Material Transfer Agreement

between

BERLIN INSTITUTE OF HEALTH AT CHARITÉ (BIH)
Anna-Louisa-Karsch-Str. 2, 10178 Berlin, Germany

(hereinafter referred to as "SUPPLIER")

and

Freie Universität Berlin
(hereinafter referred to as "RECIPIENT")

MATERIAL: described in Appendix A

RECIPIENT Scientist CONTACT:

Freie Universität Berlin
represented by Dr. Christine Reuter, Head of Legal Affairs in Research & Transfer,
Kaiserswerther Straße 16 – 18
14195 Berlin

on behalf of the Department of Biology, Chemistry, Pharmacy
Institute of Chemistry and Biochemistry
Takustr.3/6, 14195 Berlin
Principal Investigators: Prof. Nan Ma/ Dr. Yi-An Yang
Email: nan.ma@fu-berlin.de/ yianyang@zedat.fu-berlin.de
FUB Contract no.: 2023000420

SUPPLIER'S Scientist CONTACT:

BIH Core Unit pluripotent Stem Cells and Organoids (CUSCO)
Charité Campus Virchow Klinikum (CVK)
Dr. Harald Stachelscheid
Augustenburger Platz 1
13353 Berlin
Email: harald.stachelscheid@bih-charite.de

1. **Definitions**
   a. MATERIAL: ORIGINAL MATERIAL together with all fragments and mixtures thereof and together with PROGENY and UNMODIFIED DERIVATIVES;

MATERIAL shall not include MODIFICATIONS or other substances created by the RECIPIENT through the use of the MATERIAL which are not MODIFICATIONS, PROGENY or UNMODIFIED DERIVATIVES.

b. PROGENY: Unmodified descendant from the MATERIAL (for instance virus from virus, cell from cell, organism from organism)
c. UNMODIFIED DERIVATIVES: Substances created by RECIPIENT constituting an unmodified functional subunit or product expressed by the ORIGINAL MATERIAL
d. MODIFICATIONS: Substances created by the RECIPIENT which contain or incorporate the MATERIAL

The MATERIAL as listed in **Appendix A** is considered proprietary to BIH.

2. Background.

RECIPIENT desires to obtain the MATERIAL and/or information described in **Appendix A** (the "MATERIAL") from SUPPLIER for use by RECIPIENT solely for non-human experiments described in **Appendix A** (the "TESTS") under the terms and conditions of this Agreement. The obligations of RECIPIENT herein described will apply to any biological MATERIAL that incorporates the MATERIAL or any recombinant version thereof.

3. The MATERIAL and the TESTS.

RECIPIENT acknowledges that SUPPLIER retains ownership of the MATERIAL, including any MATERIAL contained or incorporated in MODIFICATIONS. SUPPLIER will use commercially reasonable efforts to provide RECIPIENT with the quantity of the MATERIAL described in **Appendix A**. RECIPIENT will use the MATERIAL solely for the TESTS and for no other purpose. Furthermore, the use for any commercial purpose, such as for production is prohibited under this Agreement. In particular, no rights are provided to use the MATERIAL or any related patents for profit-making or commercial provision of a service to a third party in exchange for consideration. RECIPIENT will not use the MATERIAL for testing in or treatment of human subjects. RECIPIENT acknowledges that the MATERIAL is experimental and will comply with all laws and regulations applicable to its handling and use. Any MATERIAL remaining upon completion of the Research either will be returned to SUPPLIER or discarded, consistent with SUPPLIER'S instructions. RECIPIENT agrees to not distribute or release the MATERIAL to any other person or entity, except laboratory personnel of RECIPIENT. RECIPIENT shall ensure that no one will be allowed to take or send the MATERIAL to any other location than mentioned above, unless written permission is obtained from SUPPLIER.

