TIGM.org
TEXAS A&M INSTITUTE FOR GENOMIC MEDICINE

Questions? Call us
(888) 377-TIGM
or (979) 845-8446

Dear Colleague,

Over the past year TIGM has continued expanding its capabilities. In collaboration with TAMU institutes and facilities, TIGM can now offer centralized access to a variety of phenotyping services. Our production efforts are as strong as ever; To date, TIGM has provided more than 295 mouse lines and more than 3,700 ES cell lines to research community. TIGM continues to offer a variety of services to the domestic and international research communities and high-throughput screening of our ES cell library. Important scientific breakthroughs are made with both direct and indirect involvement of TIGM; more than 90 peer-reviewed papers have been published by either TIGM scientists or external researchers who utilized TIGM resources have been published. We now have more than 220 mouse lines in our repository all available at cost recovery rates. These are in addition to 170 NIH- and Wellcome-Trust-subsidized lines also available through TIGM.

Sincerely,

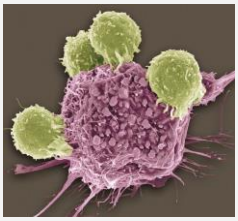
Ben Morpurgo, Ph.D.
Executive Director, TIGM

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 610 mouse and ES cells orders to more than 290 academic and commercial institutions in over 26 countries. 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 7,500 individual investigators from more than 900 academic and research institutions and commercial entities representing 40 countries, have queried TIGM with information requests.

TIGM on the road



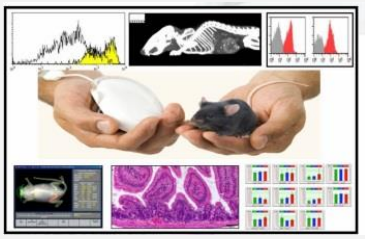
TIGM will be presenting at the **4th Annual, Advances In Oncology - From Clinical Science to Clinical Practice Conference** to be held at Brown Foundation Institute of Molecular Medicine, 1825 Pressler Street, Houston, Texas on October 11th 2013. Please come by and visit. TIGM scientists will be available to discuss our technology and resources.

TIGM will also host **Practical Workshop in Mouse Genome Informatics (MGI)** provided by our colleagues from The Jackson Laboratory on October 2, 2013 between 1 and 3 pm at TAMU VMTH, Room 28. MGI is a free, highly curated database resource for genetic, genomic and phenotypic information pertaining to the laboratory mouse and mouse models of human disease. Please RSVP @ **info@tigm.org**, see you there!

High-throughput ES Cell Screening

Use our cells to identify active compounds, antibodies or genes which modulate a particular biomolecular pathway

In addition to creating knockout mice, TIGM's mutant ES repository is a also powerful tool for high throughput target discovery and validation. Researchers are currently screening cells to investigate reaction of these cells to radiation, environmental contaminants, toxins and bacterial and viral pathogens to determine if the mutations found within specific lines mitigate normal response. Lines which are found to show a different reaction to the test material are then grown into mice and tested to validate the initial results. The advantage of using ES cells in gene target screening is that they can model specific tissues/cell types using a totally in vitro system. In partnership with the Texas A&M AgriLife Genomics and Bioinformatics Service Facility(TAGS), TIGM now offers high throughput ES screening as a fee-for service or a collaboration.



Phenotyping Services

TIGM serves as a centralized access hub to various phenotyping labs at TAMU

Such services include:

Metabolic Phenotyping

- glucose, lipid and protein metabolism
- insulin resistance
- body composition
- nutrient absorption
- hormones, cytokines and adipokines
- serum chemistry
- reactive oxygen species and glutathione metabolism
- insulin and other signaling pathway components
- organ function
- assays to measure defects in cardiovascular, kidney, nervous system, muscle, and skin (wound healing)

Imaging

- fluorescence (Bruker In-Vivo Xtreme, Xenogen - IVIS ® Lumina II, NightOWL)
- luminescence (Bruker In-Vivo Xtreme, Xenogen - IVIS ® Lumina II, NightOWL)
- radioisotopic (Bruker In-Vivo Xtreme)
- high resolution X-ray (Bruker In-Vivo Xtreme)

Behavior analysis

- Activity Chambers

- Preference testing
- Rotorod
- Open field
- Water maze
- Fear conditioning
- Irwin Screen

Pathology
- Gross Observations
- Organ Tissue Weights
- Histopathology

Expression studies
- Taqman
- Microarrays

Oncology
- Skin Proliferation
- Xenografts

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/**

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

TIGM Core Services

Custom services for your research

In addition to providing access to phenotyping services at TAMU, TIGM also offers many 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:

- Knockout mouse production
  - Blastocyst injections
  - Chimera breeding
  - Germline confirmation
- Pronuclear Injection
- 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
  - Speed Congenics

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International Mouse Repository

TIGM adds new lines

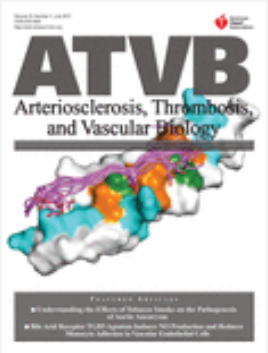
After producing a mouse line, TIGM cryopreserves the sperm and makes those lines available to the international community in compliance with most publishers and NIH resource sharing requirements. We also ask our ES cell customers to ship the mouse lines back to us because we value each knockout line 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 167 C57/BL6N and 55 129/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. We also provide access to 48 Wellcome Trust- and 125 NIH-subsidized lines in 129/SvEv x C57BL6/N background, which are available as sperm ($5,000 USD) to academic and non-profit institutions and can be rederived at an extra cost.

