Title of Qualification: Qualification of Cryostem Freezing Medium

Test Material Name and Lot #
Cryostem Serum-free, animal components-free Freezing Medium, lot 1617350

Control Material Name and Lot #
WiCell Cryopreservation Medium 11Nov16SS

Cell Culture Medium Used
- Medium Name: mTeSR1
- Component |
  | Manufacturer | Lot # |
  |---------------|-------|------|
  | Basal Medium | StemCell Technologies | 15J66194 |
  | 5X Supplement | StemCell Technologies | 15J66193 |
  | 250X Supplement | StemCell Technologies | 15J66192 |
  | Human FGF-2 | Waisman Biomanufacturing | WC-FGF2-FP-004 |

Platform/Matrix (MEFs, matrigel, etc)
Matrigel

Technician
[Redacted]

Start and End Dates of Qualification
11Nov16 and 13Dec16

PSC line, lot, and thaw used
IMR90-4-WB0088-T47356

Pre- Karyotype
- Normal Karyotype Sample #: 11978

Post-Karyotype for all three test vials
- Normal Karyotype Sample #: 12049, 12050, and 12051

QC Qualification Sample ID
11931

Experimental design:
Cryostem Serum-free, animal components-free Freezing Medium (lot 1617350) was tested for the ability to appropriately cryopreserve human pluripotent stem cells (PSCs) without affecting the undifferentiated state and expansion rate of the PSCs post thaw. PSCs were cryopreserved using Cryostem Freezing Medium (Test) and WiCell’s standard cryopreservation medium (Control). Both the Cryostem bank and control bank of cells originated from the same parent culture of recently karyotyped cells. Vials from each bank were thawed in triplicate on three separate occasions. Resulting morphology was assessed, as well as plating efficiency and expansion directly out of thaw and following the first passage. Cells were counted on day 1 post-thaw (P1 D1) and immediately pre-passage (P1 D3), as well as day one post passage (P2 D1) and immediately pre-passage at the second passage (P2 D3). In addition, at the conclusion of the assay (P2 D3), all cultures were submitted for karyotype and assayed via flow cytometry to determine the percent of undifferentiated cells. Testing was performed per WiCell’s SOP-QU-005-F, Quality Control Testing of Cell Culture Reagents. Documentation was recorded in notebook 187 pages 190-192 and notebook 190 pages 1-31.

Equipment:
- BioSafety Cabinet
  | 3-digit equipment ID: 089 | Room #: 119 |
- Incubator
  | 3-digit equipment ID: 124 | Room #: 119 |
- Microscope
  | 3-digit equipment ID: 194 | Room #: 119 |
- Micropipettor
  | S/N: F0623217G | Room #: 119 |

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Print Date: 3-Jan-17
Images of PSCs just prior to counting at 2x magnification:

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PID1</td>
<td><img src="image1" alt="Control Image" /></td>
<td><img src="image2" alt="Treatment Image" /></td>
</tr>
<tr>
<td>PID3</td>
<td><img src="image3" alt="Control Image" /></td>
<td><img src="image4" alt="Treatment Image" /></td>
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</tbody>
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Print Date: 3-Jan-17
Proliferation Data:

Average Cells/Well Post Thaw

![Graph showing proliferation data with bars for Control and Treatment groups.]

Marker Expression:

Minimal expression acceptable: ≥ 85% positive for Oct3/4 and SSEA4 markers for undifferentiated PSCs.

![Graph showing undifferentiated marker expression with bars for Control and Treatment groups.]

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Conclusions:
No negative effect on cell proliferation, differentiation, morphology or karyotype was noted for human pluripotent cells cryopreserved using Cryostem Serum-free, Animal Components-free Freezing Medium (lot 1617350). Cells thawed from a lot cryopreserved using Cryostem have met all WiCell requirements for quality. Cryostem equivalent to lot 1617350, when used as directed, is appropriate for use in pluripotent cell culture cryopreservation.

