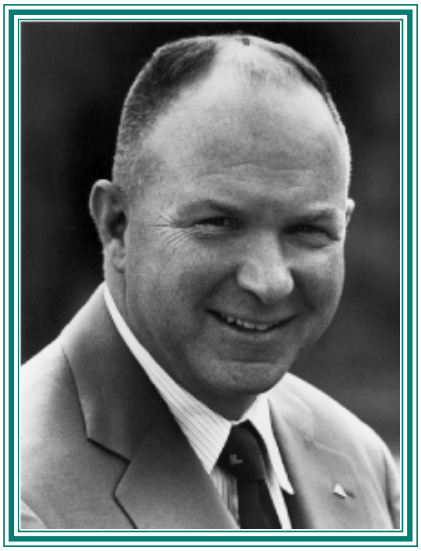
The Jackson Laboratory
BAR HARBOR, ME USA

JAX | NOTES™

For Users of JAX® Mice

Warren Cook is Named President of JAX Research Systems



Mr. Warren C. Cook has been named president of JAX Research Systems a newly expanded division of The Jackson Laboratory. JAX Research Systems includes three operational areas: (1) the JAX® Mice division; (2) development of new products and services to support biomedical research and (3) intellectual property and technology transfer. Mr. Cook joined The Jackson Laboratory in January 1999.

Mr. Cook, 53, has international experience in business management, organizational development, and finance. From 1976 to 1986, he was president and chief executive officer of Chemfab Corporation in Merrimack, New Hampshire, a producer of high-temperature materials composites. Mr. Cook most recently served as chief operating officer for American Skiing Company of Newry, Maine, operators of alpine ski, snowboard, and golf resorts nationwide, including Maine's Sunday River and Sugarloaf/USA.

"The world is increasingly turning to mice as the paramount research discovery tool for understanding and improving human health," says Jackson Laboratory Director Dr. Kenneth Paigen. "Already, a quarter of the federal biomedical research effort depends on mice, and that is growing. At The Laboratory, we are increasingly challenged in our role as an essential national resource. We look to Warren Cook in this new position to help us develop and distribute the tools researchers need to cure diseases and save lives. The potential for new growth and new jobs is considerable." As president of JAX Research Systems, Mr. Cook will report directly to Dr. Paigen.

MOUSE MODELS

USING NOD/LtJ MALES IN DIABETES RESEARCH

The NOD mouse is the most genetically defined system for studying insulin-dependent diabetes mellitus (IDDM), type 1 diabetes. Increases in funding from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Juvenile Diabetes Foundation have recently increased the demand for NOD/LtJ mice (Stock No. 001976) and related strains (*e.g.* NON/LtJ, NOR/LtJ, and NOD/LtSz-*Prkdc*^{scid}/J, and NOD mice congenic for IDDM-resistant MHC haplotypes).

The Jackson Laboratory continues to expand colonies of these strains to meet this demand. While NOD/LtJ females are more widely used than males because the onset of IDDM symptoms occurs earlier and with a higher incidence (90-100% by 30 weeks of age), NOD/LtJ males can be particularly useful for certain applications described in this article.

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Using NOD/LtJ Males in Diabetes Research (continued)

- NOD/LtJ males develop IDDM at a frequency of between 40-60% by 30-40 weeks of age. The fact that diabetes progression is more protracted in NOD males makes them very useful to assess the presence of diabetogenic catalysts in the microbial or dietary environment that can precipitate IDDM.

- NOD/LtJ males are also useful in pharmaceutical studies. Because of the more protracted rate of diabetogenesis in NOD males, a longer window of time is available for testing pharmaceutical or enviromental agents that repress the disease process. In NOD/LtJ females, leukocyte accumulation in and around pancreatic islets begins as early as 3 weeks, with precipitous declines in pancreatic insulin levels and development of overt hyperglycemia evident by 12 weeks of age. The early development of insulitis in females leaves little time to manipulate the course of disease by the time purchased female mice are received then acclimated to a new vivarium. In this regard, NOD/LtJ males also offer an advantage as recipients in islet transplantation studies. *Note:* NOD/LtSz-*Prkdc*^{scid}/J males are ideal syngeneic islet donors for transplantation studies into male recipients since they are free of T- and B-lymphocyte infiltrates.

- NOD/LtJ males may be used for "accelerated transfer" of IDDM. Young, prediabetic irradiated males may be used as hosts in adoptive transfer experiments by intravenously or intraperitoneally injecting populations of leukocytes or purified T lymphocytes from diabetic or prediabetic donor NOD mice. *Please note:* splenic leukocytes from female donors should not be transferred into male recipeints because female T lymphocytes will respond to male sex-limited (H-Y) antigen. However, syngeneic T cell lines and clones without anti-H-Y specificities can be used in accelerated transfer studies into males.

- NOD/LtJ males are as useful as NOD/LtJ females for some *in vitro* studies. For example, immune functions of leukocyte subpopulations (*e.g.* macrophages or B-lymphocytes) isolated from NOD/LtJ males generally show the same deficiencies as those from females.

Selected Reviews

Authors in bold indicate Jackson Laboratory scientists

- **Leiter EH**. 1998. NOD mice and related strains: research applications in diabetes, AIDS, cancer, and other diseases. In: *Medical Intelligence Unit*, Leiter EH, Atkinson MA (eds), Landes, Austin, pp. 208.

- **Leiter EH**. 1997. The NOD mouse: a model for insuli-dependent diabetes mellitis. *Current Protocols in Immunology* 24(Suppl):15.9.1-15.9.23.

