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Web Site: www.jax.org/jaxmice
Tel: 1-800-422-MICE or 207-288-5845

JAX | NOTES

JAX WEST FACILITY NOW OPERATIONAL

In July 1999, The Jackson Laboratory and the University of California at Davis (U.C. Davis) established a research collaboration in the area of mouse genomics and biology. As part of this agreement, a shared animal facility on the U.C. Davis campus was renovated and is now ready to import mice for custom breeding projects.

This facility is called JAX West. Susan Airhart has recently taken the position of Vice President and General Manager, JAX West. The facility is operated under highly controlled, barrier-protected conditions. This facility operates using animal health and genetic quality control programs modeled after those at The Jackson Laboratory in Bar Harbor, Maine.

JAX® West Facility on U.C. Davis Campus



The Jackson Laboratory intends to expand JAX West on the U.C. Davis campus in the coming months. Plans are being evaluated for a 15,000 box facility (with ultimate capacity for 30,000 boxes) that will allow The Laboratory to better meet the needs of biomedical researchers in the Western United States. ●

NEW WEST COAST FIELD REPRESENTATIVE

We are pleased to announce that German Vergara is our new West Coast Field Development Representative. Mr. Vergara joins us most recently from Pfizer Global Research (formerly Parke-Davis). German has over 10 years of experience working with genetically engineered mice.

JAX® SERVICES

The Jackson Laboratory is pleased to announce the expansion and refinement of custom services. The technical expertise and experience of our staff serve as a foundation and springboard for development and expansion of specialized custom services. Over the last year several services have been expanded, reconfigured or enhanced. Refinement of custom services should provide the biomedical research community with more rapid and affordable access to customized JAX® Mice.

Custom Breeding & Dedicated Supply

The Jackson Laboratory provides breeding services to create a vast array of custom strains. Most JAX® Mice strains can be bred in special crosses*, and also, customers' mice can be crossed to JAX® Mice. For customers in Western United States selected custom breeding projects and Dedicated

Supply needs may be located at the JAX West facility in Davis, California. For more information contact Alicia Valenzuela or Rose Robidoux at custombreeding@jax.org

Speed Congenic & Genomic Scanning Services

Marker assisted selection of mice for the development of speed congenic strains continues to be a successful and robust service for JAX® Mice customers. In response to community needs we are pleased to offer genome scanning services. The Jackson Laboratory can undertake complete speed congenic breeding projects or perform SSLP-based genomic scans from tissue or DNA. For those customers who wish to inquire about speed congenics or who have genome scanning needs, contact Charles Wray, PhD at cgw@jax.org for additional information. ●

*Although most JAX mice can be used in custom breeding projects, some strains are not suitable due to inherent breeding difficulties.

JAX® | GEMM™ Genetically Engineered & Mutant Mice



NEWS

In response to increased demand, we have expanded the breeding colonies for the following strains:

BALB/c-TgN(DO11.10)10Loh

Stock Number: 003303

Standard Supply: Level 3: Up to 3 mice of each sex per order per month.

Applications: Studies in immunology & inflammation research.

C.129S7(B6)-I β ng^{tm1Ts}

Stock Number: 002286

Standard Supply: Level 2: Up to 25 mice of each sex can be shipped per month.

Applications: Studies in cancer, hematological, immunology & inflammation research.

B6;129S-Il6^{tm1Kopf}

Stock Number: 002254

Standard Supply: Level 3: Up to 3 mice of each sex per order per month.

Applications: Studies in cancer, immunology & inflammation research.

B6.129S7-Ldlr^{tm1Her}

Stock Number: 002207

Standard Supply: Level 2: Up to 25 mice of each sex can be shipped per month.

Applications: Studies in cardiovascular, metabolism, human disease research.

B6.129P2-Tcrd^{tm1Mom}

Stock Number: 002120

Standard Supply: Level 3: Up to 3 mice of each sex per order per month.

Applications: Studies in hematological, immunology & inflammation research.

C.129S2(B6)-Cmkar2^{tm1Mum}

Stock Number: 002724

Standard Supply: Level 3: Up to 3 mice of each sex per order per month.

Applications: Studies in cancer, immunology & inflammation, internal/organ research.

For availability information or to place an order, call Customer Service at 1-800-422-MICE or 207-288-5845 or email orderquest@jax.org.

FASTER ORDER FULFILLMENT AND A STEADY STREAM OF NEW STRAINS

We are pleased to inform you of significant improvements gained in supplying the research community with JAX® GEMM™ (genetically engineered & mutant mice) strains. Substantial progress has been made in reducing the backlog for these mice with a **76% reduction** in mice backlogged over 6 months. Equally exciting is our improvement in turnaround time for new orders with over **90% of mice shipped within 2 ½ months** following order receipt. In addition, we continue to introduce new JAX® GEMM™ strains at a rapid rate, averaging 12 additional new strains made each month.

JAX® GEMM™ Strain Statistics

Reduction in Backorders

- 76% decrease in backorder over the past 6 months

Improved Order Fulfillment Time

- 90% of orders are shipped within 2 ½ months after receipt of order

New strains introduced each month

- Average of 12 per month

Many Strains More Readily Available

To help you plan for experiments involving JAX® Mice we have established a "Standard Supply Level" system. This system indicates the quantities of mice that we can typically ship to you from the existing distribution colonies during a fixed period of time. Most strains made available at The Jackson Laboratory are introduced initially at Level 4 (supplied as 3 breeder pairs or 6 mice) in order to provide access to new strains to as many researchers as possible.