4. Confidentiality.

RECIPIENT shall treat in confidence, for a period of five (5) years from the date of its disclosure, any written information pertaining to the MATERIAL provided to RECIPIENT by SUPPLIER or SUPPLIER'S Scientist(s). Excluded from this obligation shall be any information

(a) that was previously known to RECIPIENT prior to receipt of information from SUPPLIER;

(b) that lawfully is, or becomes publicly available during said five (5) year period through no fault of RECIPIENT;

(c) which is disclosed to RECIPIENT without confidentiality obligations by a third party having the right to make such disclosure; or

(d) which is independently developed by RECIPIENT without the use of or reference to any information received from SUPPLIER.

RECIPIENT has to prove that the matter of any violation is information in compliance with 3 a - d.

5. Research Results.

RECIPIENT will conduct TESTS with the MATERIAL and gather research results (such results are referred to as the "Research Results"). RECIPIENT will inform SUPPLIER of Research Results related to the MATERIAL, by personal communication and by providing SUPPLIER with written information describing the Research Results. In case of joint inventions, SUPPLIER and Recipient shall conclude in good faith a separate agreement concerning the use, patenting and commercialization of those joint inventions. RECIPIENT shall grant to SUPPLIER an irrevocable non-exclusive royalty-free license to practise the Research Results as well as any invention, improvement or modification resulting from the use of the MATERIAL for internal scientific research purposes.

6. Publication and Acknowledgement.

The RECIPIENT shall have the right, consistent with academic standards, to publish or present the results of the research work performed in accordance with this Agreement. The RECIPIENT shall disclose planned publications to SUPPLIER at least thirty (30) days prior to submission for publication. If SUPPLIER does not send an objection during this thirty (30) days, RECIPEINT will be free to submit for publication without delay.
In presentations or publications concerning the use of the Material, the RECIPIENT will acknowledge the SUPPLIER and the named SUPPLIER´s contact as the source of the MATERIAL (e.g. *"The cell line was provided by the Berlin Institute of Health (BIH) at Charité, Core Unit pluripotent Stem Cells and Organoids, Dr. Harald Stachelscheid"*). When research work is performed in collaboration, co- authorship of SUPPLIER is required.

7. No Warranty.

RECIPIENT acknowledges that any MATERIAL delivered to it under this agreement is experimental in nature. SUPPLIER makes no representations nor extends any warranties of any kind, either expressed or implied, with respect to the MATERIAL. There are no express or implied warranties of merchantability or fitness for a particular purpose, nor does SUPPLIER represent that the use of the MATERIAL will not infringe any patent, copyright, trade secret, trademark or other rights of third parties.

8. Indemnification.

SUPPLIER shall not be liable to RECIPIENT for any loss, claim, or demand made by RECIPIENT, or made against RECIPIENT by any other party, due to, or arising from, the use of the MATERIAL by the RECIPIENT. To the extent permitted by law, RECIPIENT shall indemnify, defend and hold harmless SUPPLIER, its trustees, assignees, agents and employees from any claim asserted against them arising from the negligence or wilful misconduct in the use of the MATERIAL by RECIPIENT or its agents or employees.

9. No obligations.
No rights or licenses to trademarks, inventions, copyrights or patents are implied or granted under this Agreement.

10. Final Agreement.
This Agreement and **Appendix A** attached hereto and hereby incorporated herein, contains the final, complete and exclusive agreement of the parties relative to the subject matter hereof and supersedes all prior and contemporaneous understandings and agreements relating to its subject matter. This Agreement may not be changed, modified, amended or supplemented except by a written instrument signed by both parties.

11. Start and Termination.
This Agreement starts with the date of signature of RECIPIENT. Either party may terminate this Agreement upon thirty (30) days' prior written notice to the other party. Upon termination, RECIPIENT will immediately return to SUPPLIER its Confidential Information, and any unused samples of the MATERIAL, and all of RECIPIENT's rights to use the MATERIAL will end. Following termination, neither party will have any further obligations under this Agreement, except that Sections 2, 3, 5 and 6 will survive.

12. Miscellaneous.
This Agreement shall be governed by the laws of Germany, excluding its conflicts of laws principles. Place of jurisdiction is Berlin, Germany.

