Claims:

1. A method of generating a mammal cell line of haploid cells comprising obtaining a plurality of haploid cells in an aggregated embryonic stage of development, preferably a blastocyst stage, isolating cells of said plurality, expanding isolated cells of said plurality, selecting and isolating one or more single cells with a haploid genome from said expanded cells, thereby obtaining a cell of a cell line of stably haploid cells, wherein the haploid cells are maintained or grown on feeder cells and subsequently adapted to feeder cell free culture conditions by gradually reducing and removing the feeder cell density.

2. The method of claim 1 further comprising culturing said cells of the cell culture and isolating haploid cells from said cell culture after up to 50 passages and expanding said isolated haploid cells as new continued cell culture.

3. The method of claim 1 or 2 wherein the parental cell is heterozygous or homozygous, preferably heterozygous.

4. A method for generating a pluripotent haploid embryonic stem cell line derived from a parthenogenetic morula or blastocyst, the method comprising:
(a) activating non-fertilized oocytes from a female subject *in vitro* to induce parthenogenetic development;
(b) culturing said activated oocytes of step (a) to generate morulae and/or blastocysts;
(c) isolating embryonic stem cells from said morulae and/or blastocysts of step (b) and, optionally, transferring said embryonic stem cells to a cell culture medium that inhibits differentiation of said embryonic stem cells;
(d) subjecting the embryonic stem cells of step (c) to FACS analysis and identifying and/or enriching embryonic stem cells displaying a haploid DNA content; and
(e) optionally, repeated FACS purification of the embryonic stem cells displaying a haploid DNA content and expansion of said em-

bryonic stem cells,
thereby generating a haploid embryonic stem cell line,
wherein the cells are maintained or grown on feeder cells and subsequently adapted to feeder cell free culture conditions by gradually reducing and removing the feeder cell density.

5. The method of claim 4, wherein said non-fertilized oocytes of step (a) are ***in vitro*** matured oocytes.

6. The method of claim 4 or 5, wherein the oocytes of step (a) are activated by exposure of the oocytes to ethanol (preferably 5%) or strontium chloride ($SrCl_2$) (preferably 25mM).

7. The method of any one of claims 4 to 6 wherein steps (d) and/or (e) is/are repeated at least 5 times.

8. The method of any of claims 1 to 7, wherein the female subject is or the cells are of a mammalian, preferably selected from a human, a non-human primate such as macaca (e.g. Macaca fascicularis, Macaca mulatta) or the genus calithrix or great apes (e.g. gorillas, chimpanzees, and orangutans), a mouse, rat, goat, cat, dog, sheep or camel.

9. The method of any of claims 1 to 8, wherein the haploid embryonic stem cells of said cell line are characterized by having a 1n chromosome set in the G1 phase and a 2n chromosome set in the G2 phase of the cell cycle.

10. The method of any of claims 1 to 9, wherein at least 60 % of the generated embryonic stem cells of said cell line are haploid.

11. The method of any of claims 1 to 10, wherein the haploid embryonic stem cells of said cell line are characterized by expression of one or more of the embryonic stem cell markers Alkaline Phosphatase, Oct4, Sox2, Nanog, Klf4, Rex1, Klf2, cMyc Sall4, and/or SSEA-1.

12. The method of any of claims 1 to 11, wherein the haploid embryonic stem cells of said cell line show stable growth for at least 50 passages.

13. The method of any of claims 1 to 12, wherein the haploid embryonic stem cells of said cell line maintain haploidy for at least 7 passages.

14. The method of any of claims 1 to 13, further comprising differentiating the haploid embryonic stem cells of said cell line.

15. The method of any of claims 1 to 14, further comprising genetically modifying the haploid embryonic stem cells of said cell line.

16. The method of any one of claims 1 to 15, wherein comprising maintaining the cells by culturing inner cell mass, cells derived from the inner cell mass or trophoblasts or blastocyst outgrowths, or wherein isolating cells of said plurality comprises individualizing cells of the multicellular stage, e.g. the entire blastocyst, preferably by trypsinization of the multicellular stage, preferably blastocyst.

17. The method of any one of claims 1 to 16, wherein an individual cell is proliferated and grown into a cell culture (subcloning).

18. The method of any one of claims 1 to 17, wherein the cells are maintained or grown in feeder cell free culture conditions after being maintained on a feeder layer.

19. A cell culture of cells with a hapoid genome, preferably a morula- or blastocyst-derived embryonic stem-like cell line, i) generated by the method of any of claims 1 to 18, which are adapted to feeder cell free culture conditions, or ii) comprising at least 60 % haploid embryonic stem cells, which adapted to feeder cell free culture conditions <u>by gradually reducing and removing the feeder cell density</u>.

20. Any one of the preceding claims, wherein the blastocyst-derived embryonic stem-cells are derived from the inner cell mass (ICM) of the blastocyst or from the trophoblast, preferably Oct4 overexpressing trophoblast.

21. Method for mutation analysis comprising providing a cell of claim 19, preferably a mammal cell, comprising introducing a mutation into a genetic locus of interest in said cell and observing modified activity of the cell related to said genetic locus, preferably wherein one or more genes of interest have been inactivated.

22. A haploid mammal cell of a cell culture according to claim 19 comprising a knock-out of the gene Drosha and/or Rarg.

23. Method of generating cells comprising a phenotype of interest, comprising randomly mutating a plurality of cells of claim 19, preferably mammal cells and selecting cells having the phenotype of interest.

24. Method of claim 23, wherein the phenotype of interest is or cell survival or cell growth when said cells are contacted with a toxin or growth inhibitor.

25. Method of claim 24, where said toxin is ricin.

26. Method of any one of claims 23 to 25, wherein the plurality of cells comprises at least 1000 cells.

27. A haploid cell having a resistance to a toxin, preferably ricin, obtainable by a method of claims 23 to 26.

28. A method of screening a cell for genetic targets having activity in toxin resistance comprising generating cells with a toxin resistance according to claims 24 to 26 further comprising identifying a mutation in said cells having toxin resistance as compared to cells without said random mutation.

29. A method of identifying a therapeutic agent against a toxin, comprising identifying a genetic target according to claim 28 and contacting a therapeutic candidate molecule with said genetic target or the gene product of said target, preferably in an isolated cell, and identifying binding events of the candidate with the genetic target or gene product or modified resistance of the cell to the toxin.

30. The method of claim 29, wherein the toxin is ricin and preferably the genetic target is selected from Gpr107, Fut9, Tcf7l1, Slc35c1, Fgfr2, Galnt2, Mid1, B4galt1, B4galnt3, Plcd3, Ror2, Samd4b, Gcnt2 or Ggta1.