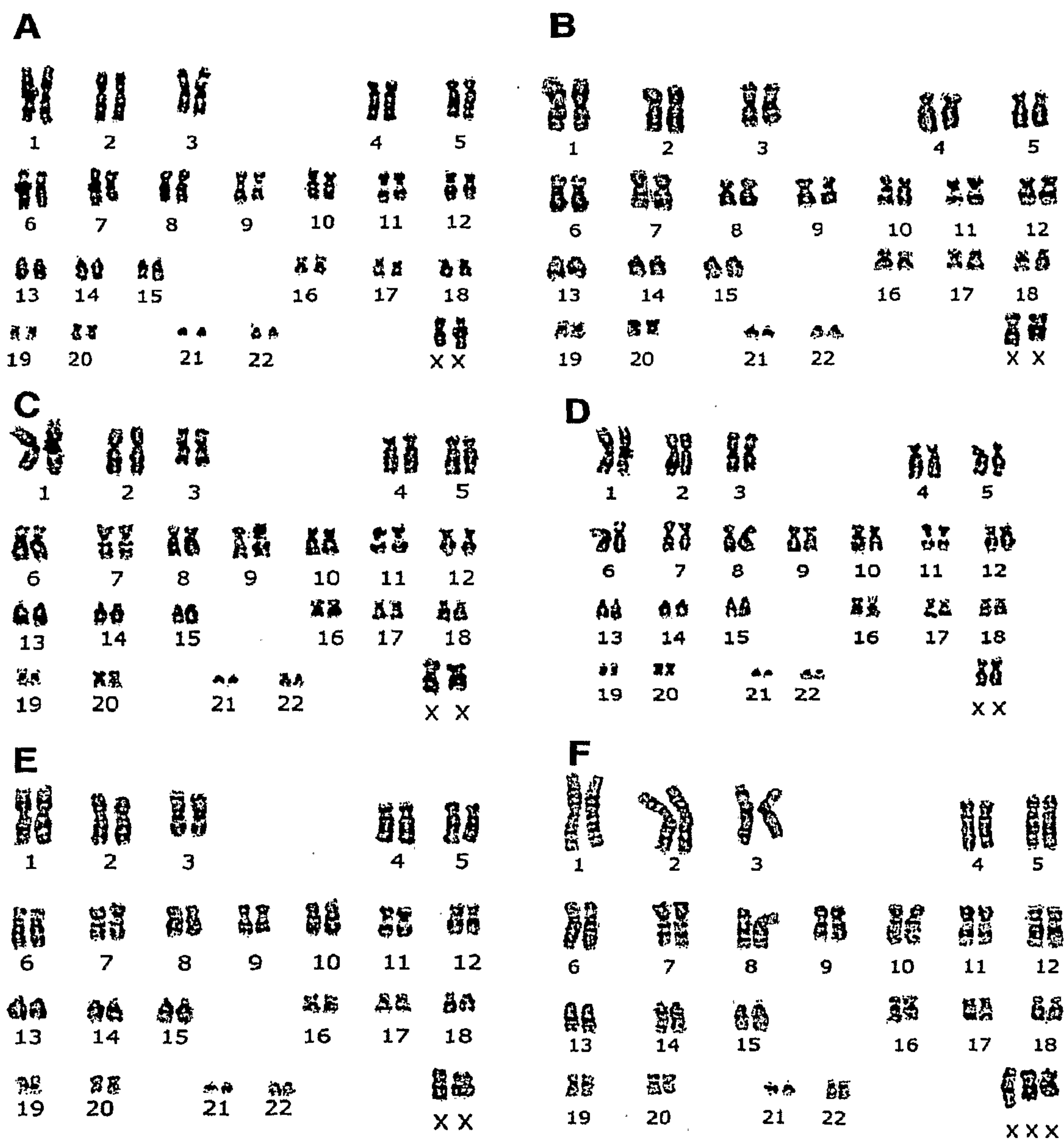


FIG. 7