- **Serreze DV, Leiter EH**. 1995. Insulin-dependent diabetes mellitus in NOD mice and BB rats: origins in hematopoietic stem cell defects and implications for therapy. In: *Lessons From Animal Diabetes*, Shafrir E (ed), Smith Gordon Press, pp. 59-73.

- **Serreze DV, Leiter EH**. 1994. Gentic and pathogenic basis of autoimmune diabetes in NOD mice. *Curr Opin Immunol* 6:900-906.

For more information and other useful references, please refer to JAX Notes No. 452 Winter 1993, accessible from the JAX Mice Web Site at www.jax.org/jaxmice (select JAX Mice Library) or go directly to url: jaxmice.jax.org/html/jaxnotes/jaxn452a.shtml.

NOD/LtSz-*Prkdc*^{scid}/J: An Improved *scid* Mouse for Cancer and Immunological Research

Severe combined immune deficiency in the mouse is a result of a mutation in the protein kinase, DNA activated, catalytic polypeptide gene (*Prkdc*^{scid}). Mice homozygous for this mutation, hereafter referred to as *scid*, are available from The Jackson Laboratory as congenics on several different inbred strain backgrounds (C57BL/6J, BALB/cByJ, C3H/SmnJ and NOD/LtSz). The lack of functional T and B cells in these mice has made them useful for many experiments involving reconstitution of human hematopoietic cells. However, most inbred strains express normal levels of natural killer (NK) cells, hemolytic complement and myeloid function precluding long term repopulation of homozygous *scid* mice with human cells. In addition, *scid* mutant mice on some background strains produce immunoglobulin and functional T-cells at low levels.

To develop a mouse stock with defective lymphoid function and nonadaptive immunologic function the *scid* mutation was backcrossed to NOD/Lt for ten generations. The NOD/Lt strain is characterized by a functional deficit in NK cells, absence of circulating complement and defects in the differentiation and function of APC's. Although NOD/Lt mice develop T cell-mediated autoimmune, insulin-dependent diabetes mellitus, NOD/LtSz-*scid* mice remain insulitis and diabetes-free. However, because of the high incidence of thymic lymphomas, the mean lifespan of NOD/LtSz-*scid* mice is only 8.5 months under specific pathogen-free conditions.

The NOD/LtSz-*scid* has been used to successfully transplant a variety of normal and malignant human cell populations and tissues. Splenic engraftment of human CEM T-lymphoblastoid cells was fourfold greater in NOD/LtSz-*scid* mice than in the C.B-17/Sz-*scid* mice. Although C.B-17/Sz-*scid* mice exhibit robust NK cell activity, this activity is markedly reduced in NOD/LtSz-*scid* mice. The macrophage population in NOD/LtSz-*scid* is functionally less mature than in C.B-17/Sz-*scid* mice. Although C.B-17/Sz-*scid* and C57BL/6Sz-*scid* mice have elevated serum hemolytic complement activity compared with their respective wildtype controls, both NOD/LtSz-+/+ and NOD/LtSz-*scid* mice lack this activity. Age-dependent increases in serum Ig levels (> 1 μg/ml) were observed in only 2 of 30 NOD/LtSz-*scid* mice vs. 21 of 29 C.B-17/Sz-*scid* animals. The multiple defects in innate and adaptive immunity unique to the NOD/LtSz-*scid* mouse provide an excellent *in vivo* environment for reconstitution with human hematopoietic cells.

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An Improved scid Mouse (continued)

NOD/LtSz-*Prkdc*^{scid}/J mice (stock # 001303) are exclusively available from The Jackson Laboratory.

This article was adapted from: **Shultz LD**, **Schweitzer PA**, **Christianson SW**, **Gott B**, **Schweitzer IB**, **Tennent B**, **McKenna S**, **Mobraaten L**, Rajan TV, Greiner DL, **Leiter**, **EH**. 1995. Multiple Defects of Innate and Adaptive Immunologic Function in NOD/LtSz-*scid* Mice. *J Immunol* 154:180-191.

Defects in Innate Immunity

	NOD/LtSz - *scid*	C.B-17/Sz - *scid*
NK cell activity	**Low**	**High**
Complement activity	**Absent**	**High**
Macrophage development	**Impaired**	**Normal**
Anitgen presenting cell function	**Impaired**	**Normal**

Helpful Reading

Authors in bold indicate Jackson Laboratory scientists

Strain-dependent leakiness of the scid mutation

- **Christianson SW**, Greiner DL, **Schweitzer IB**, **Gott B**, **Beamer GL**, **Schweitzer PA**, Hesselton RM, **Shultz LD**. 1996. Role of natural killer cells on engraftment of human lymphoid cells and on metastasis of human T-lymphoblastoid leukemia cells in C57BL/6J-*scid* mice and in C57BL/6J-*scid bg* mice. *Cell Immunol* 171:186-199.
- Nonoyama S, Smith FO, Bernstein ID, Ochs HD. 1993. Strain-dependent leakiness of mice with severe combined immune deficiency. *J Immunol* 150:3817-24.

