

Dear Colleague,

Over the past year, with the support of Texas A&M AgriLife Research, TIGM has continued offering a variety of services to the domestic and international research communities. To date, TIGM has provided more than 390 mouse lines and more than 3,700 ES cell lines to the scientists around the world. We significantly diversified our CRISPR/Cas9 production capabilities that now include generation of conditional (floxed) alleles. Important scientific breakthroughs are made with both direct and indirect involvement of TIGM; more than 230 peer-reviewed papers have been published by either TIGM scientists or external researchers who utilized TIGM resources. We now have more than 270 mouse lines in our repository all available at cost recovery rates; our database listings are being updated regularly. In collaboration with TAMUS institutes and facilities, TIGM offers centralized access to a variety of phenotyping services. For more information please visit the new site at: <http://www.tigm.org/>

Sincerely,

Ben Morpurgo, Ph.D.
Director, TIGM

TIGM Becomes a Part of Newly-Funded Texas A&M Environmental Health Science Center

TIGM will help A&M scientists generate novel mouse models and perform environmental health studies

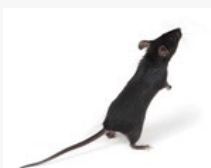
Texas A&M has received a five-year grant from the National Institute of Environmental Health Sciences (NIEHS) under the EHS Core Centers Program to open its very own environmental health science center, of which TIGM will be a core component.

The Texas A&M Center for Environmental Health Research (TICER) is one of 24 university-based EHS Core Centers that are spread out in 16 states across the nation. These centers are meant to be hubs of scientific collaboration and state-of-the-art technologies that can advance environmental health science research, promote translational research and community outreach, and train new investigators in the field.

NIEHS fosters these collaborations by supplying the funding necessary to establish new and augment existing infrastructure that can support the facilities, equipment, and resources to be shared among researchers. Texas A&M University itself has also pledged almost \$3 million over the next five years in support of the new center.

TICER's overall goal is to enhance public health by identifying, understanding, and reducing environmental health risks and to increase the impact of environmental health research at Texas A&M. Organized around four research themes, the Center aims to bring researchers together from multiple disciplines. This is in effort to promote the formation of unique collaborations and exchange of novel ideas that could lead to high impact discoveries.

The Center's vision will be realized in part through an integrated set of Facility Cores that exist to support implementation of research strategies and use of technologies for Center members. TIGM resources and facilities will be available to TICER members through one of these cores, including access to TIGM knockout mice and stocked cell lines.



Production Update

TIGM is a major international resource for mice & cells

Since 2006, TIGM has served as a major resource to the international scientific community. To date, TIGM has delivered more than 700 mouse and ES cells orders to more than 300 academic and commercial institutions in over 26 countries. Our repository now includes 270 cryopreserved lines and our mouse lines and ES cells have been featured in over 230 peer-reviewed publications and patents. Overall, more than 5,200 individual gene trapped ES cell clones have been expanded at TIGM; more than 3,700 of those were provided to external researchers. In addition, a total of over 8,600 individual investigators from more than 900 academic and research institutions and commercial entities representing 40 countries, have queried TIGM with information requests

Search for your gene at: <http://www.tigm.org/advanced-search/>

TIGM on the road



TIGM will present at the American Heart Association's Scientific Sessions to be held in Philadelphia, Pennsylvania from November 16-18 2019. Please come to see our poster "Sex As A Biological Variable Is Evident Following Deletion Of Intestinal Apolipoprotein A1" at the Best of Basic Science Session AT.APS.01.

More information is here: <https://www.abstractsonline.com/pp8/#!/7891/presentation/26909>



CRISPR/CAS9-Based Genome Editing

TIGM has successfully created conditional KO lines using 2g-2o approach

In a recent release in Genome Biology (Gurumurthy et al., <https://doi.org/10.1186/s13059-019-1776-2>), researchers from 17 institutions around the world pooled their results regarding the use of CRISPR to make conditional (loxP) knockout mouse models using 2 single guide RNAs (sgRNA) and 2 single-stranded oligonucleotides (ssODN) (2sgRNA-2ssODN). Despite the fact that after extensive testing the consortium found that only 0.87% of mice were correctly targeted – indicating a very low efficiency with this method – TIGM appears to be the only Core lab that has consistently produced conditional KOs by injecting 2sgRNA-2ssODN.

We have been continuously optimizing the CRISPR/CAS9 injections conditions over the past several years and successfully produced a variety of mutants – from single nucleotide changes and small precise deletions to conditional KOs. We can provide turn-key solution from mutation design to genotyping and sequence confirmation of mutants. Please contact us to discuss a possibility to make a CRISPR mouse.

For more details about services offered by TIGM please visit: <http://www.tigm.org/services/>

Core Services

Custom services for your research

TIGM currently has breeding colonies for these stock strains: C57BL/6J, C57BL/6N, FVB, CD1 (ICR), Balb/c, 129/SvEv, and SCID. Those can be expanded in order to provide mice at cost to investigators.