In response to demand from the user community, many of our breeding colonies are then expanded to support the demand of the research community. In this light, we are very excited to inform you that **the majority of our strains previously available at Standard Supply Level 4 (up to 3 breeder pairs or 6 individual mice**

within 1 to 6 months) will now be offered in greater quantities - **3 breeder pairs or 10 mice within 1 to 3 months**. This new level will be designated as Standard Supply Level 3a. See Table 2, page 5 for a complete list of standard supply levels.

Receive Advance Notice of New Strains by Registering Your Interest

Maintaining optimal levels of availability for over 2500 strains of JAX® Mice and responding quickly to changes in demand is complex and challenging. Please help us better predict demand and optimal colony size for strains "Under Development" by registering your interest in any of these strains.

Registering your interest also ensures that you receive advance notice (typically 3 weeks) of the pending availability of a strain. Upon receiving advance notice, you will have the opportunity to place an advance order prior to the strain being publicized as ready for distribution. Advance orders are filled on a "first come - first served basis" in the original order that interest was registered.

To register your interest: 1) contact Customer Service (tel: 800 422-MICE or fax 207 288-6150) or 2) submit our web form (go to www.jax.org/jaxmice and select "Register interest in new strains under development" from the home page text).

Technical Information Scientists Wanted!

Our Technical Information Services team is looking for new members as the group continues to grow. If you are interested in supporting your scientific colleagues with technical advice on selection and use of mouse models for research, then consider joining our team (see position #067/OJ at www.jax.org/employee/documents/techinfo041400.html or email jobs@jax.org).

Mouse Models News

NEW AUTOSOMAL DOMINANT DIABETES MODEL

Strain Origin and Diabetic Phenotype

Ins2^{Akita} is an autosomal dominant mutation that produces juvenile-onset hyperglycemia in the absence of obesity. Discovered in C57BL/6N mice in Akita, Japan (Yoshioka *et al.*, 1997), the mutation was initially named *Mody4* because mutant mice exhibit features observed in certain human maturity-onset diabetes of the young (MODY) families. The model was initially described as a model for early-onset NIDDM (Yoshioka *et al.*, 1997).

Heterozygous male mice from the source colony developed hypoinsulinemia and severe hyperglycemia by weaning age. Diabetic symptoms in heterozygous females were less severe. Additional characteristics included a decrease in both pancreatic beta cell mass and in secretory responses to glucose (Yoshioka *et al.*, 1997; Kayo and Koizumi, 1998).

Histologic analysis showed a dearth of islets; those detected were extremely atrophic and devoid of granulated beta cells. This histopathology was similar to those observed in mice rendered insulin-dependent diabetic by treatment with chemical diabetogens. Despite the juvenile onset of hyperglycemia, heterozygous diabetic males and females were viable and fertile.

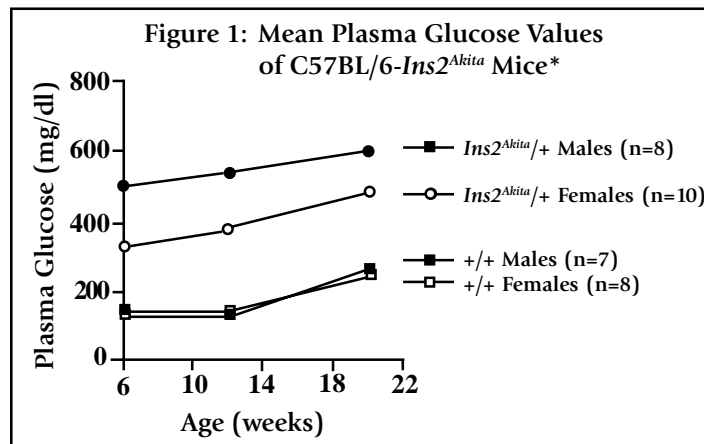
The Jackson Laboratory imported C57BL/6Njcl-*Ins2^{Akita}* mice in 1999. As was noted in Japan, heterozygous mutant mice at The Jackson Laboratory maintain viability for relatively long periods in the face of chronic hyperglycemia, with females developing more slowly progressing hyperglycemia than males (Figure 1). Hyperglycemic *Ins2^{Akita}* male mice are also sensitive to exogenously administered insulin (Figure 2). Homozygous mutant mice rarely survive beyond 12 weeks of age.

The insulin II gene (*Ins2*) located on Chr 7 is the mouse ortholog of the human insulin gene (*INS*). Mice possess another active insulin gene, *Ins1* (Chr 19), which lacks an intron present in the C-polypeptide-encoding region of the human gene. *Ins1* and *Ins2* show different expression patterns during development and in the adult pancreas; both are imprinted in a tissue-specific manner.

