ANIMAL MODELS CORE

Genetic mouse models are revolutionizing our understanding of human diseases and address important biological questions. Many of the most prevalent and devastating bone disorders still lack any animal models for studies of pathogenesis or treatment. Pharmacologic, dietary and gene therapy regimens all require disease models for full development. Present day mouse models have significant advantages for development of such disease models, including: well defined genetic characteristics and mapping data, short generation time, large litter size, definable and measurable environmental influences, maintenance of pathogen free status, and relatively inexpensive husbandry. The ability to create specific mutations in the mouse germline via ES cell technology further supports the mouse as an ideal mammalian research model.

The overall goal of the CMBD Animal Models Core is to produce mouse models that provide a mammalian system to study the pathophysiology of bone disease and the efficacy of potential treatment interventions. To this end, the Core has the following aims:

Aim 1. To develop mouse models relating to the mission of the CMBD.

- CMBD Core Committee (membership to be determined) will consult with the UAB Transgenic Mouse Facility Director bi-annually to prioritize mouse models to be developed with available resources. For example, transgenic mice expressing cre recombinase (or inducible cre) in target tissues of interest may be developed.
- Using constructs developed by the TMF or by CMBD investigators, the TMF will generate and identify transgenic founder animals (or chimeric animals derived from gene targeting in ES cells) to be analyzed by CMBD investigators expressing interest in the animal model. Each animal model will be cryopreserved, and made available to any CMBD investigator desiring its use.

Aim 2. Provide expert assistance and reagents for Pilot & Feasibility Projects.

- Provide expert services to help inexperienced investigators design the most effective transgene constructs, strategies for molecular analyses of transgenic mice, and breeding strategies required for perpetuation of transgenic mouse lines.
- Provide necessary reagents and expert advice for their use in order to train students, postdoctoral fellows, and research staff interested in transferring gene targeting technologies to individual laboratories

Aim 3. Provide consultation on development of genetically engineered mice.

- Provide expert consultation services to help investigators design most effective transgenic mouse model needed for CMBD research lab. Support will include: transgenic construct designs, strategies for molecular analyses of transgenic mice, and grant writing support pertaining to animal model.
- Provide educational resources for genetic manipulation of the mouse genome via on-campus seminars and lectures by UAB Transgenic Core personnel, and via external speakers.

Services Offered by the Transgenic Mouse Facility:

- DNA microinjection (pronuclear)

- Gene Targeting (with & without screening)
- ES cell microinjection (blastocysts)
- In vitro fertilization (IVF)
- Embryo cryopreservation
- Sperm cryopreservation
- Long-term storage of cryopreserved
- Assisted reproduction / rederivations
- Consultation and training

For additional information or assistance in developing transgenic mouse models, or utilizing any of the services offer by the TMF, please visit their website (www.uab.edu/transgenics), or contact Dr. Kesterson directly (205-934-7206).

New Resources: Perhaps the greatest resource currently available to researchers for the creation of "knockout" mouse models is the generation of libraries of ES cell clones. Members of the International Knockout Mouse Consortium (IKMC) are working together to mutate all protein-coding genes in the mouse using a combination of gene trapping and gene targeting in C57BL/6 mouse embryonic stem (ES) cells. Available ES cell clones for the estimated 40% of genes currently "knocked out" (as of June 2011) can be identified through both BLAST sequence searches and keyword queries.

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