Cell Line Information Pack (CLIP)

Cell line name	UKKi008-A

Purpose

The purpose of this Cell Line Information Pack (CLIP) is to communicate cell line specific information to potential users of the cell line, and to confirm that a User has received it upon the purchase of an EBiSC cell line.

Information

The CLIP may provide a variety of types of information related to an individual cell line. Of particular importance are Third Party Obligations (TPOs), which are ethical or legal obligations of a Depositor related to the use of the cell line. TPOs may impose ethical or legal limitations on the ability of a User to use the cell line, or require steps to be taken before it can be used. TPOs are likely to be:

- Obligations under license to an intellectual property rights (patent) holder, or
- Restrictions on use imposed by the donor of the primary tissue from which the cell line was made.

Third Party Obligations: donor consent provisions

None.

Third Party Obligations: IP or license provisions

iPS-AJ: This EBiSC Cell line was generated under the technology disclosed in patents related to iPS cells which are owned by Kyoto University and are licensable from iPS Academia Japan., Inc.("iPS AJ"). Commercial user (for-profit entity) acknowledges that, prior to receipt and use of this EBiSC Cell line, such commercial user needs to have an appropriate patent license from iPS AJ even for its research use. Academic user (academic or not-for-profit entity) acknowledges that such academic user does not need a patent license from iPS AJ for its research use, provided, however, that when such academic user uses this EBiSC Cell line for other than its independent research use, such academic user acknowledges that the academic user might need to obtain an appropriate patent license from iPS AJ. For inquiries to iPS AJ, please contact at license@ips-ac.co.jp.

In addition, cell lines UKKi008-A, UKKi009-A and UKKi009-B were generated using a plasmid encoding for the hyperactive variant of the transposase "Sleeping Beauty", inter alia the variant SB100x, which is patented by The Max-Delbrück-Center (MDC) for Molecular Medicine Berlin-Buch, Germany (Prof. Dr. Zsuzsanna Izsvak). The commercial use of cells generated with this material may require prior written consent of MDC and be subject to obtaining a commercial license from MDC. The MTA between UKK and MDC for transposon plasmid SB100x is in the attached Annex.

Other information

Any publications or public dissemination of results using EBiSC iPSCs should be accompanied by the following acknowledgement: "The EBiSC Bank acknowledges KLINIKUM DER UNIVERSITAET ZU KOELN as the source of the human induced pluripotent cell line UKKi008-A which was generated with support from the EBiSC project. The EBiSC has received support from the Innovative Medicines Initiative (IMI) Joint Undertaking (JU) under grant agreement n°115582 and from the IMI-2 JU under grant agreement No 821362, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013), European

Union's Horizon 2020 research and innovation programme and EFPIA."

SIGN AND RETURN THIS DOCUMENT WITH YOUR COMPLETED ACCESS AND USE AGREEMENT

User acknowledgement

Please sign below to indicate that you have read and acknowledge the information contained in this CLIP.

Name _____ **Position** _____

Signature _____ **Date** _____

Annex 1. Material transfer agreement between UKK and MDC for transposon plasmid SB100x

MDC MAX-DELBRÜCK-CENTRUM FÜR MOLEKULARE MEDIZIN BERLIN-BUCH

in der
HELMHOLTZ-GEMEINSCHAFT e.V.

MATERIAL TRANSFER AGREEMENT FOR THE DISTRIBUTION OF BIOLOGICAL MATERIAL

to non-profit recipients

The Parties to this Agreement are:

MDC	
Organisation	MAX-DELBRÜCK-CENTRUM FÜR MOLEKULARE MEDIZIN
Street	Robert-Rössle-Straße 10
ZIP-Code, City	13125 Berlin
Country	Germany
MDC Scientist	Dr. Zsuzsanna Izsvak
And	
RECIPIENT	
Organisation	Institute for Neurophysiology, University of Cologne
Street	Robert Koch Str. 39
ZIP-Code, City	50931 Cologne
Country	Germany
For	
RECIPIENT SCIENTIST	
Name and Title	Tomo Saric, M.D., Ph.D.
Street	Robert Koch Str. 30
ZIP-Code, City	50931 Cologne
Country	Germany

The Max-Delbrück-Center for Molecular Medicine Berlin-Buch (in the following: "MDC") holds know how and patent applications on the hyperactive variants of the transposase "Sleeping Beauty", inter alia the variant SB100x.

The RECIPIENT SCIENTIST would like to use the MATERIAL (as defined below) to generate induced pluripotent stem cells and their genetically modified progeny (in the following 'Research Program'). The Research Program is outlined in more detail in Schedule 1.

RECIPIENT is a non-profit organization.

I. Definitions:

1. ORIGINAL MATERIAL:
The Material specified at Schedule 1.

2. MATERIAL:
ORIGINAL MATERIAL, PROGENY and UNMODIFIED DERIVATIVES.

3. PROGENY:
Unmodified descendant from the MATERIAL.

4. UNMODIFIED DERIVATIVES:
Substances created by the RECIPIENT which constitute an unmodified functional subunit or product expressed by the ORIGINAL MATERIAL.