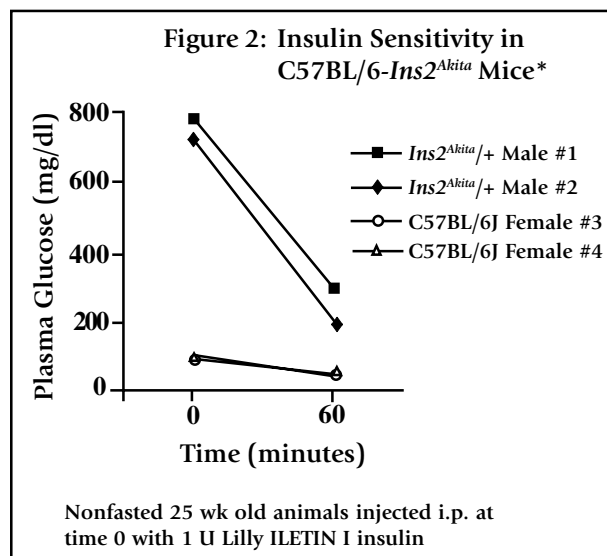
The *Akita* spontaneous mutation disrupts *Ins2*. Sequencing of the gene confirms the presence of a missense mutation at residue 96 converting a cysteine (TGC) to a tyrosine (TAC) at amino acid residue 7 of the mature A chain (Wang *et al.*, 1999). The A7 cysteine is essential, forming a disulfide bond with the corresponding B chain cysteine.

The *Akita* leads to defective proinsulin chain folding and triggers massive compensatory "quality control" mechanisms in the endoplasmic reticulum (*e.g.* chaperonin influx). These responses are so massive that not only is proinsulin processing from the mutant allele blocked, but also folding and processing of *Ins1* gene products are strongly inhibited. This disruption in normal processing in the regulated secretory pathway leads to beta cell failure to secrete normal levels of mature insulin, and hence early development of hypoinsulinemia.

The failure of the islet beta cell mass to develop normally further suggests a role for insulin as an autonochoous beta cell growth factor. The knowledge of the molecular basis for the syndrome led to the gene symbol change from *Mody4* to *Ins2^{Akita}*.



It is interesting to note that known point mutations in the human *INS* gene lead to a mild form of late-onset diabetes inherited in an autosomal dominant manner. However, the symptoms in humans, primarily glucose intolerance and hyperinsulinemia or hyperproinsulinemia, do not match those seen in the *Ins2^{Akita}* mice.



hyperinsulinemia or hyperproinsulinemia, do not match those seen in the *Ins2^{Akita}* mice.

Potential Research Uses

Islets from *Ins2^{Akita}* mice are depleted of beta cells and those remaining release very little mature insulin. This, and the finding that mutant mice respond to exogenously administered insulin, indicate that *Ins2^{Akita}* mice will serve as an excellent substitute for mice made insulin-dependent diabetic by treatment with alloxan or streptozotocin.

(Dominant Diabetes Model continued on page 4)

*Unpublished data from The Jackson Laboratory distribution colony

(Dominant Diabetes Model continued from page 3)

Chemically-induced diabetic mice are widely used to study the effects of chronic hyperglycemia and diabetic complications. However, these chemical diabetogens produce unwanted toxic side effects on multiple organ systems in addition to destroying pancreatic beta cells. These side effects can complicate experimental interpretations making it difficult to discern damage produced by hyperglycemia from direct toxin-induced damage.

Ins2^{Akita} mice spontaneously develop an insulin-responsive hyperglycemia, but will survive with chronic hyperglycemia without insulin therapy. The phenotype suggests that mutant mice are an ideal diabetic recipient for allogeneic or xenogeneic islets in studies designed to investigate induction of transplantation tolerance. Indeed, preliminary studies at The Jackson Laboratory indicate that intra-renal transplantation of 400 syngeneic C57BL/6 wild-type islets can correct the hyperglycemia (E. Leiter, personal communication).

Current Availability

C57BL/6- *Ins2^{Akita}* (Stock Number 003548) are maintained by backcrossing heterozygous male mice to C57BL/6J females. Mice are currently distributed at a Standard Supply Level 4 (supplied as 3 breeder pairs or 6 individual mice per order). However, the colony size will be increased in response to registered interest.

To order or for questions on current availability call Customer Service at 800 422-MICE (6423) or 207 288-5845. For further technical information, including colony maintenance, please refer to the JAX® Mice Database on the web at www.jax.org/jaxmice/pricelist (search on Stock Number, 003548, or on the gene symbol, *Ins2*) or contact our Technical Information group.

References

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Interested in Diabetes and Obesity Mouse Models?

Contact Carol Linder
(ccl@jax.org)
to register for email notifications and updates

129X1/SvJ GENETICALLY CONTAMINATED. WHAT DOES THAT REALLY MEAN?

In a series of strain name changes, 129/SvJ (Stock No. 000691) became 129X1/SvJ (Festing *et al.*, 1999). The name change reflects a genetic contamination that occurred early in its history (Simpson *et al.*, 1997; Threadgill *et al.*, 1997). What is the nature of this contamination and how does it affect its use?

129X1/SvJ mice were transferred from the laboratory of Dr. Roy Stevens (Sv) at The Jackson Laboratory to the production colonies in 1982. Historical data and genetic analysis indicate that an accidental outcrossing of 129X1/Sv occurred prior to that transfer, sometime between 1977 and 1978.

