

MICHIGAN

ANIMAL MODELS CONSORTIUM

The Michigan Animal Models Consortium (MAMC) provides services associated with the development, analysis and maintenance of mouse models of human disease. This consortium combines the technological and intellectual expertise and state of the art resources located at the AAALAC-accredited Van Andel Research Institute (VARI). By providing efficient and cost effective animal modeling services, the MAMC goals are to enhance life sciences research, facilitate research funding opportunities and promote commercial product development throughout the State of Michigan.

SERVICES

Animal Model Development

■ *Mouse Transgenics*

Production of mice containing foreign genes by microinjection of DNA into the pronuclei of fertilized eggs. Approximately 300–400 eggs are injected with transgenes that can be inserted in a variety of vectors such as plasmids or BACs. An average of ten transgenic founder mice are routinely obtained from these procedures with three founders guaranteed.

■ *Mouse Gene Targeting*

Assistance with the design, development and implementation of gene targeting experiments where a wild-type gene is replaced by either a mutated form of the gene (gene knockout) or a different functional gene (gene knock in). DNA con-

structs are electroporated into mouse embryonic stem cells (ES) and ES cell clones are selected and screened for the mutated form of the gene. Mutant ES cells are cultured and microinjected into wild-type blastocysts to produce chimeric mice. The chimeric mice are bred and the offspring carrying the gene mutation are intercrossed to produce mice with the desired targeted mutation.

■ *Xenotransplantation*

Human cancer cells are injected into immunodeficient mice to produce human-derived tumors. Protocols are designed to test anti-tumor treatment regimens that can lead to prognostic, diagnostic, or therapeutic procedures in humans.

Animal Model Analysis

■ *Cytogenetics*

Application of cytogenetic and molecular genetic methods to detect chromosomal rearrangements and instability. The detection of subtle and complex chromosomal rearrangements commonly found in tumors can be analyzed by using spectral karyotyping (SKY) which is a high quality 24-color FISH paint assay. The tumor findings can be greatly complemented by array comparative genomic hybridization (array CGH) that is useful for detecting chromosomal instability such as the loss or gain of genetic material. Other cytogenetic techniques that

can be performed on cytological samples include; G-banding, fluorescent in situ hybridization (FISH), murine trisomy 8 screening, transgene localization, and breakage studies.

■ *Necropsy*

Mice are dissected post-mortem and tissues are fixed for histological analysis. Necropsy reports are generated using voice-recognition software.

■ *Imaging and Microscopy*

Histological sections are prepared from mouse tissues using microtomes and cryostats, processed and stained using automated instruments, and then microscopically analyzed.

■ *Veterinary Pathology*

Tissue specimens are fixed, embedded and stained for microscopic analysis. A board-certified veterinary pathologist holding the D.V.M. and Ph.D. degrees provides expert microscopic analysis and project consultation.

■ *Robotic DNA Isolation*

DNA is isolated from mouse tail biopsies using the AutogenPrep 960 instrument.

Animal Model Maintenance

■ *Embryo/Sperm Cryopreservation*

Cryopreservation of mouse embryos and sperm combined with in vitro fertilization services to reconstitute cryopreserved strains.

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■ **Mouse Rederivation**

All mouse strains entering the specific pathogen-free breeding facility are rederived to specific pathogen-free mouse status using embryo transfer techniques.

■ **Animal Housing Services**

Mice are housed in a specific pathogen-free Vivarium

■ **Animal Technical Services**

Veterinary services such as injections, measurements, mating set-up, and tail biopsies are performed by the animal technician staff.

■ **Contract Breeding Services**

Wild-type mouse strains and genetically engineered animal models are maintained for research purposes by breeding the strains in a specific pathogen-free environment.

■ **Cancer Model Repository**

Mouse cancer models of research interest are maintained through breeding strategies.