Technician Signature: ___________________________ Date: 03 Jan 17
Reviewer Signature: ___________________________ Date: 03 Jan 17
QA Signature: ___________________________ Date: 04 Jan 17
Chromosome Analysis Report: 054060

Date Reported: Monday, December 12, 2016
Cell Line: iPSC(IMR90)-4-WB49934 12049
Passage#: 44
Date of Sample: 12/7/2016
Specimen: iPSC
Results: 46,XX

Cell Line Gender: Female
Reason for Testing: QC 11931 Cryostem freezing medium 1617350 test vial #3
Investigator:

Cell: 12
Slide: 3
Slide Type: Karyotype

Total Counted: 20
Total Analyzed: 8
Total Karyogrammed: 4
Band Resolution: 500 - 550

Interpretation:
This is a normal karyotype. No clonal abnormalities were detected at the stated band level of resolution.

Completed by:
Reviewed and Interpreted by:
A signed copy of this report is available upon request.

Date:______________  Sent By:____  Sent To:______________  QC Review By:____

Limitations: This assay allows for microscopic visualization of numerical and structural chromosome abnormalities. The size of structural abnormality that can be detected is ≥3-10Mb, dependent upon the G-band resolution obtained from this specimen. For the purposes of this report, band level is defined as the number of G-bands per haploid genome. It is documented here as "band level", i.e., the range of bands determined from the four karyograms in this assay. Detection of heterogeneity of clonal cell populations in this specimen (i.e., mosaicism) is limited by the number of metaphase cells examined, documented here as "% of cells counted".

This assay was conducted solely for listed investigator/institution. The results may not be relied upon by any other party without the prior written consent of the Director of the WiCell Cytogenetics Laboratory. The results of this assay are for research use only. If the results of this assay are to be used for any other purpose, contact the Director of the WiCell Cytogenetics Laboratory.

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Chromosome Analysis Report: 054059

Date Reported: Monday, December 12, 2016
Cell Line: iPS(IMR90)-4-WB49934 12050
Passage#: 44
Date of Sample: 12/7/2016
Specimen: iPSC
Results: 46,XX

Cell Line Gender: Female
Reason for Testing: QC 11931 Cryostem freezing medium 1617350 test vial #2
Investigator:

Interpretation:
This is a normal karyotype. No clonal abnormalities were detected at the stated band level of resolution.

Completed by:
Reviewed and Interpreted by: 

A signed copy of this report is available upon request.

Cell: 14
Slide: 1
Slide Type: Karyotype
Total Counted: 20
Total Analyzed: 8
Total Karyogrammed: 4
Band Resolution: 475 - 575

Date: Sent By: Sent To: QC Review By:

Limitations: This assay allows for microscopic visualization of numerical and structural chromosome abnormalities. The size of structural abnormality that can be detected is >3-10Mb, dependent upon the G-band resolution obtained from this specimen. For the purposes of this report, band level is defined as the number of G-bands per haploid genome. It is documented here as "band level", i.e., the range of bands determined from the four karyograms in this assay. Detection of heterogeneity of clonal cell populations in this specimen (i.e., mosaicism) is limited by the number of metaphase cells examined, documented here as "% of cells counted".

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Chromosome Analysis Report: 054058

Date Reported: Monday, December 12, 2016
Cell Line: iPS(IMR90)-4-WB49934 12051
Cell Line Gender: Female
Passage#: 44
Reason for Testing: QC 11931 Cryostem freezing medium 1617350 test vial #1
Date of Sample: 12/7/2016
Specimen: iPSC
Investigator:
Results: 46,XX

Cell: 35
Slide: 2
Slide Type: Karyotype

Total Counted: 20
Total Analyzed: 9
Total Karyogrammed: 4
Band Resolution: 500 - 550

Interpretation:
This is a normal karyotype. No clonal abnormalities were detected at the stated band level of resolution.

Completed by:
Reviewed and Interpreted by:

A signed copy of this report is available upon request.

Date: ________________  Sent By: ___  Sent To: ________________  QC Review By: ___

Limitations: This assay allows for microscopic visualization of numerical and structural chromosome abnormalities. The size of structural abnormality that can be detected is >3-10M, dependent upon the G-band resolution obtained from this specimen. For the purposes of this report, band level is defined as the number of G-bands per haploid genome. It is documented here as “band level”, i.e. the range of bands determined from the four karyograms in this assay. Detection of heterogeneity of karyotypic cell populations in this specimen (i.e., mosaicism) is limited by the number of metaphase cells examined, documented here as “# of cells counted”.

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