In 1979 Dr. Stevens reported a mutation in coat color from *A^w* to *a* (white-bellied agouti to nonagouti) in his 129/Sv substrain. This change at the agouti locus would only be apparent when outcrossing the strain. This is because 129X1/SvJ are

carrying both the pink-eyed dilution and tyrosinase recessive mutations (*p Tyr^{c-ch}/p Tyr^c*) making their coat color either albino or light chinchilla. A mutation from *A^w* to *a* now seems improbable given the molecular structure and postulated evolution of agouti alleles (Bultman *et al.*, 1994). Skin graft rejection and SSCP (simple sequence length polymorphism) data analysis comparing 129X1/SvJ mice to other 129 strains support the genetic contamination hypothesis; however the contaminating strain could not be determined by genetic analysis (Simpson *et al.*, 1997).

Unfortunately, the genetic differences present in 129X1/Sv mice and other genetically diverse 129 strains did not result in changes in the protein markers normally used to ensure genetic integrity (see Simpson *et al.*, 1997 for a complete list). Although all 129 strains tested had a major histocompatibility complex haplotype of *b* (*H2^b*), dramatic skin graft rejection occurred between some 129 strains (Simpson *et al.*, 1997).

(129X1/SvJ continued on page 5)

Table 1: Origins of ES cell lines

| 129 Strains | ES Cell Line |
|--|--|
| 129P2/OlaHsd | E14TG2a HM-1 (<i>Hprt^{b-m1}</i>) |
| 129P3/JEMs | mEMS32 |
| 129X1/SvJ (Stock No. 000691) | RW-4 PJ1-5 |
| * 129X1/SvJ x 129S1/Sv- ^p ^{+Tyr-c} <i>Kitl^{SL1}</i> /+ (Stock No. 000691 & 000090) | R1 (+ <i>Kitl-SJ</i>) |
| * 129S1/Sv- ^p + ^{Tyr-c} <i>Kitl^{SL1}</i> /+ (Stock No. 000090) | W9.5 (+ <i>Kitl-SJ</i>) CJ7 (+ <i>Kitl-SJ</i>) |
| 129S2/SvPas | D3 |
| 129S4/SvJae | J1 |
| 129S4/SvJaeSor | AK7 |
| 129S6/SvEv | EK.CCE CP-1 |
| 129S6/SvEvTac | TC1 |
| 129S7/SvEvBrd- <i>Hprt^{b-m2}</i> | AB1 (+ <i>Hprt-bm2</i>) AB2.1 (+ <i>Hprt-bm2</i>) |
| *Origin of 129S1/SvImJ (+ <i>Kitl-SJ</i>) (Stock No. 002448) (Simpson, <i>et al.</i> , 1997) | |

(129X1/SvJ continued from page 4)

Since their transfer to the production colonies of The Jackson Laboratory, 129X1/SvJ mice have been strictly inbred and have not been subject to any accidental or intentional outcrossings. All data analysis (including a genome wide scan with SSLP DNA markers) indicates that the strain is currently completely inbred and is not segregating for any detectable loci (except the forced heterozygosity of alleles at the tyrosinase locus that is characteristic of both 129X1/SvJ and 129P3/J).

Despite its early history, 129X1/SvJ have been widely used in a large number of experiments and are the strain of choice when using certain embryonic stem (ES) cell lines. No differences have been detected between the 129X1/SvJ and the RW-4 ES cell line derived from it. In addition, the R1 ES cell line was derived from a cross between 129X1/SvJ and 129S1/Sv-^{+p} +^{Tyr-c} *Kitl*^{Sl-J}/+ strains. It is important to note that both of these ES cell lines were created in the early 1990s and analysis confirms the absence of genetic heterogeneity between the ES cell lines and the parental strains (Simpson *et al.*, 1997).

The Jackson Laboratory regularly distributes seven different 129 strains, most of which have been used in creating genetically targeted mutant mice (see Table 1 on page 4). For a complimentary wall chart on Gene Targeting with 129 Strains, please complete and return the enclosed business reply card. Further questions may be directed to our Technical Information group.

For more information about the revised nomenclature of 129 mice please refer to JAX Bulletin No. 1 (June 30, 1999) available on the web at jaxmice.jax.org/html/nomenclature/129nomenclature.pdf

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Authors in bold indicate Jackson Laboratory scientists

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Nomenclature News Mgf GENE NAME CHANGES TO *Kitl*

In June 2000, the gene symbol, *Mgf*, mast cell growth factor, was withdrawn and replaced with *Kitl*, kit ligand (See Table 2 for a list of strains). This change was prompted by requests from the scientific community and based on

mast cell growth not being truly representative of the gene's function. While *KITL* does act as a growth factor for mast cells, this is only one of several important functions of this gene.

KITL is the ligand for the protein *KIT* produced by the *Kit* oncogene. The effects of mutations in the *Kitl* gene are like those seen with mutations in the *Kit* gene. *KITL* functions in migration, proliferation, and differentiation of hematopoietic stem cells, primordial germ cells and melanocytes. *KITL* acts on very primitive cells of the hematopoietic lineage. It affects myelopoiesis and lymphopoiesis, stimulates mast cell growth, and promotes differentiation of the erythroid line.