EQUIPMENT

■ **Transgenics**

2 microinjection workstations each composed of a Nikon Eclipse inverted microscope with a Dage-MTI RC 100 video camera, Sony PVM-137 video monitor, 2 Leitz micromanipulators, a TMC vibration isolation table and Bunton and Stoeling microinjectors. The two surgical workstations consist of a wall and table mounted Zeiss OPMI 1-FC surgical microscopes and two Nikon SMZ645 stereomicroscopes. A Defonbrune type microforge with Meiji Techno EMZ optics and a Kopf Pipette Puller are used to fabricate the microinjection needles. The lab also contains a Forma 3110 Hepa filtered, CO₂ incubator.

■ **Gene Targeting**

2 microinjection workstations each consisting of a Leica DMIRB-HC inverted microscope, an Optronics DEI-750D digital video camera, a Sony 14" monitor, a model 5000 Micro Devices cooling stage, 2 Leitz micromanipulators, Eppendorf

Cell Tram Air and Cell Tram Vario microinjectors, and a TMC vibration isolation table. Two Leica MZ9.5 zoom stereomicroscopes are available for dissections and the surgical workstation consists of a Zeiss OPMI 1-FC table mounted surgical microscope. An ES cell culture facility equipped with 4 Forma 3110, Hepa filtered CO₂ incubators, a 6 ft Baker Biological SterilGARD ClassII, type B biological safety cabinet, a Baker, 4 ft horizontal laminar flow clean bench, a Nikon Eclipse TS500 inverted microscope, a Leica ZFLI-II research fluorescence stereomicroscope with a Nikon spot digital camera, a Leica MZ6 zoom stereomicroscope, a BioRad Gene Pulser II electroporation system with capacitance extender, a BioRad Gene Pulser Xcell electroporation system, a Sorvall Legend refrigerated centrifuge, a Forma -80°C freezer, a -20°C Freezer, and a MVE XLC 1211 liquid nitrogen freezer. A CF-150B cell fusion instrument is available for producing tetraploid embryos.

■ **Xenograft Models:**

Electronic Laboratory Animal Monitoring System

■ **Cytogenetics**

Olympus BX51 fluorescence microscope with filter sets from Chroma Technology Corporation; COOL-1300 SpectraCube imaging system (Applied Spectral Imaging); Hamamatsu Cooled CCD Camera C4880-85 (Hamamatsu Photonics K.K., Japan); CytoLabView software including BandView, FISHView, and SKYView, (Applied Spectral Imaging); Zeiss Axioplan 2 Imaging universal microscope; Ikaros karyotyping and Isis in situ imaging system software (MetaSystems Group Inc.).

■ **Histology/Veterinary Pathology**

Zeiss 510 Nonlinear optics multiphoton confocal scanning microscope, Zeiss 410 Laser scanning inverted confocal microscope, Zeiss 310 Laser scanning upright confocal microscope, Laser capture

microdissection station, Olympus Microtome 4060E, Ventana Tissue Processor Leica Embedding Center, Leica Cryostat EG1140H, Vibratome.

■ **Embryo/Sperm cryopreservation**

A MVE XLC 1211 liquid nitrogen freezer and a ThermoElectron CryoMed controlled rate freezer.

■ **Animal Housing**

The vivarium is equipped with an MTP tunnel washer with a dump station and automated bedding dispenser, an MTP rack washer, Getinge/Castle walk through and small autoclaves, Thoren ventilated caging systems, an Edstrom automatic water system with alarm, and an MTP bottle filler. Vivarium records are maintained using the Topaz Technologies Scion Database. DNA samples are prepared with an AutogenPrep 960.

ACCESS

All MAMC services are available to clients on a fee-for-service basis. Potential clients are strongly advised to view the website <http://www.vai.org/Research/Services/mamc.aspx> and contact the service directors prior to submitting an application form for the services. All services are provided in the order that the application is received. Training and consultation is available on a fee-for-service basis after consultation with the service provider.

CONTACT INFORMATION

HUB

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