CRM Induced Pluripotent Stem (iPS) Cell Material Transfer Agreement

I. Parties:

1. PROVIDER: Center for Regenerative Medicine, National Institutes of Health, Bethesda, MD (NIH/CRM), a trans-NIH initiative administratively housed within the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)/NIH.

2. RECIPIENT: _____

3. RECIPIENT SCIENTIST: _____

II. Definitions:

1. COMMERCIAL PURPOSES: The use, sale, lease or license of a material for fee in connection with any business or undertaking intended for profit.

2. INDUCED PLURIPOTENT STEM CELLS ("iPS CELLS"): Adult cells (such as skin cells or lymphoblasts) "reprogrammed" to assume an embryonic stem cell-like state, by being forced to express genes and factors important for maintaining the defining properties of embryonic stem cells.

3. MATERIAL(S): ORIGINAL MATERIAL, PROGENY, and UNMODIFIED DERIVATIVES.

4. MODIFIED DERIVATIVES: Substances that are not intact cells that RECIPIENT isolated or derived from NON-PLURIPOTENT MODIFICATIONS or PLURIPOTENT MODIFICATIONS and that are not UNMODIFIED DERIVATIVES.

5. NON-PLURIPOTENT MODIFICATIONS: Cells that are created by the RECIPIENT from ORIGINAL MATERIAL, PROGENY or PLURIPOTENT MODIFICATIONS, but only if such cells are NOT capable of responding to extrinsically acting cues (such as growth factors, changing media conditions, and other similar cues) to differentiate into various cell types from each of the three embryonic germ layers (endoderm, ectoderm, mesoderm). For clarity, NON-PLURIPOTENT MODIFICATIONS may be multipotent, restricted progenitor cells, or may be terminally differentiated cells, but are NOT pluripotent. NON-PLURIPOTENT MODIFICATIONS may or may not have been genetically manipulated by the RECIPIENT in the manner described in the definition of PLURIPOTENT MODIFICATIONS.

   ORIGINAL MATERIAL(S): The iPS CELLS provided by the PROVIDER to the RECIPIENT, as described in Appendix ONE.

6. PLURIPOTENT MODIFICATIONS: iPS CELLS that are created by the RECIPIENT from ORIGINAL MATERIAL or PROGENY. PLURIPOTENT MODIFICATIONS differ from ORIGINAL MATERIAL and PROGENY as a result of a manipulation (genetic or otherwise) to the ORIGINAL MATERIAL or PROGENY performed by the RECIPIENT. Some examples of such genetic manipulations include: integration of a reporter gene, or correction of a genetic defect of the ORIGINAL MATERIAL. For clarity, PLURIPOTENT MODIFICATIONS are capable of self-renewal in culture and of responding to extrinsically acting cues (such as growth factors, changing media conditions, and other similar cues) to differentiate into various cell types from each of the three embryonic germ layers (endoderm, ectoderm, mesoderm).

7. PROGENY: Unmodified descendant iPS Cells from the ORIGINAL MATERIAL. Progeny retain the ability to self-replicate and the ability to differentiate into cell types from all three germ layers.

8. THIRD PARTY or THIRD PARTIES: Any person or entity that is not a PARTY to this AGREEMENT and is not a RECIPIENT.

9. UNMODIFIED DERIVATIVES: Substances that are not intact cells that RECIPIENT either: (a) isolated or derived from ORIGINAL MATERIAL, PROGENY or other UNMODIFIED DERIVATIVES or (b) isolated or derived from NON-PLURIPOTENT MODIFICATIONS, PLURIPOTENT MODIFICATIONS or MODIFIED DERIVATIVES that are indistinguishable from substances that could have been isolated or derived from ORIGINAL MATERIAL, PROGENY or other UNMODIFIED DERIVATIVES.

III. Terms and Conditions of this Agreement:

1. The RECIPIENT agrees that the MATERIAL:

   (a) will not be used in human subjects, in clinical trials, or for diagnostic purposes involving human subjects without the written consent of the PROVIDER;

   (b) will be used only in compliance with applicable laws and regulations;

   (c) will, in the case of entities receiving funding from agencies of the United States to conduct human stem cell research, be used only in compliance with applicable National Institutes of Health Guidelines on Human Stem Cell Research: http://stemcells.nih.gov/policy;

   (d) will not be used in research in which the MATERIALS are introduced into non-human primate blastocysts;

   (e) will not be used in research involving the breeding of animals where the introduction the MATERIALS may contribute to the germ line; and

(f) is subject to the additional terms and conditions in the appendices attached hereto.

2. The RECIPIENT acknowledges that the MATERIAL may be the subject of a patent application or covered by patent rights in one or more countries. Except as provided in this Agreement, no express or implied licenses or other rights are provided to use the MATERIAL, NON-PLURIPOTENT MODIFICATIONS, PLURIPOTENT MODIFICATIONS, MODIFIED DERIVATIVES or any related patents for COMMERCIAL PURPOSES.

3. No ownership rights to the MATERIAL, including any MATERIAL contained or incorporated in NON-PLURIPOTENT MODIFICATIONS, PLURIPOTENT MODIFICATIONS or MODIFIED DERIVATIVES are conveyed to the RECIPIENT under this Agreement.

4. Exclusive of any third-party rights that may exist, the RECIPIENT retains ownership of: (a) NON-PLURIPOTENT MODIFICATIONS and (b) those substances created through the use of the MATERIAL, NON-PLURIPOTENT MODIFICATIONS or PLURIPOTENT MODIFICATIONS, but which are not PROGENY or UNMODIFIED DERIVATIVES.