KITL is also essential to the proliferation and maintenance of primordial germ cells, and these cells are absent from the gonads of homozygous *Kitl* mutants. *KITL* is necessary for oocyte growth and for the binding of germ cells to Sertoli cells in the testis. *KITL* is required for maintenance of the tissue environment for neural crest precursors of

(*Mgf Gene Name continued on page 6*)

Table 2: JAX® GEMM™ Strains Carrying *Kitl* Mutation

| Mutation | Strain Name (Former Name) | Stock No. Standard Supply Level | *Standard Supply Levels |
|-------------------------------|---|---|-------------------------|
| <i>Kitl</i> ^{Sl} | B6.Cg-Ca <i>Kitl</i> ^{Sl} (B6.Cg-Ca <i>Mgf</i> ^{Sl}) | 000124 Level 5 * | |
| | C3FeLe.Cg-a/a-Ca' <i>Kitl</i> ^{Sl} Hm (C3FeLe.Cg-a/a-Ca' <i>Mgf</i> ^{Sl} Hm) | 000291 Level 5 * | |
| | WC/ReJ- <i>Kitl</i> ^{Sl} /+ (WC/ReJ- <i>Mgf</i> ^{Sl} /+) | 000693 Level 3 * | |
| | <i>Kitl</i> ^{Sl-con} | C3Sn.Cg- <i>Kitl</i> ^{Sl-con} (C3Sn.Cg- <i>Mgf</i> ^{Sl-con}) | 001380 Level 5 * |
| <i>Kitl</i> ^{Sl-d} | B6.D2- <i>Kitl</i> ^{Sl-d} /+ (B6.D2- <i>Mgf</i> ^{Sl-d} /+) | 000160 Level 3 * | |
| | WB.D2- <i>Kitl</i> ^{Sl-d} /+ (WB.D2- <i>Mgf</i> ^{Sl-d} /+) | 000161 Level 5 * | |
| | <i>Kitl</i> ^{Sl} <i>Kitl</i> ^{Sl-d} | WCB6F1/J <i>Kitl</i> ^{Sl} / <i>Kitl</i> ^{Sl-d} (WCB6F1/J <i>Mgf</i> ^{Sl} / <i>Mgf</i> ^{Sl-d}) | 100401 Level 3 * |
| <i>Kitl</i> ^{Sl-J} | 129S1/Sv- ^{+p} + ^{Tyr-c} <i>Kitl</i> ^{Sl-J} /+ (129S1/Sv- ^{+p} + ^{Tyr-c} <i>Mgf</i> ^{Sl-J} /+) | 000090 Level 5 * | |
| <i>Kitl</i> ^{Sl-1GJ} | STOCK <i>Kitl</i> ^{Sl-1GJ} (STOCK <i>Mgf</i> ^{Sl-1GJ}) | 000979 Level 5 * | |
| <i>Kitl</i> ^{Sl-20J} | C57BL/6J- <i>Kitl</i> ^{Sl-20J} (C57BL/6J- <i>Mgf</i> ^{Sl-20J}) | 003252 Level 5 * | |

JAX® MICE WEB SITE HIGHLIGHTS

www.jax.org/jaxmice

Keep Abreast of New JAX® Mice Each year The Jackson Laboratory provides the biomedical research community with an average of 100 new mouse models. Now you can easily browse a Web-accessible "New JAX® Mice Strains" list.

This list is continually updated and includes strains that have been released for distribution within the most recent six month period and also strains recently released from hold.

To find this list on the JAX® Mice Web site: 1) go to our home page at www.jax.org/jaxmice; 2) select the link: "Strains Newly Available" from the home page text.

Register Your Interest in New Strains Under Development At any one time, The Jackson Laboratory also has over 100 strains at various stages of importation, development and colony expansion.

To view this list of strains on the JAX® Mice Web site and to indicate your future interest in obtaining them: 1) go to our home page at www.jax.org/jaxmice; 2) select the link: "Register interest in new strains" from the homepage text

This new strain interest information is critically important and used to help determine the optimal size of a breeding colony for a new strain to support the needs of the worldwide research community.



Send your order inquiries to orderquest@jax.org

(Mgf Gene Name continued from page 5)

melanocytes. This dependence is transitory and ceases with differentiation.

Phenotypic effects of the steel mutations (*Kitl^{Sl}*) of the mouse cause deficiencies in pigment cells, germ cells, and blood cells. The severity of the phenotypic effects of the *Kitl^{Sl}* alleles is correlated with the degree of alteration of KITL.

Generally, mice that are homozygous for the *Kitl^{Sl}* mutation or combinations of two *Kitl^{Sl}* mutations have a white hair coat and black eyes and are afflicted by severe macrocytic anemia. One or both sexes are sterile. Heterozygotes have a diluted coat color with a small amount of white spotting, are fertile, and may be slightly anemic.

For further information about strains carrying the *Kitl* mutations please refer to the JAX® Mice Database at www.jax.org/jaxmice/pricelist (search on gene symbol, *Kitl*, or the individual stock numbers). Additional information on the *Kitl* gene may also be found at www.informatics.jax.org/searches/marker.cgi?11236.

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ONGOING NOMENCLATURE CHANGES

Gene names and symbols are updated when genes are cloned or when gene families are refined. While this causes a great deal of confusion, it is important for users of JAX® GEMM™ strains to have access to the most up-to-date information about the nature of the mutation. For example, when positional cloning identified the leptin gene as the cause of the obese spontaneous mutation, this discovery opened an entirely new pathway advancing diabetes and obesity research.