***Transplantation experiments using* NOD/LtSz-*Prkdc*^{scid}**

- Baersch G, Mollers T, Hotte A, Dockhorn-Dworniczak B, Rube C, Ritter J, Jurgens H, Vormoor J. 1997. Good engraftment of B-cell precursor ALL in NOD-SCID mice. *Klin Padiatr* 209:178-85.
- Greiner DL, **Shultz, LD**. 1998. The use of NOD/LtSz-*scid/scid* mice in biomedical research. In: *NOD Mice and Related Strains: Research Applications in Diabetes, AIDS, Cancer and Other Diseases*, **Leiter E**, Atkinson M (eds), R. G. Landes Company, pp. 173-203.
- Greiner DL, Hesselton RA, **Shultz LD**. 1998. SCID mouse models of human stem cell engraftment. *Stem Cells* 16:166-177.
- **Pelsue SC**, Leif J, Rajan TV. 1995. Improved engraftment of human spleen cells in NOD/LtSz-*scid/scid* mice as compared with C.B-17-*scid /scid* mice. *Am J Path* 146: 888-902.
- Hogan CJ, Shpall EJ, McNulty O, McNiece I, Dick JE, **Shultz LD**, Keller G. 1997. Engraftment and Development of Human CD34^{+}-Enriched Cells From Umbilical Cord Blood in NOD/LtSz-*scid/scid* Mice. *Blood* 90:85-96.
- Larochelle A, Vormoor J, Lapidot T, Sher G, Furukawa T, Li Q, **Shultz LD**, Olivieri NF, Stamatoyannopoulos G, Dick JE. 1995. Engraftment of immune-deficient mice with primitive hematopoietic cells from b-thalassemia and sickle cell anemia patients: implications for evaluating human gene therapy protocols. *Hum Mol Genet* 4:163-172.
- Ramirez M, Rottman GA, **Shultz LD**, Civin CI. 1998. Mature human hematopoietic cells in donor bone marrow complicate interpretation of stem/progenitor cell assays in xenogeneic hematopoietic chimeras. *Exp Hematol* 26:332-44.
- Wang JC, Lapidot T, Cashman JD, Doedens M, Addy L, Sutherland DR, Nayar R, Laraya P, Minden M, Keating A, Eaves AC, Eaves CJ, Dick JE. 1998. High level engraftment of NOD/SCID mice by primitive normal and leukemic hematopoietic cells from patients with chronic myeloid leukemia in chronic phase. *Blood* 91:2406-14.

Another *scid* Model of Interest - NOD/LtSz-*Prkdc*^{scid}/J *B2m*^{tm1Unc}

The Jackson Laboratory is in the process of establishing a production colony of NOD/LtSz-*Prkdc*^{scid}/J *B2m*^{tm1Unc} (Stock # 002570). This mouse was generated by backcrossing the Class I deficient *B2m* targeted mutation on to the NOD/LtSz-*Prkdc*^{scid} strain. You can help us determine the most appropriate colony size by contacting Customer Service with your interest in this strain: tel:1-800-422-MICE or 207-288-5845; fax: 207-288-6150.

Reference

Authors in bold indicate Jackson Laboratory scientists

- **Christianson SW**, Greiner DL, Hesselton RA, Leif JH, Wagar EJ, **Schweitzer IB**, Rajan TV, **Gott B**, **Roopenian DC**, **Shultz LD**. 1997. Enhanced human CD4+ T cell engraftment in beta2-microglobulin-deficient NOD-*scid* mice. *J Immunol* 158:3578-86.

A Mouse Model for Hereditary Glaucoma

Aging DBA/2J mice (Stock No. 000671) develop progressive eye abnormalities that closely mimic human hereditary glaucoma. Defects include iris pigment dispersion, iris atrophy, anterior synechia (adhesion of the iris to the cornea), and

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A Mouse Model for Hereditary Glaucoma (continued)

elevated intraocular pressure (IOP). The onset of disease symptoms begins between 3 and 4 months of age with 56% of females and 15% of males showing signs of iris pigment epithelium loss and transillumination of the peripheral iris. By 6 to 7 months of age, all mice demonstrate significant widespread transillumination and thickening of the iris border. Elevation of IOP is evident in some females by 6 months of age. By 9 months of age both sexes exhibit elevated IOP with pressures higher in females (mean: 20.3 ± 1.8 mmHg) compared to males (mean: 16.2 ± 1.4 mmHg).

REFERENCE

Authors in bold indicate Jackson Laboratory scientists

- **John SW, Smith RS**, **Savinova OV**, **Hawes NL**, **Chang B**,Turnbull D, **Davisson M, Roderick TH,** Heckenlively JR. 1998. Essential iris atrophy, pigment dispersion, and glaucoma in DBA/2J mice. *Invest Ophthalmol Vis Sci* 39:951-62. Published erratum appears in *Invest Ophthalmol Vis Sci* 1998 39:1641.

THE FIRST MOUSE MODEL FOR ERYTHROPOIETIC PROTOPORPHYRIA

The BALB/c-*Fech*^{Pas} strain (Stock No. 002662) is the first mouse model for studying erythropoietic protoporphyria (EPP). This strain carries a chemically induced mutation in the mouse homolog of the human gene (*FECH*) mutated in patients with EPP. BALB/c-*Fech*^{m1Pas} mice are deficient in ferrochelatase and exhibit increased photosensitivity that mimics the human disease. For animal husbandry purposes, please note that the degree of sensitivity is dependent on the wavelength of light produced in the mouse room (specific range: 400-410 nm), the type of caging system used (*e.g.* filter bonnets, PIV racks, and/or opaque boxes may reduce exposure), and the distance of the mouse box from the light source (top versus bottom shelf placement). Additionally these mice reportedly develop severe hepatobiliary disease, including jaundice, a complication found in approximately 5% of EPP patients.

REFERENCES

Authors in bold indicate Jackson Laboratory scientists

- Tutois S, Montagutelli X, Da Silva V, Jouault H, Rouyer-Fessard P, Leroy-Viard K, Guenet JL, Nordmann Y, Beuzard Y, Deybach JC. 1991. Erythropoietic protoporphyria in the house mouse. A recessive inherited ferrochelatase deficiency with anemia, photosensitivity, and liver disease. *J Clin Invest* 88:1730-1736.