In addition to CRISPR/CAS9 injections, TIGM continues offering a traditional array of custom services. If you need to generate a constitutive or conditional knockout TIGM offers a complete knockout package that include vector design and construction, electroporation into C57BL/6 or 129/SvEv cells, clone screening and confirmation of targeted events, blastocyst injection and heterozygous mouse production. Alternatively, each step of this process can be ordered separately.



Other services include:

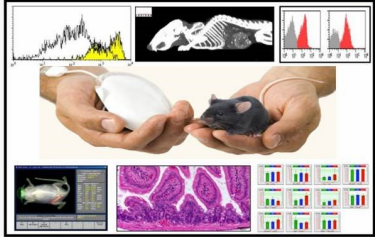
- Pronuclear Injection (including CRISPR/Cas9)
- ES cell services
 - Electroporation
 - Clone isolation and identification of targeted ES cell clones by PCR
- Sperm and Embryo Cryopreservation
- Rederivation
 - via embryo transfer
 - via IVF
- Frozen or Live Embryo Transfer
- Cryostorage

- Breeding services
 - line expansion
 - colony management
- Animals from stock colonies: C57BL/6, ICR, FVB, Balb-c, 129/SvEv, SCID
- Tissue sharing

We can also perform simple animal studies as well as tissue collections, and arrange for analysis using a variety of services available at Texas A&M (such as histology, microarray, blood proteins and hormones, to name a few).

Please contact us at info@tigm.org or (979) 845-TIGM (979-845-8446) to discuss your project needs or find out how we can help you with your research.

For more details about services offered by TIGM please visit: <http://www.tigm.org/services/>



Phenotyping Services

In collaboration with Rodent Preclinical Phenotyping Core at Texas A&M Institute for Genome Sciences and Society (TIGSS) and The Department of Veterinary Pathobiology (VTPB) at Texas A&M College of Veterinary Medicine &

Biomedical Sciences

The areas of expertise include:

- Oncology
- Metabolic
- Cardiovascular
- Skeletomuscular
- Behavior
- Pathology
- Histology
- Chemical analyses
- Imaging
- Expression studies

TIGM can also provide a variety of breeding services that can be used to obtain information about Genetics, Viability and Fertility of mouse lines. We can also perform simple animal studies as well as tissue collections and arrange for their analysis.

For more details about services offered by TIGM please visit: <http://www.tigm.org/services/>

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International Mouse Repository

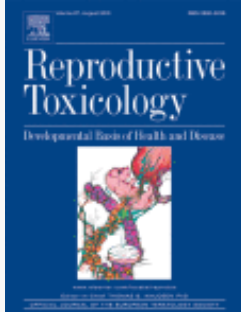


After producing a mouse line, TIGM cryopreserves the sperm and makes those lines available to the international community in compliance with most publishers and NIH resource sharing requirements. We also ask our ES cell customers to ship the mouse lines back to us because we value each knockout line and want to ensure every single mutation is preserved for future use by the scientific community. In addition to contributing to the scientific community, by depositing your mouse in TIGM the line will be available to you or your colleagues anytime in the future should you need it. Should someone contact you to obtain the published mouse, you can send them to us and we will take care of the rest. Depositing your lines at TIGM also means significant cost savings to you as it allows to eliminate the colony once your research is complete and you can be confident that it will be available should you decide to revisit the work. The TIGM International Mouse Repository currently has 213 C57/BL6N and 57 129/SvEv x C57BL6/N cryopreserved lines most of which are available to the public on a cost recovery basis (\$3,500 USD per mouse line) under the same Terms and Conditions as any of our other lines.

The current list of lines in the repository can be found at <http://www.tigm.org/repository/>

Thanks everyone who returns the mouse lines to TIGM International Mouse Repository. Your contributions continue to benefit the research community.

Publications



234 peer-reviewed publications; 11 in 2019

TIGM provides excellent research environment and outstanding services allowing scientists perform a variety of studies. In a recent paper published by Dr. Bedi in the August, 2019 issue of Reproductive Toxicology, Texas A&M scientists used our facilities and animals to determine the impact of alcohol exposure on male reproductive physiology and the association of sperm-inherited noncoding RNAs with the transmission of the observed growth defects ([Alterations in sperm-inherited noncoding RNAs associate with late-term fetal growth restriction induced by preconception paternal alcohol use](#)). Alcohol exposure did not appreciably alter male reproductive physiology or fertility. However, chronic alcohol use reproducibly induced late-term fetal growth restriction in the offspring, which correlated with a shift in the proportional ratio of transfer RNA-derived small RNAs to Pw i-interacting RNAs, as well as altered enrichment of microRNAs miR21, miR30, and miR142 in alcohol-exposed sperm. TIGM will continue assisting scientists with their studies.