Table 3 below provides a list of selected gene symbol changes affecting mouse strains maintained at The Jackson Laboratory. A comprehensive cross-reference chart of former gene/allele symbols to cloned gene symbols is available from the JAX® Mice home page by selecting the "Gene and Strain Nomenclature" link. ●

Table 3: Selected Gene/Allele Designation Changes

| New Symbol | Former Symbol |
|------------------------------|---------------------------|
| <i>Tnfrsf6^{gld}</i> | <i>Fas^{gld}</i> |
| <i>Tnfrsf6^{lpr}</i> | <i>Fas^{lpr}</i> |
| <i>Foxn1^{nu}</i> | <i>Hfh11^{nu}</i> |
| <i>Pdeb^{rd1}</i> | <i>rd1</i> |
| <i>Prkdc^{scid}</i> | <i>scid</i> |

Jackson Laboratory Research News TWO NEW MOUSE MODEL CENTERS AT THE JACKSON LABORATORY

Earlier this year, the National Institutes of Health awarded a \$16.3 million grant to The Jackson Laboratory to start a center for models of neurological diseases. Neurogeneticist Dr. Wayne Frankel, a Jackson Laboratory Staff Scientist will head this new program. The grant will fund a Neuroscience Mutagenesis Facility to create at least 50 new mouse models a year in neural disease areas including motor function, epilepsy, obesity, hearing, vision, learning, and memory deficits. The new program will also involve collaborations with investigators from within the Laboratory and from other institutions, including the Monell Chemical Senses Center, University of Pennsylvania, University of Vermont, and Northern Illinois University.

The National Institutes of Health also awarded a four-year \$14 million grant to The Jackson Laboratory to establish a center for mouse models of heart, lung, blood, and sleep disorders. Jackson Laboratory Staff Scientist Luanne L. Peters, PhD, is the new center's program director. The center has two key goals: (1) developing new models and databases for biomedical researchers worldwide; and (2) advancing understanding of the genetic mechanisms underlying healthy function and diseases of the heart, lungs and blood, as well as the physiology of sleep. ●

SELECTED PUBLICATIONS AUTHORED BY JACKSON LABORATORY SCIENTISTS

Authors in bold indicate Jackson Laboratory scientists

Bioinformatics Research

● Ashburner M, Ball CA, **Blake JA**, Botstein D, Butler H, Cherry JM, **Davis AP**, Dolinski K, Dwight SS, **Eppig JT**, Harris MA, **Hill DP**, Issel-Tarver L, Kasarskis A, Lewis S, Matese JC, **Richardson JE**, **Ringwald M**, Rubin GM, Sherlock G. 2000. Gene ontology: tool for the unification of biology. *Nat Genet* 25:25-29.

● **Paigen K, Eppig JT**. 2000. A mouse phenome project. *Mamm Genome* 11:715-717.

Cancer Research

● Marton I, Johnson SE, Damjanov I, **Currier KS, Sundberg JP, Knowles BB**. 2000. Expression and immune recognition of SV40 Tag in transgenic mice that develop metastatic osteosarcomas. *Trans Res* 9:115-125.

● **Tennent BJ**, Cardiff RD. 2000. Mice, mutations and mammary glands. *Mol Med Today* 143-144.

● Reilly KM, Loisel DA, **Bronson RT**, McLaughlin ME, Jacks T. 2000. *Nf1; Trp53* mutant mice develop glioblastoma with evidence of strain-specific effects. *Nat Genet* 26:109-113.

Genetics Research

● **Akeson EC, Davisson MT**. 2000. Mitotic chromosome preparations from mouse cells for karyotyping. IN: Current Protocols in Human Genetics. Wiley, 2000:4.10.1-4.10.19

● Chen Y, **Schimenti J**, Magnuson T. 2000. Toward the yeastification of mouse genetics: chemical mutagenesis of embryonic stem cells. *Mamm Genome* 11:598-602.

Diabetes and Obesity Research

● **Reifsnnyder PC, Churchill G, Leiter EH**. 2000. Maternal environment and genotype interact to establish diabetes in mice. *Genome Res* 10:1568-1578.

● **Serreze DV**, Ottendorfer EW, Ellis TM, Gauntt CJ, Atkinson MA. 2000. Acceleration of type 1 diabetes by a coxsackievirus infection requires a preexisting critical mass of autoreactive T-cells in pancreatic islets. *Diabetes* 49:708-711.

Hematology and Stem Cell Research

● Kollet O, Peled A, Byk T, Ben-Hur H, Greiner D, **Shultz L**, Lapidot T. 2000. $\beta 2$ microglobulin-deficient ($B2m^{null}$) NOD/SCID mice are excellent recipients for studying human stem cell function. *Blood* 95:3102-3105.

● **Wandersee NJ, Birkenmeier CS, Gifford EJ, Mohandas N, Barker JE**. 2000. Murine recessive hereditary spherocytosis, sph/sph, is caused by a mutation in the erythroid aspectrin gene. *Hematol J* 1:235-242.

● **Zho Y, Lin Y, Zhn G, Louie J, Harrison DE, Anderson WF**. 2000. Murine hematopoietic stem cell characterization and its regulation in BM transplantation. *Blood* 96:3016-3022.

Sensorineural Research

● **Milam AH, Hendrickson AE, Xiao M, Smith JE, Possin De, John SK, Nishina PM**.

2000. Localization of tubby-like protein 1 in developing and adult human retinas. *Invest Ophthalmol Vis Sci* 41:2352-2356.