- Boulechfar S, Lamoril J, Montagutelli X, Guenet JL, Deybach JC, Nordmann Y, Dailey H, Grandchamp B, de Verneuil H. 1993. Ferrochelatase structural mutant (*Fech*^{m1Pas}) in the house mouse. *Genomics* 16:645-648.

- **Kiupel M**, Montagutelli X, **Sundberg JP**. 1998. The ferrochelatase deficiency (*Fech*^{m1Pas}) mouse mutation: a mouse model for erythropoietic protoporphyra, Jackson Laboratory *JAX Communication*^{TM}. Contact Customer Service for a copy.

A MOUSE MODEL FOR WOUND HEALING AND REGENERATION

Dr. Ellen Heber-Katz and her colleagues at the Wistar Institute in Philadelphia, PA recently reported that MRL/MpJ mice (Stock No. 000486) have the ability for rapid and complete wound closure, a process resembling regeneration. Ear punches, a commonly used method for murine identification, to MRL/MpJ or MRL/MpJ-*Fas*^{lpr} mice (Stock No. 000485) are completely closed in less than four weeks. An intriguing finding in mammals as the regenerated tissue has normal architecture including cartilage, skin, blood vessels and fur. Similarly, these mice are able to significantly regenerate tail tissue following excision.

Genetic analysis of this wound healing trait implicates the involvement of multiple genes, possibly 6, mapped to locations on chromosomes 8, 12, 15, 13 and 7. All but one of these putative genes, located on chromosome 8, are inherited from the MRL/MpJ parent strain. Interestingly, the genes regulating the wound healing trait appear to be independent from those leading to autoimmune disease in these mice.

REFERENCES

- McBrearty BA, Clark LD, Zhang XM, Blankenhorn EP, Heber-Katz E. 1998. Genetic analysis of a mammalian wound-healing trait. *Proc Natl Acad Sci USA* 95:11792-7.

- Clark LD, Clark RK, Heber-Katz E. 1998. A new murine model for mammalian wound repair and regeneration. *Clin Immunol Immunopathol* 88:35-45.

NIH, JACKSON LABORATORY AND DUPONT PHARMACEUTICALS SIGN CRE-LOX TECHNOLOGY USE AGREEMENTS

During late 1998, the National Institutes of Health, The Jackson Laboratory and DuPont Pharmaceuticals Company signed landmark agreements on the use of DuPont's proprietary Cre-lox technology. The agreements resolve long-standing issues of access by academics to commercially owned technology.

Under the agreements, The Jackson Laboratory can accept and breed Cre-lox mice whose genetic makeup has been defined using DuPont's proprietary technology and distribute them to the scientific community. Cre-lox derived strains will also be added to The Jackson Laboratory's national repository of genetically defined mice.

"We're very pleased to be able to make this valuable technology more widely available to scientists," Jackson Laboratory Director Dr. Kenneth Paigen said. "This agreement helps advance an important part of our mission: to provide genetic resources to the world's research community in a manner that promotes basic discovery." *(continued on page 5)*

Cre-lox Agreements (continued)

The agreements distinguish between academic and commercial uses of the technology. DuPont has agreed to make the technology available without cost to NIH researchers and grantee institutions for non-commercial purposes. Recipient nonprofit institutions need an academic license with DuPont to transfer the NIH materials or to practice further under the Cre-lox patents. Discoveries made within the academic realm through use of the Cre-lox technology will not be subject to any payments to DuPont so long as the discovery is made outside of any benefit accruing to a commercial entity.

"The agreement between DuPont and the NIH is a milestone in the cooperative relationship between academia and industry," said Dr. Harold Varmus, Director of the National Institutes of Health. "It will allow science to continue to move forward freely as it uses a valuable commercially owned research tool for the benefit of medicine and the public."

The Jackson Laboratory has accepted several Cre-lox strains that are now in our importation and rederivation program, and thus, not yet available (see the list above). To help us anticipate your needs for specific Cre-lox strains, please register your interest with Customer Service by calling 1-800-422-MICE or 207-288-5845.

LIST OF CRE-LOX STRAINS IN DEVELOPMENT AT THE JACKSON LABORATORY

Stock Name	Stock Number	Reference
TgN(CrehCMV) #	002471	Lakso M, Sauer B, Mosinger B, Jr., Lee EJ, Manning RW, Yu S-H, Mulder KL, Westphal H. 1992. Targeted oncogene activation by site-specific recombination in transgenic mice. *Proc Natl Acad Sci USA* 89:6232-6236.
TgN(CreMx1)1Cg	002527	Kuhn R, Schwenk F, Aguet M, Rajewsky K. 1995. Inducible gene targeting in mice. *Science* 269:1427-1429.
TgN(balancer1)2Cgn	002858	Betz UAK, Vosshenrich CAJ, Rajewsky K, Muller W. 1996. Bypass of lethality with mosaic mice generated by Cre-loxP-mediated recombination. *Curr Biol* 6:1307-1316.
TgN(balancer2)3Cgn	002859	Betz UAK, Vosshenrich CAJ, Rajewsky K, Muller W. 1996. Bypass of lethality with mosaic mice generated by Cre-loxP-mediated recombination. *Curr Biol* 6:1307-1316.
DBA/2-TgN(xstpxLacZ)32And C57BL/6-TgN(xstpxLacZ)36And	002981 002982	Zinyk DL, Mercer EH, Haris E, Anderson DJ, and Joyner AL.1998. Fate mapping of the mouse midbrain-hindbrain constriction using a site-specific recombination system. *Curr Biol* 8(11):665-668.
B6,129-*Gtrosa26*^{tm1Sor} (nomenclatuire subject to change)	003309	Soriano P. 1999. Generalized *lacZ* expression with the ROSA26 Cre reporter strain. *Nat Genet* 21:70-71.
FVB/N-TgN(EIIa-Cre)C5379Lmgd	003314	Lakso M, Pichel JG, Gorman Jr, Sauer B, Okamoto Y, Lee E, Alt FW, Westphal H. 1996 . Efficient *in vivo* manipulation of mousegenomic sequences at the zygote state. *Proc Natl Acad Sci USA* 93:5860-5865.