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

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

Publications

94 peer-reviewed publications; 13 in 2013



Even though about 30% of knockouts turn out to be embryonic lethal, they can still be a source of invaluable scientific information. In a recent paper published in the July issue of Arteriosclerosis, Thrombosis, and Vascular Biology and featuring a mouse produced from a TIGM's C57BL/6 gene trapped clone, Roy L. Sutliff and colleagues showed that polymerase delta interacting protein 2 (Poldip2) heterozygous mutation reduces H_2O_2 production in vivo, leading to increases in extracellular matrix, greater vascular stiffness, and impaired agonist-mediated contraction (Polymerase Delta Interacting Protein 2 Sustains Vascular Structure and Function). Based on these finding the researchers concluded that unaltered expression of Poldip2 is necessary for vascular integrity and function. The Poldip2 knockout line is available at TIGM repository.

We look forward to listing your publication acknowledging the use of TIGM mouse models on our website. More than 90 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:

Propitious Modulation Fibroblast Quiescence Mediated by Cytokine Expression Mediated from Embryonic Stem Cells. Ron Shane, Andrei Golovko, Benjamin Morpurgo, Alexa Dillberger, Taylore Bonn, and Amber Buz-Zard. The E-Journal of Age Management Medicine, October 2012,.Vol. 7, No 10.

Publications featuring mice created and provided by TIGM:

TIMP3 is the primary TIMP to regulate agonist-induced vascular remodelling and hypertension. Basu R, Lee J, Morton JS, Takawale A, Fan D, Kandalam V, Wang X, Davidge ST, Kassiri Z. Cardiovasc Res. 2013 Jun 1;98(3):360-71. doi: 10.1093/cvr/cvt067. Epub 2013 Mar 21. [Request Info on Timp4 knockout]

Chromosomal Instability Triggered by Rrm2b Loss Leads to IL-6 Secretion and Plasmacytic Neoplasms. Chang L, Guo R, Huang Q, Yen Y. Cell Rep. 2013 May 1. doi:pii: S2211-1247(13)00164-2. 10.1016/j.celrep.2013.03.040. [Request Info on Rrm2b knockout]

Genetic deletion of Rnd3 results in aqueductal stenosis leading to hydrocephalus through up-regulation of Notch signaling. Lin X, Liu B, Yang X, Yue X, Diao L, Wang J, Chang J. Proc Natl Acad Sci U S A. 2013 Apr 29. [Request Info on Rnd3 knockout]

GPR55, a G-Protein Coupled Receptor for Lysophosphatidylinositol, Plays a Role in Motor Coordination. Wu CS, Chen H, Sun H, Zhu J, Jew CP, Wager-Miller J, Straiker A, Spencer C, Bradshaw H, Mackie K, Lu HC. PLoS One. 2013;8(4):e60314. doi: 10.1371/journal.pone.0060314. Epub 2013 Apr 2. [Request Info on Gpr55 knockout]

A null mutation of mouse Kcna10 causes significant vestibular and mild hearing dysfunction. Sue I. Lee, Travis Conrad, Sherri M. Jones, Ayala Lagziel, Matthew F. Starost, Inna A. Belyantseva, Thomas B. Friedman, Robert J. Morell. Hearing Research, Available online 22 March 2013, ISSN 0378-5955, 10.1016/j.heares.2013.02.009. [Request Info on Kcna10 knockout]

OLA1 protects cells in heat shock by stabilizing HSP70. Mao RF, Rubio V, Chen H, Bai L, Mansour OC, Shi ZZ. Cell Death Dis. 2013 Feb 14;4:e491. doi: 10.1038/cddis.2013.23. [Request Info on Ola1 knockout]

Dact2 Represses PITX2 Transcriptional Activation and Cell Proliferation through Wnt/beta-Catenin Signaling during Odontogenesis. Li X, Florez S, Wang J, Cao H, Amendt BA. PLoS One. 2013;8(1):e54868. doi: 10.1371/journal.pone.0054868. Epub 2013 Jan 22. [Request Info on Dact2 knockout]

Factor VII activating protease (FSAP) exerts anti-inflammatory and anti-fibrotic effects in liver fibrosis in mice and men. Borkham-Kamphorst E, Zimmermann HW, Gassler N, Bissels U, Bosio A, Tacke F, Weiskirchen R, Kanse SM. J Hepatol. 2013 Jan;58(1):104-11. doi: 10.1016/j.jhep.2012.09.007. [Request Info on FSAP knockout]

Haploinsufficiency of the ammonia transporter Rhcg predisposes to chronic acidosis. Rhcg is critical for apical and basolateral ammonia transport in the mouse collecting duct. Bourgeois S, Bounoure L, Christensen EI, Ramakrishnan SK, Houillier P, Devuyst O, Wagner CA. J Biol Chem. 2012 Dec 31. [Epub ahead of print] [Request Info on Rhcg knockout]

The auto-generated fragment of the usp1 deubiquitylase is a physiological substrate of the N-end rule pathway. Piatkov KI, Colnaghi L, Békés M, Varshavsky A, Huang TT. Mol Cell. 2012 Dec 28;48(6):926-33. doi: 10.1016/j.molcel.2012.10.012. Epub 2012 Nov 15.

G-protein signaling modulator-3, a gene linked to autoimmune diseases, regulates monocyte function and its deficiency protects from inflammatory arthritis. Giguère PM, Billard MJ, Laroche G, Buckley BK, Timoshchenko RG, McGinnis MW, Esserman D, Foreman O, Liu P, Siderovski DP, Tarrant TK. Mol Immunol. 2012 Dec 29;54(2):193-198

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 The **Texas A&M AgriLife Research**

Contact: **Benjamin Morpurgo**, Executive Director
670 Raymond Stotzer Pkwy, 4485 TAMU
College Station, TX 77843-4485 | 979-458-5494