● **Zhang N, Martin GV, Kelley MW, Gridley T**. 2000. A mutation in the *Lunatic fringe* gene suppresses the effects of a *Jagged2* mutation on inner cell development in the cochlea. *Curr Biol* 10:659-662.

Veterinary Pathology

● **Ward JM, Mahler JE, Maronpot RR, Sundberg JP, Fredrickson RM**. Eds. Pathology of Genetically Engineered Mice. Iowa State University Press, Ames. 2000.

Chapters by Jackson Laboratory Authors in the above publication:

➤ **Sharp JJ, Mobraaten LE, Bedigian HG**. Mutant mouse resources. pp. 3-9.

➤ **Sundberg JP, King LE Jr**. Skin and its appendages: normal anatomy and pathology of spontaneous, transgenic, and targeted mouse mutations. pp.183-215.

➤ **Smith RS, Nishina PM, Ikeda S, Jewett P, Zabeleta A, John SWM**. Interpretation of ocular pathology in genetically engineered and spontaneous mutant mice. pp. 217-231.

➤ **Bronson RT**. Pathologic characterization of neurological mutants. pp. 239-252.

➤ **Mahler M, Rozell B, Mahler JE, Merlino G, Devor-Henneman D, Ward JM, Sundberg JP**. Pathology of the gastrointestinal tract of genetically engineered and spontaneous mutant mice. pp. 269-297. ●

Questions and Answers

FREQUENTLY ASKED QUESTIONS ABOUT JAX® MICE

Q How can I find information on the JAX® Mice Web site about a specific strain, including pricing and standard supply level?

A The JAX® Mice Database offers the most up-to-date information on strain details, pricing, and standard supply levels. This resource is available 24 hours a day via the Internet at jaxmice.jax.org/pricelist, or by choosing the "Search for JAX® Mice" link prominently featured on the JAX® Mice Web site home page at www.jax.org/jaxmice.

(Q & A continued on page 8)

COURSES & CONFERENCES YEAR 2001

- Cryopreservation Courses
Embryo Handling Supplement
Dates: April 25-27
October 17-19
Cryopreservation of Mouse Germplasm
Dates: April 29 - May 3
October 21 - 26
- Colony Management
Dates: May 18-19
November 16 - 17
- Techniques in Gene Microarray Development and Analysis: Approaches to Heart, Lung, Blood and Sleep Disorders
Dates: May 22 - 26
- 42nd Annual Short Course in Medical and Experimental Genetics
Dates: July 15 - 27
- Mouse Initiatives III: Mouse Models for Human Disease
Dates: August 1 - 4
- Experimental Genetics of the Laboratory Mouse in Cancer Research
Dates: August 18 - 31
- Genetic Approaches to Complex Heart, Lung and Blood Disease
Dates: September 7 - 16
- Workshop on Mouse Molecular Neurogenetics
Dates: September 13 - 15
- Mathematical Approaches to the Analysis of Complex Phenotypes
Dates: September 30 - October 7
- Genome Nanostructure: Genetics Meets Nanoscience
Dates: October 10 - 13

For more information, contact the Office of the Courses & Conferences at:
 Tel: 207.288.6262
 Fax: 207.288.6080
 Email: education@jax.org
 Web Site: www.jax.org/courses

(Q & A continued from page 7)

Q How can I get copies of the *Animal Health Reports for Jackson Laboratory Animal Rooms?*

A The Jackson Laboratory provides Animal Health Reports for all of our production and research facilities on our Web site: 1) go to www.jax.org/jaxmice/pricelist; 2) enter the strain name or stock number of interest in the Query Form; 3) select the strain name on the results page; 4) the resulting datasheet, scroll down to the section "Animal Health Reports" and select the room number. You can also obtain an Animal Health Report for a specific strain by conducting a search on that strain: 1) go to www.jax.org/jaxmice; 2) select Animal Health and Genetic Quality from the Main Menu; 3) select Health Status by Room. These documents are presented in Portable Document File (PDF) format in order to preserve an easily understood layout of the information. To view PDF documents; you need Adobe Acrobat Reader software which is provided for free by following a link on our Web page "Health Status by Room". ●

ABIGAIL SMITH IS NEW HEAD OF LABORATORY ANIMAL SCIENCE

We are pleased to announce that Abigail L. Smith, PhD has recently joined The Jackson Laboratory as the Director of Laboratory Animal Sciences. Prior to joining the Laboratory, Dr. Smith held the positions of Professor of Pathology at the Stritch School of Medicine, Loyola University of Chicago, and as a Research Associate at the Chicago Zoological Society. Dr. Smith obtained MPH and PhD degrees in Infectious Disease Epidemiology (Virology) from Yale University and was a member of the faculty of the Section of Comparative Medicine at Yale for 17 years. She served as Chief, Laboratory of Virology & Epidemiology, in that department from 1983 to 1998.

In recognition of outstanding research contributions in the field of laboratory animal science, Dr. Smith was made an Honorary Diplomate, American College of Laboratory Animal Medicine in 1994 and received the AALAS President's Award in 1995.