FREQUENTLY-ASKED QUESTIONS

QUESTION: How can I improve the breeding performance of my mice?

ANSWER: Some mice, including the C57BL/6J inbred strain, are very susceptible to environmental stress. Breeding difficulties may be overcome in this strain and others by examining the overall mouse room conditions and trying to minimize exposure to sudden noises, excess handling, and vibrations from equipment in adjoining rooms. Often, extending the light/dark cycle from 12/12 to 14/10 can improve performance.

As well, dietary fat content and nutritional makeup affects the overall health of the mice and also their reproductive performance. The Jackson Laboratory has had success with mice maintained on NIH 31 6% feed from Purina Mills. Another factor to consider is that reproductive performance generally decreases with age. We recommend replacing older breeders (*i.e.*, greater than 8 months of age) with young mice (*i.e.*, 6-8 weeks of age) on a routine basis. If breeder pairs do not produce progeny within 6-8 weeks, try switching males and female pairs. If females are not caring for their young and environmental stress has been minimized, then consider fostering the litter to a proven surrogate mother.

QUESTION: How should I foster a litter?

ANSWER: Newborn litters are sometimes fostered onto nursing surrogate mothers for a variety of reasons. The following is a compilation of comments, suggestions and proven techniques that can be used to successfully foster a litter. It is important to note that techniques used to ensure the foster mother will accept the new pups vary and the method that works best may depend upon individual preferences and the reason for fostering.

- The first step in fostering is the selection of a suitable foster mother. Try to choose a mother that has successfully weaned a litter in the recent past. For best results it is important to match the age of the litter to be fostered with the age of the foster mother's natural litter. The foster mother's litter should be a different coat color than the litter to be fostered so the pups can be separated at weaning. If, however, the entire natural litter is removed and replaced with the foster litter this is not necessary. Always be sure the foster mother has finished delivering her young before using her as a foster mother because sometimes one or two pups may be born up to 6 hours after the majority of pups are born.
- It is critical to have the foster litter size equivalent to the natural litter size. If the litter to be fostered is especially large (*i.e.*, more than 10 pups) then the litter may need to be

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Frequently Asked Questions (continued)

divided and given to two foster mothers. A change in litter size of ± 2 or more pups can affect the milk supply of the foster mother.

- It is best to keep the foster mother in her cage, remove the natural litter, then add the foster litter to the cage. The foster mother and her foster litter can be transferred to a clean cage the next day. During the first 24 hours, avoid disturbing the foster mother and her new foster litter, but periodically check to ensure that the foster mother is caring for the new litter.

- An alternative approach to transferring a litter is to remove the entire nest containing the foster mother's natural litter. Place the nest under a heat lamp or some source of heat. Next place the foster litter in the nest, then gently mingle pups from the natural and foster litters together to spread scent. Rub feces from the foster mother on the backs of the foster pups. When the foster mother cleans the foster pups, she will most likely accept the pups as her own. Place the nest with the foster pups back in the cage of the foster mother.

JACKSON LABORATORY RESEARCH NEWS

NEW MOUSE TUMOR BIOLOGY PROTOTYPE DATABASE AVAILABLE

A prototype version of the *Mouse Tumor Biology Database* (MTB) is now available from The Jackson Laboratory's Mouse Genome Informatics (MGI) group. MTB has been designed to aid researchers in such areas as choosing experimental models, reviewing patterns of mutations in specific cancers, and identifying genes that are commonly mutated across a spectrum of cancers.

The MTB Database supports the use of the mouse as a model system of hereditary cancer by providing electronic access to:

- Tumor names and classifications
- Tumor incidence and latency data (in different strains of mice)
- Tumor pathology reports and images
- Information on genetic factors associated with tumors and tumor development
- References (published and unpublished data)
- Links to related on-line resources including:
  -The Mouse Genome Database
  -The JAX Mice Database

Future versions of the MTB database will include information on experimental protocols and tumor treatment response data reported in the published literature. The current prototype version can be accessed from the MGI home page at www.informatics.jax.org or directly using url: tumor.informatics.jax.org. User support is available for MTB by email at mgi-help@informatics.jax.org.

Above: Home page of the Mouse Tumor Biology Prototype Database

REFERENCE

Authors in bold indicate Jackson Laboratory scientists

- **Bult CJ, Krupke DM, Eppig JT**. 1999. Electronic access to mouse tumor data: the Mouse Tumor Biology Database (MTB) project. *Nucl Acids Res* 27:99-105.

The Mouse Tumor Database Project is supported by the National Cancer Institute contract 97CSX022A.

REVISED NOMENCLATURE FOR STRAIN 129 MICE

It is important to clearly distinguish different 129 sublines because of the genetic differences between them (Simpson *et al.*, 1997). In October 1998, the International Committee on Genetic Nomenclature for Mice approved a new nomenclature to distinguish different 129 family lines and related sublines.

