Claims

1. A method for selecting a dosage or a dosage range of~~screening~~ an agent as a drug candidate customised to an individual subject, comprising the steps ~~of~~:

(i) contacting at least one induced pluripotent stem cell (iPSC)-derived cardiomyocyte-like cell derived from said subject with the agent at more than two different dosages; and

(ii) determining the effect of the agent based on changes in at least one electrophysiological property of the iPSC-derived cardiomyocyte-like cell contacted with different dosages of the agent at the different dosages, compared to a control comprising at least one iPSC-derived cardiomyocyte absent the agent to give a dose response curve;~~.~~

and selecting a suitable dosage or dosage range exerting a desired effect on the induced pluripotent stem cell (iPSC)-derived cardiomyocyte-like cell(s) isolated from a subject.

2. The method according to claim 1, wherein the iPSC-derived cardiomyocyte-like cell(s) are derived from human iPSC.

3. The method according to claim 1 or 2, wherein the electrophysiological property comprises the field potential duration (FPD), minimum field potential (FPmin), conduction velocity, beating frequency and/or regularity of beating rhythm.

4. The method according to any one of the preceding claims, wherein the method comprises determining if the agent causes an increase, decrease or no changes in field potential duration (FPD) compared to said control.

5. The method according to any one of claims 1 to 3, wherein the method comprises determining if the agent causes an increase, decrease or no changes in minimum field potential (FPmin) compared to said control.

6. The method according to any one of claims 1 to 3, wherein the method comprises determining if the agent causes an increase, decrease or no changes in conduction velocity compared to said control.

7. The method according to any one of claims 1 to 3, wherein the method comprises determining if the agent causes an increase, decrease or no changes in beating frequency compared to said control.

8. The method according to any one of claims 1 to 3, wherein the method comprises determining if the agent causes a change or no changes in regularity of beating rhythm compared to said control.

9. The method according to any one of the preceding claims, comprising using a multielectrode array or a patch-clamp to measure the electrophysiological properties in step (ii).

10. The method according to any one of claims 1 to 3, wherein the method is for screening for an agent exerting an effect on cardiomyocytes.

11. The method according to claim 10, wherein the method is for screening for an agent exerting any one of the following effects:

(i) increasing the field potential duration (FPD) compared to said control;
(ii) decreasing the field potential duration (FPD) compared to said control;
(iii) increasing the minimum field potential (FPmin) compared to said control;
(iv) decreasing the minimum field potential (FPmin) compared to said control;
(v) increasing the beating frequency compared to said control;

(vi) decreasing the beating frequency compared to said control;
(vii) increasing conduction velocity compared to said control
(viii) decreasing conduction velocity compared to said control; or
(ix) disrupting the regularity of rhythmic waveform compared to said control.

12. The method according to any one of the preceding claims, wherein the method is for screening for a cardiovascular agent, an agent affecting cardiac function and/or an agent for ameliorating, controlling, eliminating, preventing, reducing and/or treating a cardiac condition.

13. The method according to any one of the preceding claims, wherein the method is for screening for anti-arrhythmic agents.

14. The method according to any one of the preceding claims for assessing the cardiotoxicity of the agent.

15. The method according to any one of the preceding claims, for selecting a dosage and/or dosage range of the agent.

16. The method according to any one of the preceding claims, wherein the method is for selecting an agent customised to an individual subject.

17. The method according to claim 16, comprising using cardiomyocyte-like cells derived from Induced pluripotent stem cells from said individual subject to screen for an agent for said individual subject.

18. ~~Induced~~ Use of induced pluripotent stem cell (iPSC)-derived cardiomyocyte-like cell(s) ~~for use~~ in screening an agent as a drug candidate.

19. ~~Induced~~ Use of induced pluripotent stem cell (iPSC)-derived cardiomyocyte-like cell(s) ~~for use~~ in a method according to any one of claims 1 to17.

20. A method for predicting risk of and/or predisposition to cardiac arrhythmia in a subject, comprising:

(i) providing at least one induced pluripotent stem cell (iPSC)-derived cardiomyocyte-like cell derived from the subject;

(ii) contacting the at least one iPSC-derived cardiomyocyte-like cell with a beta-adrenergic agonist;

(iii) further contacting the at least one iPSC-derived cardiomyocyte-like cell from (ii) with a beta-blocker;

(iv) determining a first Beat Rate Variability (BRV) for the at least one iPSC-derived cardiomyocyte-like cell based on changes in at least one electrophysiological property in the at least one iPSC-derived cardiomyocyte-like cell; and

(v) comparing the first BRV to a second BRV for at least one control.

21. The method according to claim 20, wherein if the first Beat Rate Variability is lower than the second Beat Rate Variability, this is indicative of risk of and/or predisposition to cardiac arrhythmia in the subject as compared to a normal individual.

22. The method according to claim 20 or claim 21, wherein the at least one control comprises at least one iPSC-derived cardiomyocyte-like cell derived from a normal individual.

23. The method according to any one of claims 20 to 22, wherein (iv) comprises measuring at least one electrophysiological property in the at

least one iPSC-derived cardiomyocyte-like cell, the at least one electrophysiological property comprising the power spectral density of beat-to-beat or RR intervals, ECG, blood pressure, ballistocardiograms, the pulse wave signal derived from a photoplethysmograph, field potential duration (FPD), minimum field potential (FPmin), conduction velocity, beating frequency and/or regularity of beating rhythm.

24. The method according to any one of claims 20 to 23, wherein (iv) comprises measuring the power spectral density of beat-to-beat or RR intervals in the at least one iPSC-derived cardiomyocyte-like cell.

25. The method according to any one of claims 20 to 24, wherein (iv) comprises measuring at least one electrophysiological property in the iPSC-derived cardiomyocyte-like cell(s) after (ii) and after (iii).

26. The method according to any one of claims 20 to 25, wherein the iPSC-derived cardiomyocyte-like cell(s) are derived from human iPSC.

27. The method according to any one of claims 20 to 26, wherein the beta-adrenergic agonist comprises isoprenaline.

28. The method according to any one of claims 20 to 27, wherein the beta-blocker comprises propranolol.

29. The method according to any one of claims 20 to 28, wherein the beta-blocker comprises atenolol.

30. Induced pluripotent stem cell (iPSC)-derived cardiomyocyte-like cell(s) for use in a method according to any one of claims 20 to 29.