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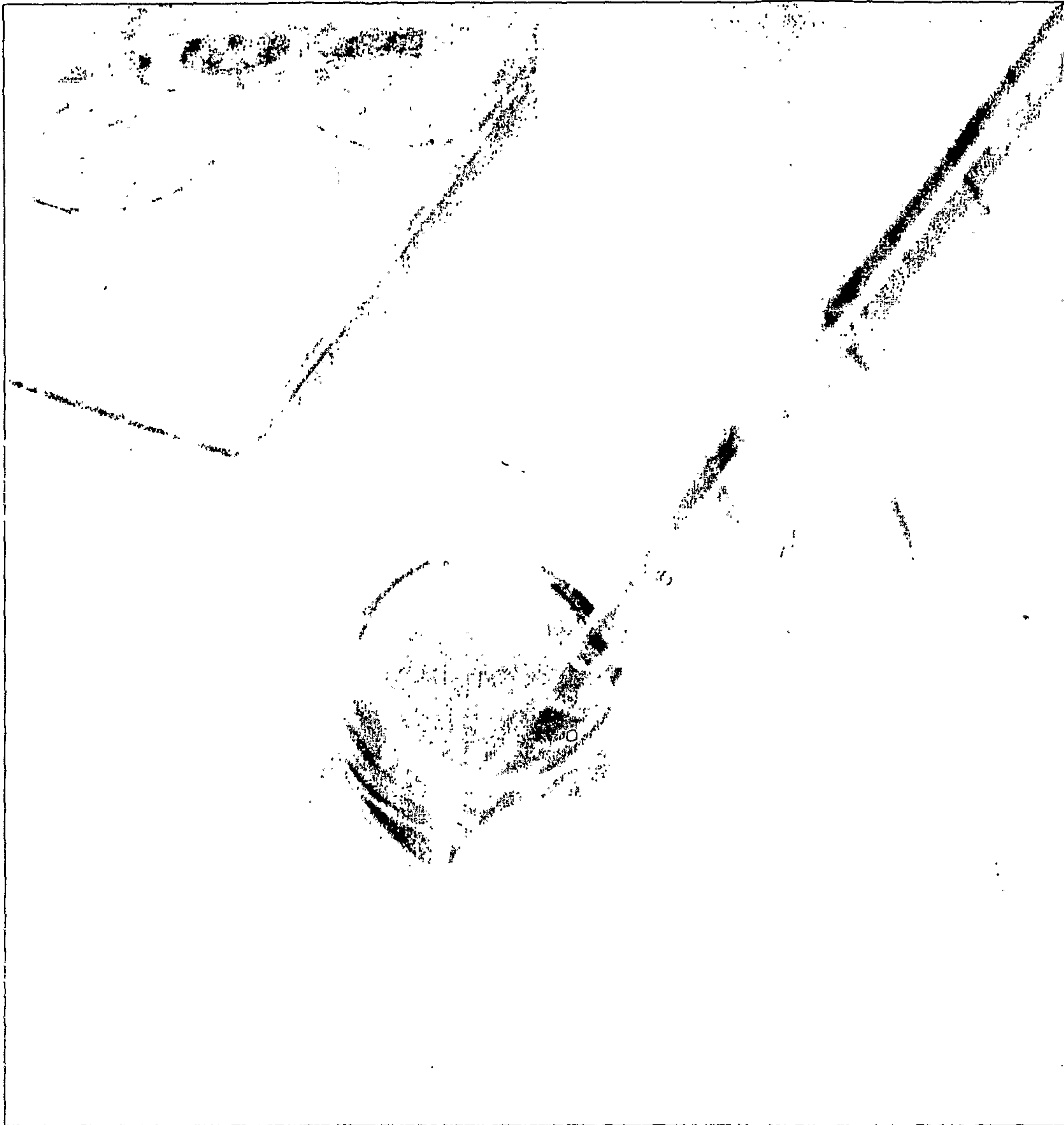


FIG. 8