5. MODIFICATIONS:
Substances created by the RECIPIENT through use of the MATERIAL.

6. COMMERCIAL PURPOSES:
The sale, lease, license, or other transfer of the MATERIAL or MODIFICATIONS to a for-profit organisation. COMMERCIAL PURPOSES shall also include uses of the MATERIAL or MODIFICATIONS by any organisation, including RECIPIENT, to perform contract research, to screen compound libraries, to produce or manufacture products for general sale, or to conduct research activities that result in any sale, lease, license, or transfer of the MATERIAL or MODIFICATIONS to a for-profit organisation.

7. NONPROFIT ORGANIZATION(S):
A university or other institution of higher education or an organisation exempt from taxation or any non-profit scientific or educational organisation.

8. CONFIDENTIAL INFORMATION
Information relating to the MATERIAL disclosed by MDC or RECIPIENT including but not limited to research results, manuscripts and invention disclosures. CONFIDENTIAL INFORMATION does not include:

(a) Information that is or becomes publicly known or available from other sources who are not under a confidentiality obligation;
(b) Information which has been made available by MDC to others without a confidentiality obligation;
(c) Information already known or available to RECIPIENT without a confidentiality obligation;
(d) Information which relates to potential hazards or cautionary warnings associated with the production, handling or use of the materials; or
(e) Information required to be disclosed by applicable law, rule or court order.

II. Terms and Conditions of this Agreement:

1. The RECIPIENT and the RECIPIENT SCIENTIST agree that the MATERIAL:
(a) is to be used solely for teaching and academic research purposes;
(b) will not be used in human subjects, in clinical trials, or for diagnostic purposes involving human subjects;
(c) is to be used only at the RECIPIENT organisation and only in the RECIPIENT SCIENTIST's laboratory under the direction of the RECIPIENT SCIENTIST or others working under his/her direct supervision; and
(d) will not be transferred to anyone else within the RECIPIENT organisation without the prior written consent of the MDC.

2. MDC hereby grants to RECIPIENT a royalty-free, non-exclusive restricted licence under all of its rights in and to the MATERIAL solely for the purpose of the Research Program (without any rights to grant sub-licences). Upon completion of the work for which this restricted license is granted, MATERIAL

which has not been destroyed will be disposed of as explicitly directed by MDC. The MDC retains ownership of the MATERIAL, including any MATERIAL contained or incorporated in MODIFICATIONS.

3. The RECIPIENT acknowledges that the MATERIAL is or may be the subject of a patent application. Except as provided in this agreement, no express or implied licenses or other rights are provided to the RECIPIENT under any patents, patent applications, trade secrets or other proprietary rights of the MDC, including any altered forms of the MATERIAL made by the MDC. In particular, no express or implied licenses or other rights are provided to use the MATERIAL, including any MATERIAL contained in MODIFICATIONS, or any related patents of the MDC for COMMERCIAL PURPOSES.

4. RECIPIENT is free to use MODIFICATIONS for COMMERCIAL PURPOSES. RECIPIENT shall notify MDC of any such commercial use and shall share with MDC any proceeds derived from such commercial use, as negotiated between RECIPIENT and MDC in good faith.

5. The use or license of the MATERIAL, including MATERIAL contained in MODIFICATIONS for COMMERCIAL PURPOSES requires the prior written consent of MDC and the RECIPIENT agrees, in advance of such use, to negotiate in good faith with the MDC to establish the terms of a commercial license. It is understood by the RECIPIENT that the MDC shall have no obligation to grant such a license to the RECIPIENT, and may grant exclusive or non- exclusive commercial licenses to others, or sell or assign all or part of the rights in the MATERIAL to any third party(ies).

6. The RECIPIENT and the RECIPIENT SCIENTIST agree to refer to the MDC any request for the MATERIAL from anyone other than those persons working under the RECIPIENT SCIENTIST's direct supervision. To the extent supplies are available, the MDC agrees to make the MATERIAL available, under a separate implementing letter to this Agreement or other agreement having terms consistent with the terms of this Agreement, to other scientists (at least those at NONPROFIT ORGANIZATION(S)) who wish to replicate the RECIPIENT SCIENTIST's research; provided that such other scientists reimburse the MDC for any costs relating to the preparation and distribution of the MATERIAL.

7. RECIPIENT is free to file patent application(s) claiming inventions made by the RECIPIENT through the use of the MATERIAL ("RECIPIENT IP") and agrees to notify MDC upon filing of a patent application claiming RECIPIENT IP. RECIPIENT hereby grants to MDC an irrevocable, royalty-free and non-exclusive license to use RECIPIENT IP for research purposes.