If you agree to accept the MATERIAL under the above conditions, please have this Agreement signed by an authorized representative of RECIPIENT and return a PDF with digital signature or two originals to:

Charité - BIH Innovation
Technologietransfer
Anna-Louisa-Karsch-Straße 2
D- 10178 Berlin Germany
technologietransfer@charite.de

The MATERIAL will be sent to you as soon as possible after the receipt of the signed Agreement.

RECIPIENT ORGANIZATION APPROVAL:

Freie Universität Berlin

Date: _____

By: Dr. Christine Reuter Digital unterschrieben von Dr. Christine Reuter Datum: 2024.02.16 11:21:25 +01'00'
Dr. Christine Reuter
Head of Legal Affairs in Research & Transfer

AGREED AND ACCEPTED BY RECIPIENT SCIENTIST

Date: _____

By: Nan Ma Digitally signed by Nan Ma Date: 2024.02.15 12:49:10 +01'00'
Prof. Nan Ma
Professor

By: _____
Dr. Yi-An Yang
Scientist

BERLIN INSTITUTE OF HEALTH AT CHARITÉ (BIH)

Date: _____

By: Christopher Baum Digital unterschrieben von Christopher Baum Datum: 2024.05.07 09:58:41 +02'00'

Berlin Institute of Health at Charité
Anna-Louisa-Karsch-Str. 2,
10178 Berlin, Germany

Date: Digital unterschrieben von Harald Stachelscheid CN: c=DE, st=Berlin, l=Berlin, o=Charite - Universitaetsmedizin Berlin, sn=Stachelscheid, givenName=Harald, cn=Harald Stachelscheid Datum: 2024.04.03 14:12:38 +02'00'

By: _____
Dr. Harald Stachelscheid
SUPPLIER Scientist

Appendix A

MATERIAL: The ORIGINAL MATERIAL covered by this agreement includes:

BIHi001-A (https://hpscreg.eu/cell-line/BIHi001-A), also named as BCRT-3/BCRT#1, a human induced pluripotent stem cell (hiPSC) line generated by Berlin Institute of Health (BIH), Germany. BIHi001-A has been validated with positive NANOG, TRA 1-60, OCT-4 and SSEA-4 expression. This hiPSC line is derived from dermal fibroblasts of a male donor.

Scientific references:

- Hossini AM et al. PI3K/AKT Signaling Pathway Is Essential for Survival of Induced Pluripotent Stem Cells. PloS one. 2016;11(5):e0154770.
- Buonocore F et al. Somatic mutations and progressive monosomy modify SAMD9-related phenotypes in humans. The Journal of clinical investigation. 2017 May 1;127(5):1700-1713.
- Fenske P et al. Autaptic cultures of human induced neurons as a versatile platform for studying synaptic function and neuronal morphology. Scientific reports. 2019 Mar 20;9(1):4890.
- Sürün D et al. Efficient Generation and Correction of Mutations in Human iPS Cells Utilizing mRNAs of CRISPR Base Editors and Prime Editors. Genes. 2020 May 6;11(5).
- Ebner-Peking P et al. Self-assembly of differentiated progenitor cells facilitates spheroid human skin organoid formation and planar skin regeneration. Theranostics. 2021;11(17):8430-8447.
- Krisch L et al. Improving Human Induced Pluripotent Stem Cell-Derived Megakaryocyte Differentiation and Platelet Production. International journal of molecular sciences. 2021 Jul 30;22(15).
- Luo Y et al. A novel approach for studying mast cell-driven disorders: Mast cells derived from induced pluripotent stem cells. The Journal of allergy and clinical immunology. 2022 Mar;149(3):1060-1068.e4.

TESTS TO BE PERFORMED WITH THE ABOVE-MENTIONED MATERIAL:

- Biocompatibility test of synthetic materials
- 2D/3D cultivation and differentiation assay
- hiPSc-derived organoid induction assay
- FACS analysis, immunostaining assay and western blot assay for protein expression level measurement
- PCR assays for gene expression level measurement