Above: Photo of 129/Sv Ems-+$^{Ter?}$/J (Stock No. 002065)

These nomenclature changes affect the strain designations for inbred 129 mice and for all transgenic and mutant mice on a 129 background strain. The Jackson Laboratory is currently working on modifying the strain designations of all relevant JAX Mice. We will begin using the new 129 nomenclature for JAX Mice in June 1999. The new strain designations will appear in our *1999 Price List & Product Guide*, available in June 1999.

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Revised Nomenclature for Strain 129 Mice (continued)

For detailed information on the 129 nomenclature change, please see our Web site at www.jax.org/jaxmice. Select **Gene and Strain Nomenclature**; click on Revised Nomenclature for Strain 129 Mice or go directly to url: jaxmice.jax.org/html/nomenclature/nomen_129.shtml.

Reference

Authors in bold indicate Jackson Laboratory scientists

- **Simpson EM**, **Linder CC**, **Sargent EE**, **Davisson MT**, **Mobraaten LE**, **Sharp J**. 1997. Genetic variation among 129 substrains and its importance for 'targeted mutagenesis' in mice. *Nat Genet* 16:19-27.

Selected Recent Publications Authored by Jackson Laboratory Scientists

Jackson Laboratory scientists publish over 150 papers annually in referred journals. We have listed below several publications from late 1998 of interest to JAX Mice customers.

Cancer Research

- **Beamer WG**, **Shultz KL**, **Tennent BJ**, Azumi N, **Sundberg JP**. 1998. Mouse model for malignant juvenile ovarian granulosa cell tumors. *Toxicol Pathol* 26(5): 704-710.

- **Chapoval AI**, **Fuller JA**, **Kremlev SG**, **Kamdar SJ**, **Evans R**. 1998. Combination chemotherapy and IL-15 administration induce permanent tumor regression in a mouse lung tumor model: NK and T cell-mediated effects antagonized by Bcells. *J Immunol* 161:6977-6984.

- **Golovkina TV**, Dudley JP, Ross SR. 1998. B and T cells are required for mouse mammary tumor virus spread within the mammary gland. *J Immunol* 161:2375-2382.

- Husler MR, Kotopoulis KA, **Sundberg JP**, **Tennent BJ**, Kunig SV, **Knowles BB**. 1998. Lactation-induced WAP-SV40 tag transgene expression in C57BL/6J mice leads to mammary carcinoma. *Transgenic Res* 7:253-263.

Cardiovascular Research

- **Pitman WA**, **Hunt MH**, **McFarland C**, **Paigen B**. 1998. Genetic analysis of the difference in diet-induced atherosclerosis between the inbred mouse strains SM/J and NZB/BINJ. *Arterioscler Thromb Vasc Biol* 18:615-620.

Developmental Biology Research

- **Eppig JJ**, **O'Brien MJ**, **Pendola FL**, Watanabe S. 1998. Factors affecting the developmental competence of mouse oocytes grown in vitro: follicle- stimulating hormone and insulin. *Biol Reprod* 59:1445-1453.

- Wakayama T, Perry AC, Zucotti M, **Johnson KR**, Yanagimachi R. 1998. Full-term development of mice from enucleated oocytes injected with cumulus cell nuclei *Nature* 394:369-374.

Diabetes and Obesity Research

- **Leiter EH**, **Reifsnyder** PC, **Flurkey K**, Partke HJ, Junger E, Herberg L. 1998. NIDDM genes in mice: deleterious synergism by both parental genomes contributes to diabetoenic thresholds. *Diabetes* 47:1287-1295.

- **Nishina PM**, North MA, **Ikeda A**, Yan Y, **Naggert JK**. 1998. Molecular characterization of a novel tubby gene family member, TULP3, in mouse and humans. *Genomics* 54:215-220.

- **Serreze DV**, **Bridgett M**, **Chapman HD**, **Chen E**, **Richard SD**, **Leiter EH**. 1998. Subcongenic analysis of the Idd13 locus in NOD/Lt mice: evidence for several susceptibility genes including a possible diabetogenic role for beta 2-microglobulin. *J Immunol* 160:1472-1478.

Genetics Research

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JAX MICE WEB SITE

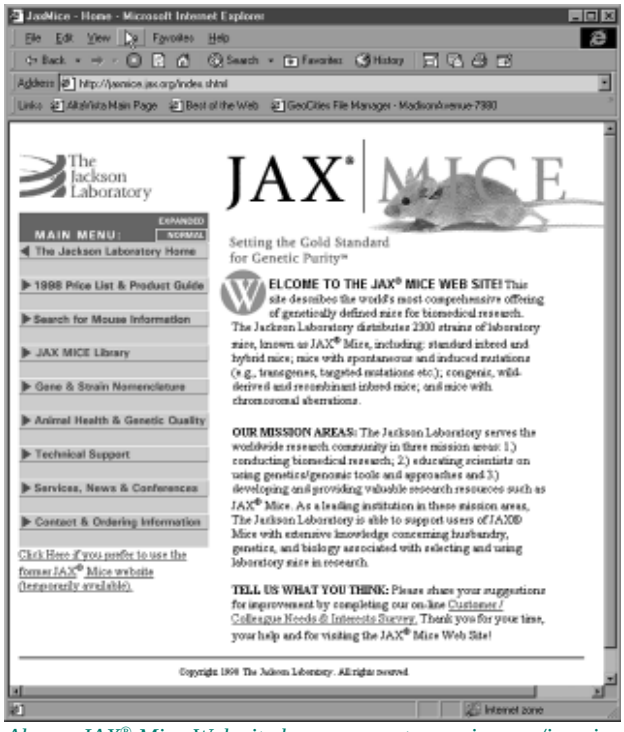
New JAX® Mice Web Site – A Great Mouse Detective!

www.jax.org/jaxmice

During 1998, we introduced a new JAX® Mice Web site which enables researchers to more efficiently find information needed to select and use JAX® Mice.

