

Texas Institute for Genomic Medicine

TERMS AND CONDITIONS FOR KNOCKOUT MOUSE LINES

1. Overview

This document describes the terms and conditions under which an investigator at an academic or other non-profit research institution may request and receive knockout mice from the Texas Institute for Genomic Medicine (“TIGM”).

2. Requests for Knockout Mice

TIGM is committed to advancing biomedical research by making a broad array of important knockout mouse lines available to the academic research community at a reasonable cost and on favorable terms. TIGM is developing the [OmniBank® II](#) gene trap library, a knockout mouse embryonic stem cell resource that will contain 350,000 cell lines in a C57BL/6 mouse genetic background. Ultimately, this library is anticipated to contain mutations in 60% to 70% of all genes. The library is designed to contain multiple clones for each gene to ensure the successful creation of knockout mice. Through its collaboration with Lexicon Genetics Incorporated (“Lexicon Genetics”), TIGM also has access to Lexicon’s [OmniBank®](#) library. This gene trap library contains more than 270,000 sequence-tagged embryonic stem cell clones in the 129/SvEvBrd mouse strain representing mutations in approximately 60% of all genes. Finally, TIGM has access to more than 1,000 established knockout mouse lines produced by Lexicon Genetics.

TIGM distributes mice under a material transfer agreement (the “MTA”) that must be signed by the recipient investigator and his or her institution’s technology transfer representative. The terms and conditions of this MTA include, among other provisions:

- An acknowledgment that, as between the parties, TIGM owns and retains all rights to the knockout mouse line requested by the recipient investigator, including progeny and cells, tissues and other biological materials derived from any of the foregoing, and is making such materials available to the recipient under license as a service to the research community.
- An agreement that the recipient shall use the knockout mouse line received from TIGM, including progeny and cells, tissues and other biological materials derived from any of the foregoing, solely for recipient’s internal non-commercial research purposes. For clarity, internal non-commercial research purposes shall exclude contract research services and any research activities in which a third party has rights to obtain the assignment, sale, lease, license (including an option for a license) or transfer of resulting invention(s); *provided, however*, that the foregoing shall not be deemed to restrict the recipient from performing research funded by the United States government in which the United States government has rights under 35 U.S.C. § 203. Recipient investigators must obtain appropriate authorization from TIGM and (as appropriate) Lexicon prior to any commercial use.
- An agreement that the recipient shall not distribute, sell or otherwise transfer to others the knockout mouse line received from TIGM, any progeny thereof, or any cells, tissues and other biological materials derived from any of the foregoing. Recipients shall refer any outside request for such materials to TIGM. To the extent supplies are available, TIGM agrees to make materials available to other scientists under the same form of MTA and under the same terms and conditions as the knockout mouse line was made available to the recipient.
- An agreement that the recipient will acknowledge TIGM in any presentations and publications reporting use of materials.
- Acknowledgements that the materials are understood to be experimental in nature, may not be used in human subjects, and may have hazardous properties and that the recipient assumes all responsibility for its use, storage or disposal of such materials.

- An agreement to use the materials in compliance with all applicable statutes and regulations.

All knockout mouse lines are made available on a non-exclusive basis. The recipient's use of materials in accordance with the terms and conditions of the agreement is fully licensed under the patent and intellectual property rights of TIGM and Lexicon in such materials.

3. Development and Delivery of Knockout Mice

When a recipient investigator and his or her institution places an order and delivers a signed MTA, TIGM will process embryonic stem (ES) cells for the requested mouse line and, provided that such ES cells pass its quality control procedures, will use commercially reasonable efforts to complete the development of mice from the requested mouse line for delivery to the recipient.

TIGM will notify the recipient promptly following its completion of the development of mice from the requested mouse line for delivery to the recipient. Upon payment and confirmation of shipping arrangements by the recipient, TIGM will deliver the following materials:

- Four (4) mice, heterozygous for the selected mutation, including at least one (1) breeding pair
- Validated genotyping protocols
- Animal health data

The recipient shall be responsible for complying with all customs, regulations, veterinary handling procedures and protocols, and obtaining any and all permits, forms or permissions that may be required for the recipient to accept shipment of mice from the requested mouse line. In addition, the recipient is responsible for the costs of shipping and, if desired, insurance.

The development of genetically-modified mice involves a number of technologically complex steps, and technical obstacles may, on occasion, prevent TIGM from producing a requested mouse line. TIGM will promptly notify the recipient of any such technical obstacle encountered and its analysis of whether the obstacle can be overcome using commercially reasonable efforts and the time required to do so. If TIGM determines that production of a requested mouse line is not feasible using commercially reasonable efforts, TIGM may, upon notice to the recipient, terminate efforts to develop and deliver mice from such requested mouse line. Upon termination of such efforts, (a) TIGM shall have no further obligation to the recipient with respect to such requested mouse line; (b) TIGM shall retain the fees, if any with respect to such requested mouse line that became payable prior to such termination; and (c) recipient shall have no further payment obligations to TIGM with respect to such requested mouse line.

4. Payments and Fees

TIGM charges fees that are intended to cover the costs of developing knockout mice for delivery to requesting investigators. It is important to note that TIGM's Genome Knockout Project did not receive funding by NIH's Knockout Mouse Project, and that the OmniBank II and OmniBank gene trap libraries have been generated entirely without funding of any kind from the NIH or other federal government agencies. Likewise, TIGM has not received the substantial NIH subsidies that cover the bulk of the costs of the Mutant Mouse Resource Center ("MMRC") program. As a result, the fees charged by TIGM must be sufficient to cover the true costs incurred in making these materials available. The NIH has obtained rights to 122 established knockout mouse lines from Lexicon Genetics, allowing TIGM to make these specific lines available for distribution to the academic research community on a subsidized basis.

Knockout mice created by microinjection of ES cells from the [OmniBank](#) and [OmniBank II](#) gene trap libraries are available to academic researchers at a cost of \$17,500 per line. In addition, TIGM can provide academic researchers with access to more than 1,000 established knockout mouse lines produced by Lexicon Genetics at a cost of \$30,000 per line. The National Institutes of Health has obtained rights to 122 of these lines from Lexicon Genetics, allowing TIGM to make them available for distribution to the academic research community for \$5,000 per line.

For each requested mouse line, TIGM will invoice \$5,000 (a) upon successful completion of its quality control procedures with respect to the ES cells for such requested mouse line, in the event mice are being developed from ES cells, or (b) upon receipt of a signed MTA, in the event mice have already been developed. TIGM will invoice the balance concurrently with its notice to the recipient of its completion of the development of mice from the requested mouse line for delivery to the recipient. Such amounts will be due on receipt of the invoice by the recipient institution.

All payments shall be made in United States dollars and shall be paid in full, without deduction of taxes or other fees that may be imposed by any government. Any payments that are not made on or before thirty (30) days after the date such amounts are due shall bear interest, to the extent permitted by applicable law, at one percent (1.0%) per month, calculated on the number of days payment is late.