For over 25 years, Dr. Smith has been an active member of the research community, primarily in the areas of rodent infectious disease research and laboratory animal science. She has served on the Executive Council of the American Committee on Laboratory Animal Diseases (ACLAD; 1987-1994) and on the Subcommittee on Rodent Viruses and Mycoplasma: Detection and Surveillance; ACLAD (1984-1998). ●

DISCOVERY STRATEGIES CONFERENCE

"Emerging Technologies for Creating and Phenotyping New Mouse Models", was the title for the 3rd conference in the annual Discovery Strategies Series sponsored by the Research Affiliates Program of The Jackson Laboratory. Another capacity audience came to the Asticou Inn in Northeast Harbor on Mount Desert Island to hear leading experts present new ways to develop and to phenotype mice.

The two-day conference featured speakers representing a variety of scientific disciplines from The Jackson Laboratory, member companies of the Research Affiliates Program, University of California at Davis, and other leading research institutions. The speakers presented some of the latest advances in technology both for creating new mouse models and for analyzing mice for phenotypes that are similar to those in human diseases. Part of the conference was devoted to advances in technologies for creating new mouse models by chemical and gene targeted mutagenesis. The speakers included the following:

- Joseph Carroll (Genetics Institute)
 - Andras Nagy (Samuel Lunenfeld Research Institute)
 - Lothar Hennighausen (NIH)
- (Discovery Strategies continued on page 9)

*(Discovery Strategies continued
from page 8)*

Tom Sato (U. Texas SW Medical Center)
John Schimenti (The Jackson Laboratory)
Tom Hampton (MouseSpecifics)
Al Johnson (Duke Univ Medical Center)
Kevin Seburn (The Jackson Laboratory)
Jose Galvez (Univ of California at Davis)
Tamara Goode (Merck Research
Laboratories)
Mary Stevens (Bayer Biotechnology)

In his closing summary remarks, Dr. Ken Paigen, Director of The Jackson Laboratory, cited the critical need for baseline measurements of a broad array of inbred strains of mice which is being addressed by the Laboratory's efforts to create a mouse "phenome" database. The new phenome database will establish baseline parameters in the biological properties of up to 50 strains of JAX® Mice inbred strains, creating a standardized dataset for comparison with new mutants and facilitating the identification of new strain dependent characteristics. ●

Discovery Strategies 2001 Conference Series

Conferences designed to address research needs of the Pharmaceutical and Biotechnology industry.

East Coast

*"Novel Mechanisms for
Regulating Gene
Expression in vivo"*

Date: August 27-29, 2001

Location: Portland Regency Hotel,
Portland, Maine

West Coast

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Neuroinflammatory
Diseases"*



Date: October 29-31, 2001

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Center, Lake Tahoe, California

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Animal Care News

NATIONAL LABORATORY ANIMAL CARE TECHNICIAN WEEK AT THE JACKSON LABORATORY

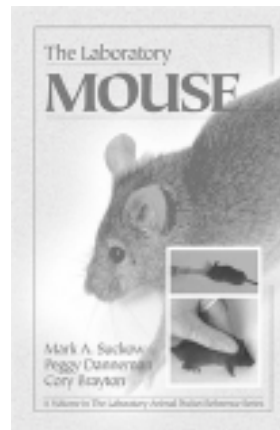


*Phil Stadel, Vice President of Operations
presenting The Jackson Laboratory Animal
Care Technician of the Year Award to
Melody Knight. The Operations Technician
of the Year Award was presented to Dan
Ryan.*

The Jackson Laboratory celebrated the Second Annual National Animal Care Technician Week from January 28 - February 3, 2001. Special events were held throughout the week to honor our animal care staff for their essential role in breeding and care for millions of JAX® Mice. The best evidence of the dedication of our animal care staff is by the hallmark quality JAX® Mice. ●

FULL AAALAC ACCREDITATION GRANTED FOR 2001

Since 1967, The Jackson Laboratory has maintained full accreditation status with AAALAC International (Association For Assessment and Accreditation of Laboratory Animal Care International) for its facility in Bar Harbor, Maine. The Jackson Laboratory conducts all animal-related work according to well-established national guidelines for animal care and welfare. ●



TITLE: Laboratory Mouse

AUTHORS: Mark A. Suckow, PhD,
Cory Brayton, DVM and Peggy
Danneman VMD

FEATURES:

- Provides instructions for the humane care of laboratory mice
- Includes numerous figures that clearly illustrate concepts
- Offers resources of relevance to laboratory mice and extensive references for further study

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OUR COMMITMENT TO IMPROVED SERVICE: CUSTOMER SATISFACTION SURVEY RESULTS

Over the past year, we have implemented many changes to improve our service to the worldwide research community. To capture your feedback on our service enhancements, we placed a Customer Satisfaction Survey on our Web site.

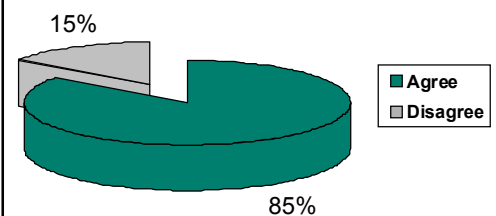
Thank you to all who have completed this survey. The survey results help guide our priorities for ongoing efforts in service enhancements.

Your feedback is essential. Please continue to share your ideas with us by contacting Customer Service or your Field Development Representative or by completing our on-line survey (www.jax.org/jaxmice).

Summary of Survey Results: JAX® Mice Service and Responsiveness Have Improved

Time Period: October 1, 2000 thru
January 12, 2001

Number of Surveys Submitted: 206



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