We look forward to listing your publication acknowledging the use of TIGM mouse models on our website. More than 230 peer-reviewed research papers have been published by TIGM scientists or using mice derived from TIGM resources. Below is a selection of the most recent publications:

Publications by TIGM scientists:

A Murine Pancreatic Islet Cell-based Screening for Diabetogenic Environmental Chemicals. Chen, J., Zhong, L., Wu, J., Ke, S., Morpurgo, B., Golovko, A., Ouyang, N., Sun, Y., Guo, S., Tian, Y. J. Vis. Exp. (136), e57327, doi:10.3791/57327 (2018)

Long noncoding RNA MALAT1 regulates generation of reactive oxygen species and the insulin responses in male mice. J. Chen, S. Ke, L. Zhong, J. Wu, A. Tseng, B. Morpurgo, A. Golovko, G. Wang, J.J. Cai, X. Ma, D. Li, Y. Tian. Biochemical Pharmacology (2018), Volume 152, 2018, Pages 94-103, doi: <https://doi.org/10.1016/j.bcp.2018.03.019>.

Role of metastasis-associated lung adenocarcinoma transcript-1 (MALAT-1) in pancreatic cancer. Cheng Y, Imanirad P, Jutooru I, Hedrick E, Jin UH, Rodrigues Hoffman A, Leal de Araujo J, Morpurgo B, Golovko A, Safe S. PLoS One. 2018 Feb 1;13(2):e0192264. doi: 10.1371/journal.pone.0192264. eCollection 2018.

Sodium-dependent organic anion transporter (Slc10a6^{-/-}) knockout mice show normal spermatogenesis and reproduction, but elevated serum levels for cholesterol sulfate. Bakhaus K, Bennien J, Fietz D, Sánchez-Guijo A, Hartmann M, Serafini R, Love CC, Golovko A, Wudy SA, Bergmann M, Geyer J.J Steroid Biochem Mol Biol. 2017 Jul 22. pii: S0960-0760(17)30184-X. doi: 10.1016/j.jsmb.2017.07.019

The eIF2A knockout mouse.. Golovko A, Kojukhov A, Guan BJ, Morpurgo B, Merrick WC, Mazumder B, Hatzoglou M, Komar AA. Cell Cycle. 2016 Sep 29:0.

Recent publications featuring mice created and provided by TIGM:

Neuroprotection in non-transgenic and transgenic mouse models of Alzheimer's disease by positive modulation of σ 1 receptors. Tangui Maurice, Jean-Noël Volle, Manon Strehaiano, Lucie Crouzier, Claire Pereira, Nikolay Kaloyanov, David Virieux, Jean-Luc Prat. Pharmacological Research, Volume 144, 2019, Pages 315-330, ISSN 1043-6618.

Neuronal growth regulator 1-deficient mice show increased adiposity and decreased muscle mass. Yeonhee Joo, Hyejin Kim, Sungjoong Lee, Soojin Lee. International Journal of Obesity, 2019, 1476-5497.

Alterations in sperm-inherited noncoding RNAs associate with late-term fetal growth restriction induced by preconception paternal alcohol use. Yudhishtar Bedi, Richard C. Chang, Rachel Gibbs, Tracy M. Clement, Michael C. Golding. Reproductive Toxicology, Volume 87, 2019, Pages 11-20, ISSN 0890-6238.

Dissociation of impulsivity and aggression in mice deficient for the ADHD risk gene Adgrl3: Evidence for dopamine transporter dysregulation. Niall Mortimer, Tatjana Ganster, Aet O'Leary, Sandy Popp, Florian Freudenberg, Andreas Reif, María Soler Artigas, Marta Ribasés, Josep Antoni Ramos-Quiroga, Klaus-Peter Lesch, Olga Rivero, Neuropharmacology, 2019, ISSN 0028-3908.

Activation of GPR55 induces neuroprotection of hippocampal neurogenesis and immune responses of neural stem cells following chronic, systemic inflammation. Jeremy D. Hill, Viviana Zuluaga-Ramirez, Sachin Gajghate, Malika Winfield, Uma Sriram, Slava Rom, Yuri Persidsky. Brain, Behavior, and Immunity, Volume 76, 2019, Pages 165-181, ISSN 0889-1591

A novel GPR55-mediated satiety signal in the oval Bed Nucleus of the Stria Terminalis. E. R. Hawken, C. P. Normandeau, J. Gardner Gregory, B. Cécyre, J.-F. Bouchard, K. Mackie & É. C. Dumont. Neuropsychopharmacology (2019)

Smarcal1 and Zranb3 protect replication forks from Myc-induced DNA replication stress. Matthew V Puccetti, Clare M Adams, Saul Kushinsky and Christine M. Eschen. Cancer Res. January 4 2019 DOI: 10.1158/0008-5472.CAN-18-2705

For the most up to date listing please see our website at

<http://www.tigm.org/publications/>

With Best Regards,

Ben Morpurgo, Ph.D.
Executive Director

Andrei Golovko, Ph.D.
Production Manager

TIGM is a research institute of [Texas A&M AgriLife Research](#)