5. Unless restricted by Appendix TWO or Appendix THREE, The RECIPIENT may transfer MATERIAL to other nonprofit or governmental parties if permission from the PROVIDER is first obtained.

6. RECIPIENT shall have the right to nonexclusively distribute:

   (a) NON-PLURIPOTENT MODIFICATIONS or PLURIPOTENT MODIFICATIONS subject to Appendix TWO and Appendix THREE restrictions, if any, and the following term:

      i. In the event that RECIPIENT enters into negotiations to provide or license PLURIPOTENT MODIFICATIONS to a THIRD PARTY for COMMERCIAL PURPOSES, then RECIPIENT will notify that THIRD PARTY of PROVIDER's ownership of MATERIALS that are contained or incorporated within the PLURIPOTENT MODIFICATIONS. It is recognized by the RECIPIENT that such COMMERCIAL PURPOSES may require a license from PROVIDER, who has no obligation to grant a license to any ownership interest in MATERIAL incorporated in the PLURIPOTENT MODIFICATIONS.

   (b) MODIFIED DERIVATIVES subject to Appendix TWO and Appendix THREE restrictions, if any, and the following terms:

      i. RECIPIENT will transfer such substances, and sufficient rights to use them, to other academic and governmental research

institutions for internal research purposes at nominal cost, and will implement arrangements to effect such transfers.

7. There is no restriction on RECIPIENT's development of commercial products resulting from the knowledge gained from research using the MATERIAL, MODIFIED DERIVATIVES, NON-PLURIPOTENT MODIFICATIONS or PLURIPOTENT MODIFICATIONS.

8. The RECIPIENT is free to file patent application(s) claiming inventions made by the RECIPIENT through the use of the MATERIAL but agrees to notify the PROVIDER upon filing a patent application claiming MATERIALS, NON-PLURIPOTENT MODIFICATIONS, PLURIPOTENT MODIFICATIONS, MODIFIED DERIVATIVES or method(s) of manufacture or use(s) of the MATERIAL.

9. RECIPIENT AND RECIPIENT SCIENTIST agree not to attempt to identify or contact the donor subject from whom the ORIGINAL MATERIAL was or may have been derived.

10. Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties and its use may require acquisition of rights from THIRD PARTIES. The PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF THE MATERIAL, ITS SOURCE, MERCHANTABILITY, TRANSFER OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE MATERIAL WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS.

11. **For U.S. State Institutions**: The RECIPIENT agrees to be responsible for any claims, costs, damages or expenses resulting from any injury (including death) damage, or loss that may arise solely from its use of the MATERIAL and to hold harmless and indemnify the PROVIDER and any THIRD PARTIES having intellectual proprietary or other rights to the MATERIAL to the extent permitted by law.

12. **For all other Institutions:** Except to the extent prohibited by law and except for U.S. Government agencies (which may not agree to an indemnification obligation), the RECIPIENT hereby agrees to hold harmless and indemnify the PROVIDER and PROVIDER against any claim arising from the RECIPIENT's receipt, storage, disposition and/or use of the MATERIAL, and any claim that the RECIPIENT's use of the MATERIAL violates any intellectual property or other rights of a THIRD PARTY, or violates any provision of local, national or international law, except to the extent permitted by law when caused by the gross negligence or willful misconduct of the PROVIDER.

13. This Agreement shall not be interpreted to prevent or delay publication of research findings resulting from the use of the MATERIAL. The RECIPIENT SCIENTIST

agrees to provide appropriate acknowledgement of the source of the MATERIAL in all publications.

14. In all oral presentations or written publications concerning the use of MATERIAL, RECIPIENT will acknowledge PROVIDER's contribution of ORIGINAL MATERIAL unless requested otherwise by PROVIDER.

15. Additional terms, if any, are in Appendix THREE.

SIGNATURES BEGIN ON THE NEXT PAGE

RECIPIENT expressly certifies and affirms that the contents of any statements made herein are truthful and accurate to the best knowledge and belief, and the official signing this Agreement on behalf of RECIPIENT further certifies and affirms that he or she has the authority to do so.

FOR RECIPIENT:

Authorized Official:

_____ _____

[Name] Date
[Title]

Address:

Read and understand by RECIPIENT SCIENTIST:

_____ _____

[Name] Date
[Title]

FOR PROVIDER:

Authorized Official

_____ _____

John O'Shea, MD Date
Scientific Director, NIAMS

Address:
Office of Technology Transfer and Development (OTTAD), NHLBI, NIH
One Rockledge Center, Suite 6070 MSC 7992
6705 Rockledge Drive
Bethesda, MD 20892-7992

Read and understand by the principal investigator:

_____ _____

Mahendra S. Rao, MD, PhD Date
Director, NIH CRM

Appendix ONE

Detailed Description of ORIGINAL MATERIAL PROVIDED TO RECIPIENT [Article I.4]

(Attach info sheet for each iPS cell line.)

Appendix TWO

Additional Terms and Conditions for RECIPIENT's Use of MATERIALS [Article III.5]

Original Material	**Distribution Restrictions** *(check all applicable boxes)*	**Modification Restrictions** *(check all applicable boxes)*	**Source** (Include Protocol #, if applicable)	**Comments**
	☐ No restrictions ☐ for nonprofit research, or government research use only For-profit entity permitted: ☐ internal research use only ☐ Commercial Purposes ☐ **NIH license required**	Non-Pluripotent Modifications ☐ Prohibited Pluripotent Modifications ☐ Prohibited		

Appendix THREE

Additional Terms
[Article III.15]

(default is “none”)