In addition to a new graphic look, this Web site provides more intuitive navigation through hundreds of web text pages as well as direct access to the Laboratory's mouse-related databases, including the *JAX® Mice Database*, the *Mouse Genome Informatics* database, and the *Induced Mutant Resource* database. The end result is that web browsers interested in laboratory mice can find what they need more quickly and easily by visiting the new JAX® Mice Web site.

The investment in this renovated Web site demonstrates The Jackson Laboratory's long-standing commitment to enabling the worldwide scientific community with helpful information resources. "The JAX® Mice Web site provides an important channel for customer communications and complements our existing strengths in technical and customer support. We look forward to introducing additional enhancements in all of our customer support areas based on customer needs and feedback," said Philip Standel, Director and General Manager of Research Resources at the Laboratory.



Above: JAX® Mice Web site home page at www.jax.org/jaxmice

Visit the JAX® Mice Web Site at **www.jax.org/jaxmice**. Please let us know what you think works well and not so well by completing our on-line *Customer Needs & Interest Survey* accessible from the JAX® Mice home page.

OTHER *NEW* JACKSON LABORATORY WEB SITES

The Jackson Laboratory's Genetic Resources Committee

The Genetic Resources Committee (GRC) advises The Jackson Laboratory administration on genetic aspects of policy issues. The GRC meets once a month to make recommendations concerning the importation or discontinuation of mouse strains, methods of strain maintenance, genetic quality control, strain nomenclature, and general policy issues. This Web site describes strain selection criteria and provides on-line access to new strain submission forms. Visit this site at **www.jax.org/resources/documents/grc/grchomeout.html**

The Transgenic/Targeted Mutation Database - TBASE

Since development of the technology to manipulate the germline of animals over a decade ago, a large number of transgenic animals have been produced worldwide for use in both basic and applied research. Additionally, development of gene targeting protocols involving homologous recombination in mouse embryonic stem cells has resulted in a considerable number of mutant lines with specific phenotypes and well-defined DNA structural changes. The purpose of TBASE is to organize information on transgenic animals and targeted mutations generated and analyzed worldwide. This Web site contains: instructions for searching TBASE, a searchable database of transgenic animals, a searchable citation database and much more. Visit this site at **tbase.jax.org**

COURSES AND CONFERENCES

The Jackson Laboratory has a 70 year history of providing educational programs as part of its mission to train the scientists of today and of the future. Our courses and conferences are designed to: (1) foster collaboration among members of the worldwide research community; (2) keep biomedical scientists abreast of new approaches in using genetics/genomics to study basic biology and human disease; and (3) provide training on using genetic research resources such as genetically defined mice and genomic bioinformatics tools.

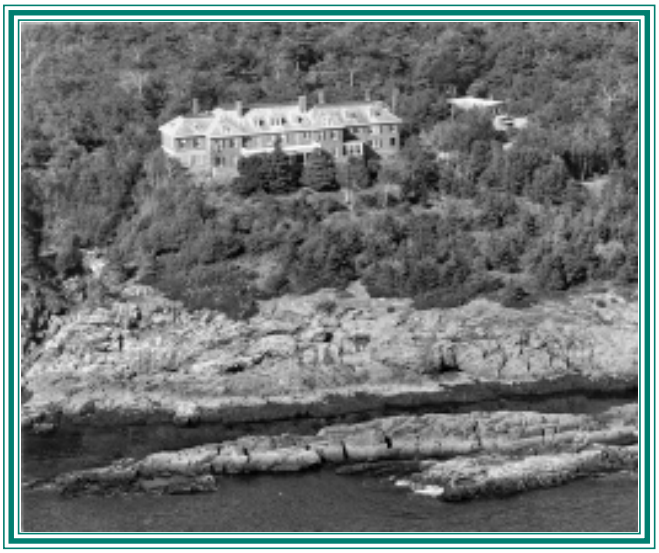
Our courses and conferences program provides a unique opportunity to keep pace with the rapidly advancing field of genomics, to meet with colleagues, and to enjoy the beauty of Acadia National Park which surrounds The Jackson Laboratory campus. Space in our courses and conferences is limited. Submission prior to application deadline is strongly recommended (see list on page 9).

(*continued on page 9*)