8. The RECIPIENT acknowledges that MDC has already established a strategy for commercial exploitation of the MATERIAL and relating intellectual property. Therefore, the Parties agree that in case RECIPIENT IP is dependent on intellectual property of MDC covering the MATERIAL, MDC shall be entitled to exclusively commercialize RECIPIENT IP on behalf of RECIPIENT as a bundle together with the MATERIAL and relating intellectual property of MDC during a period of one (1) year after notification of MDC. MDC shall inform RECIPIENT about all negotiations, shall consult with RECIPIENT upon the licensing conditions and shall disclose to potential licensees that RECIPIENT is the owner of RECIPIENT IP. Such period will be extended by a further one (1) year period if negotiations with a potential license have resulted at least in a signed term sheet. RECIPIENT is entitled to the proceeds attributable to the commercialization of such RECIPIENT IP.

9. RECIPIENT agrees upon request of MDC to provide MDC with a report of observations related to the MATERIAL describing the results of such research using the MATERIAL provided MDC will treat RECIPIENT'S report as CONFIDENTIAL INFORMATION. RECIPIENT shall notify MDC upon completion of the Research Program.

10. At MDC's request, RECIPIENT agrees to provide MDC for its internal research with reasonable quantities of materials developed, made or discovered in the course of the Research Program. Such transfer shall be free of charge, but an appropriate handling/shipping fee may be charged by RECIPIENT.

11. In the event that RECIPIENT SCIENTIST desires to publish or make an oral presentation of the results of the Research Program using the MATERIAL, RECIPIENT SCIENTIST will give full acknowl-

edgement of the origin of the MATERIAL. RECIPIENT SCIENTIST will provide MDC with a manuscript of the paper and MDC will treat said manuscript as CONFIDENTIAL INFORMATION.

12. Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. RECIPIENT shall use the MATERIAL at its own risk. All claims based on legal or other defects of the MATERIAL are hereby excluded. The MDC MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OR MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE MATERIAL WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS.

13. Except to the extent prohibited by law, the RECIPIENT assumes all liability for damages which may arise from its use, storage or disposal of the MATERIAL. The MDC will not be liable to the RECIPIENT for any loss, claim or demand made by the RECIPIENT, or made against the RECIPIENT by any other party, due to or arising from the MATERIAL by the RECIPIENT, except to the extent permitted by law when caused by the gross negligence or wilful misconduct of the MDC.

14. The RECIPIENT agrees to use the MATERIAL in compliance with all applicable statutes and regulations, including guidelines regarding the use, transport, security and disposal of such MATERIAL.

15. This Agreement shall enter into force on the date of the last signature. It will terminate on the earliest of the following dates:

(a) on completion of the RECIPIENT's current research with the MATERIAL, or

(b) on thirty (30) days written notice by either party to the other.

All rights and obligations designed to have effect after termination of this Agreement, in particular RECIPIENT's obligations according to Section II 1 and 2 above, shall survive termination of this Agreement.

16. CONFIDENTIAL INFORMATION will be retained in confidence for five (5) years after disclosure, and shall not be disclosed by RECIPIENT or MDC to anyone other than employees having a need to know such information.

17. The MATERIAL is provided at no cost, or with an optional transmittal fee solely to reimburse the MDC for its preparation and distribution costs.

18. The MDC will forward the MATERIAL to the RECIPIENT SCIENTIST upon receipt of the signed copy from the RECIPIENT organisation.

19. This Agreement shall be governed by and construed in accordance with German law without reference to its conflict of laws rules and under exclusion of the UN Convention on the International Sale of Goods. For all controversies arising under this Agreement, the parties submit to the exclusive jurisdiction of the courts of Berlin, Germany.

IN WITNESS whereof the Parties have caused this agreement to be executed below by duly authorised representatives

MAX-DELBRÜCK-CENTRUM FÜR MOLEKULARE MEDIZIN

Name and Title: Dr. Christine Rieffel-Braune, Administrative Director

Signature

Date

MDC SCIENTIST

Name and Title: Zsuzsanna Izsvak, PhD, Group leader

Signature

Date

RECIPIENT

Name and Title

Signature

Date

RECIPIENT SCIENTIST

Name and Title: Tomo Saric, M.D., Ph.D.

Signature

Date

Schedule 1

1. Description of the ORIGINAL MATERIAL:

PCMV-SBx100 plasmid expressing the 100-fold hyperactive Sleeping Beauty transposase gene under the CMV promoter

2. The ORIGINAL MATERIAL is covered by patent applications.

3. Description of the Research Program:

RECIPIENT'S SCIENTIST will use ORIGINAL MATERIAL in order to generate induced pluripotent stem cells from somatic cells of patients with inherited diseases to study the molecular mechanism of this disease in vitro and to screen for potentially toxic substances and test and develop new drugs. In addition, the sleeping beauty transposon system will be used for generation of stable transgenic ES and iPS cells to express fluorescent or bioluminescent marker and/or antibiotic selection genes under the control of ubiquitous or lineage-specific promoters. These transgenic ES and iPS cell lines will be used for generation of highly purified populations of differentiated cells, such as cardiac myocytes, for assessment of their functional integrity and vitro and capacity to structurally and functionally engraft into host tissue(s) upon transplantation in vivo.