CLAIMS:

1. A method for making a fertile female XY mouse in an F0 generation, comprising:

(a) maintaining a donor XY mouse ES cell in a medium comprising

(i) a base medium, and

(ii) supplements suitable for maintaining mouse ES cells in culture,

wherein the base medium exhibits a characteristic selected from the group consisting of: an osmolality of from 200 mOsm/kg to less than 329 mOsm/kg, a conductivity of about 11-13 mS/cm, a salt of an alkaline metal and a halide in a concentration of about 50-110 mM, a carbonic acid salt concentration of about 17-30 mM, a total alkaline metal halide salt and carbonic acid salt concentration of about 85-130 mM, and a combination of any two or more thereof;

(b) introducing the donor XY mouse ES cell into a host embryo;

(c) gestating the host embryo; and,

(d) obtaining an XY female mouse progeny, wherein upon attaining sexual maturity the XY female mouse is fertile.

2. The method of claim 1, wherein the donor XY mouse ES cell comprises a genetic modification.

3. The method of claim 2, wherein the genetic modification comprises one or more of an endogenous nucleic acid sequence, a substitution of one or more nucleic acids, a replacement of an endogenous nucleic acid sequence with a heterologous nucleic acid sequence, a knockout, and a knock-in.

4. The method of any one of claims 1-3, wherein the genetic modification is a knock-out of a STEAP2 gene.

5. The method of any one of claims 1-4, wherein the base medium exhibits 50 ± 5 mM NaCl, 26 ± 5 mM carbonate, and 218 ± 22 mOsm/kg.

6. The method of any one of claims 1-5, wherein the base medium exhibits about 3 mg/mL NaCl, 2.2 mg/mL sodium bicarbonate, and 218 mOsm/kg.

7. The method of any one of claims 1-4, wherein the base medium exhibits 87 ± 5 mM NaCl, 18 ± 5 mM carbonate, and 261 ± 26 mOsm/kg.

8. The method of any one of claims 1-4 and 7, wherein the base medium exhibits about 5.1 mg/mL NaCl, 1.5 mg/mL sodium bicarbonate, and 261 mOsm/kg.

9. The method of any one of claims 1-4, wherein the base medium exhibits 110 ± 5 mM NaCl, 18 ± 5 mM carbonate, and 294 ± 29 mOsm/kg.

10. The method of any one of claims 1-4 and 9, wherein the base medium exhibits about 6.4 mg/mL NaCl, 1.5 mg/mL sodium bicarbonate, and 294 mOsm/kg.

11. The method of any one of claims 1-4, wherein the base medium exhibits 87 ± 5 mM NaCl, 26 ± 5 mM carbonate, and 270 ± 27 mOsm/kg.

12. The method of any one of claims 1-4 and 11, wherein the base medium exhibits about 5.1 mg/mL NaCl, 2.2 mg/mL sodium bicarbonate, and 270 mOsm/kg.

13. The method of any one of claims 1-4, wherein the base medium exhibits 87 ± 5 mM NaCl, 26 ± 5 mM carbonate, 86 ± 5 mM glucose, and 322 ± 32 mOsm/kg.

14. The method of any one of claims 1-4 and 13, wherein the base medium exhibits about 5.1 mg/mL NaCl, 2.2 mg/mL sodium bicarbonate, 15.5 mg/mL glucose, and 322 mOsm/kg.

15. A method of producing a transgenic mouse homozygous for a genetic modification in the F1 generation, comprising crossing an F0 XY fertile female mouse of any one of claims 1-14 with a cohort F0 XY male mouse, wherein the F0 XY fertile female mouse and the F0 XY male mouse each is heterozygous for the genetic modification, and obtaining a F1 progeny mouse that is heterozygous for the genetic modification.

16. The method of claim 15, wherein the genetic modification comprises one or more of an endogenous nucleic acid sequence, a substitution of one or more nucleic acids, a replacement of an endogenous nucleic acid sequence with a heterologous nucleic acid sequence, a knockout, and a knock-in.

17.The method of claim 16, wherein the F0 XY fertile female mouse is made according to claim 6.

18. A transgenic mouse homozygous for a genetic modification produced according to any one of claims 15-17.

19. A fertile female XY mouse produced according to any one of claims 1-14.

20. The fertile female XY mouse of claim 19, wherein the base medium exhibits 50 ± 5 mM NaCl, 26 ± 5 mM carbonate, and 218 ± 22 mOsm/kg.

CLAIMS

1. A method for making and breeding a fertile female XY mouse in an F0 generation, comprising:

(a) maintaining donor XY mouse ES cells in a medium comprising:

(i) a base medium, and

(ii) supplements suitable for growing the mouse ES cells in culture with maintenance of pluripotency,

wherein the donor XY mouse ES cells do not comprise a Tdy-negative sex reversal genetic modification and wherein the base medium comprises an osmolality of 218 mOsm/kg, a sodium chloride concentration of 50-110 mM and a sodium bicarbonate concentration of 13-25 mM;

(b) introducing a donor XY mouse ES cell from step (a) into a pre-morula stage host mouse embryo;

(c) introducing the host mouse embryo of step (b) into a recipient female mouse and gestating the house mouse embryo;

(d) obtaining an F0 XY mouse progeny comprising a F0 XY phenotypically female mouse, wherein upon attaining sexual maturity the F0 XY female mouse is fertile; and

(e) breeding the F0 XY fertile female mouse to produce progeny.

2. The method of claim 1, wherein the donor XY mouse ES cell comprises a genetic modification.

3. The method of claim 2, wherein the genetic modification comprises a substitution of one or more nucleic acids.

4. The method of claim 2, wherein the genetic modification is a knock-out of a STEAP2 gene.

5. The method of claim 1, wherein the base medium comprises 87 ± 5 mM sodium bicarbonate, and 261 ± 26 mOsm/kg.

6. The method of claim 1, wherein at least 34% of the F0 XY mouse progeny derived from the donor XY mouse ES cell are phenotypically female XY mice.

7. The method of claim 1, wherein at least 15% of the F0 XY mouse progeny derived from the donor XY mouse ES cell are phenotypically female XY mice.

8. The method of claim 1, wherein all of the females derived from the donor XY mouse ES cell in the F0 generation have a XY genotype.

9. The method of claim 1, wherein the breeding comprises crossing the F0 XY fertile female mouse with a cohort F0 XY male mouse, wherein the F0 XY fertile female mouse and the F0 XY male mouse each is heterozygous for a genetic modification, and obtaining an F1 progeny mouse that is homozygous for the genetic modification.