1999 Courses & Conferences

- **Maine Biological and Medical Sciences Symposium**
  Symposium dates: May 5-7, 1999
  Application deadline: April 1, 1999
- **Courses for Cryopreservation of Mouse Germplasm**
  Embryo Handling: May 12-14, 1999
  Cryopreservation: May 17-21, 1999
  In Vitro Fertilization: May 24-25, 1999
  Application deadline: February 1, 1999
- **Mouse Initiatives: Advanced Functional Genomics**
  Meeting dates: June 29-July 3, 1999
  Application deadline: April 1, 1999
- **The 40th Annual Short Course in Medical and Experimental Mammalian Genetics**
  Course dates: July 18-30, 1999
  Symposium: July 30, 1999
  Application deadline: March 15, 1999
- **Biotechnology: Products, Policy and the Public – Third World Issues**
  Meeting dates: August 11-14, 1999
  Application deadline: June 1, 1999
- **Experimental Genetics of the Laboratory Mouse in Cancer Research**
  Course dates: August 21 - September 1, 1999
  Application deadline: June 1, 1999
- **Genetic Approaches in Complex Heart, Lung and Blood Diseases**
  Course dates: September 1-10, 1999
  Application deadline: July 1, 1999
- **Third Workshop on Mouse Molecular Neurogenetics**
  Workshop dates: September 21-26, 1999
  Application deadline: July 12, 1999
- **Mouse Retinal Degenerations Symposium & Workshop**
  Workshop dates: September 27-30, 1999
  Application deadline: July 1, 1999
- **Modeling Human Mammary Cancer in Mice**
  Meeting dates: October 2-6,1999
  Application deadline: August 1, 1999
- **Techniques for Modeling Human Cancer in Mice**
  Workshop dates: October 6-9, 1999
  Application deadline: August 1 ,1999
- **Cryopreservation I: Embryo and Gamete Collection, *in Vitro* Fertilization, Embryo Transfer**
  Course dates: October 18-22, 1999
  Application deadline: August 1, 1999
- **Cryopreservation II: Freezing, Storage, and Thawing of Mouse Germplasm**
  Course dates: October 25-29, 1999
  Application deadline: August 1, 1999

For more information, see www.jax.org/courses; call 207-288-6262; fax: 207-288-6080 or email: education@jax.org



Above: The Jackson Laboratory's Highseas Conference Center

Customer Relations

New Call Reception System

In the Customer Service area, we have developed a new call reception system. Using this new system, your calls to our Customer Service Department are now answered by a telephone receptionist. The receptionist triages incoming calls by asking a few questions, especially as related to the mouse type(s) of interest. Based on the nature of your call, the receptionist then transfers you to the most appropriate specialist(s) to help with your needs. We hope you are finding our new call reception system helpful. Please feel free to share your comments with our Customer Service Representatives.

New People and New Positions

New personnel have recently joined our Customer Relations and Technical Support group. As well, some personnel that you have known through the years have recently taken new postions within The Jackson Laboratory.

Elizabeth Bunker is our new Manager of Customer Service. Ms. Bunker has worked at The Jackson Laboratory for nine years as an Operations Manager and Engineer. Her extensive experience in managing the daily operations of The Jackson Laboratory mouse production support functions will help ensure JAX Mice customer satisfaction.

Peggy Danneman, VMD, MS is our new Acting Director of Laboratory Animal Health. Dr. Danneman joins us most recently from University of Tennessee, Memphis, where she was Associate Professor of Comparative Medicine. Dr. Danneman also served on the graduate faculties at the University of Michigan and the Pennsylvania State University.

Craig Gladstone is our new Field Development Manager. Prior to coming to The Jackson Laboratory, Mr. Gladstone held several sales and marketing management positions at Advanced ChemTech, Dynatech Laboratories, and Lab Systems.

(*continued on page 10*)

Jeffery Lake, PhD is our new Technical Support Manager. Dr. Lake joins us most recently from Emory University where he held positions as Assistant Professor and Director of the Transgenic Mouse Facility of the Winship Cancer Center.

Carol Linder, PhD, formerly the Technical Support Manager, is now our Senior Techncial Information Scientist. In this new position, Dr. Linder will focus on creating printed and web information to help JAX Mice customers select the best mouse model systems for their experimental studies.

John Sharp, PhD, formerly the Manager of our Induced Mutant Resource, is the new Research Resources Technical Director. As in his former position, Dr. Sharp will continue to manage new transgenic and "knockout" strain acquisition and development activities. Additionally, Dr. Sharp will oversee the areas of Technical Support and Genetic Quality Control.

Barbara Witham, formerly Manager of Customer Service and Distribution, is now working as a Field Representative. In this position, Ms. Witham brings a wealth of JAX Mice knowledge directly to our customers at their home institutions.

New Customer Service Staff: In response to your needs for enhanced service, we are expanding our customer service staff. We have several new representatives in training. The next issue of *JAX NOTES* will provide more information on our Customer Service Group.

JAX® Mice Contact Information

Ordering & Customer Service
Tel: 800-422-MICE or 207-288-5845
Fax: 207-288-6150

Technical Support
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JAX MICE Web Site
www.jax.org/jaxmice

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JAX NOTES *JAX NOTES* is a quarterly publication produced by the Marketing Communications group at The Jackson Laboratory: Susan Bean (Marketing Communications Coordinator); Carol Linder, PhD (Sr. Technical Information Scientist); Megan Macauley (Manager); and Linda Neleski (Technical Information Coordinator).

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Share Your Ideas: If you would like a special topic addressed in a future issue of *JAX NOTES*, please contact Megan Macauley with your idea (tel: 207-288-6446; fax: 207-288-6150; email: mjm@jax.org).

Mailing List: If you would like to be added to the *JAX NOTES* mailing list, please contact Customer Service using information above or complete and return the enclosed business reply card.

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MAILING LISTS: *JAX NOTES:* add me ___ delete me ___ *Price List & Product Guide:* add me ___ delete me ___

LITERATURE REQUESTS

Please send *Price List & Product Guide* ___

Please send Mouse Model Lists: (send by mail ___ or email ___) Check research area of interests below:

___ Apoptosis ___ Cancer ___ Diabetes & Obesity ___ Immunolology & Inflammation
___ Breast Cancer ___ Cardiovascular Biology ___ Endocrine Deficiency ___ Neurobiology Research

We want to know what you think! **If you have any suggestions on how The Jackson Laboratory can better serve your needs, please share your ideas:** _____

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