

JAX® NOTES



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Reliable New Sperm Cryopreservation Service Developed at The Jackson Laboratory

The Jackson Laboratory recently developed the first truly reliable and cost-effective sperm cryopreservation and recovery service for transgenic and knockout mice. The service uses new techniques developed at the Jackson Laboratory and is suitable for cryopreserving and recovering the sperm from transgenic and knockout strains with C57BL/6, FVB, DBA/2, and C3H backgrounds, F1 hybrid backgrounds of these strains, and B6;129 hybrid backgrounds. This service promises to be a reliable, space-saving, and cost-effective alternative to maintaining transgenic and knockout strains on the shelf. Its advent is timely and should be welcome news to biomedical researchers. The new Service offers several advantages over previous sperm cryopreservation and recovery techniques:

Better fertilization rates. The fertilization rates (percent of oocytes fertilized) by sperm cryopreserved and recovered using traditional methods have averaged only about 5%. The fertilization rates by sperm frozen using The Jackson Laboratory's new techniques are nearly 50%, comparable to the 65% average fertilization rates by fresh sperm (Fig. 1).

More live births. The percentage of embryos developing into live mice is comparable to that from using fresh sperm and twice that from using sperm cryopreserved and recovered by traditional techniques (Fig. 2).

Saves mouse room space. Low-use colonies can now be removed from the shelf through cryopreservation, freeing up space for other projects. If the colony is needed again in the future, it can be quickly and economically recovered and expanded from frozen sperm.

More mice. The new service enables large numbers of same-age mice (or frozen embryos) to be quickly produced from frozen sperm. All mice are produced at a high health status and are certified specific pathogen free (SPF).

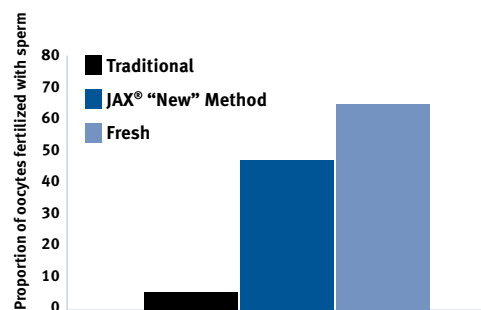


Figure 1. Percent of eggs fertilized by sperm cryorecovered by traditional methods, the new JAX® Sperm Cryo Service, and fresh sperm (data for C57BL/6).

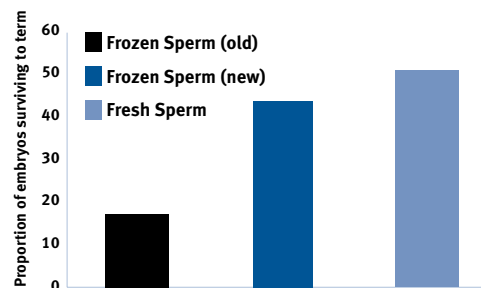


Figure 2. Percent of embryos surviving to term if fertilized by sperm cryorecovered by traditional methods, the new JAX® Sperm Cryo Service, and fresh sperm (data for C57BL/6).

More versatile. Whereas previous techniques worked to a degree with DBA/2, C3H, and F1 hybrids between DBA/2 and C57BL/6 (and very poorly with transgenics and knockouts), the new techniques can successfully cryopreserve and recover the sperm of transgenic and knockout strains with C57BL/6, FVB, DBA/2, and C3H backgrounds, F1 hybrids of these backgrounds, and B6;129 hybrid backgrounds (Fig. 3).

Cryopreserving Your Strain

Our standard service for cryopreserving sperm from transgenic and knockout strains with C57BL/6, FVB, DBA/2, and C3H backgrounds, F1 hybrid backgrounds of these strains, and B6;129 hybrid backgrounds costs \$1,800. The feasibility and cost of cryopreserving sperm from strains with

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800.422.MICE (6423)
www.jax.org/jaxmice

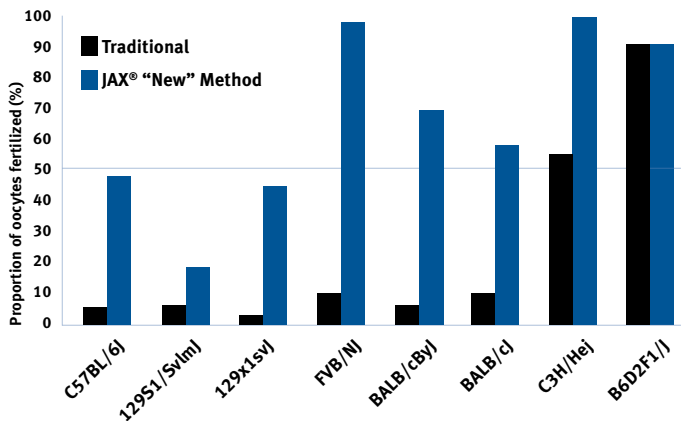


Figure 3. The Jackson Laboratory's new Sperm Cryo Service techniques result in better fertilization rates and work with more strains than do traditional sperm cryo techniques.

other backgrounds will be evaluated upon request. To cryopreserve a strain's sperm, only two fertile 10- to 16-week old males are needed. For the standard service, a minimum of 16 straws of sperm per strain will be cryopreserved and stored for three years, in three liquid nitrogen tanks, at two sites. Additional years of storage can be purchased for \$175/yr. Throughout the cryopreservation process, stringent quality control checks are implemented, including sperm motility tests and an IVF fertilization test to two-cell embryos. Optional recovery of live born mice (for verification of recoverability) is only \$500 per strain and is strongly recommended.

Recovering Your Strain

The service's standard procedure for recovering a strain from cryopreserved sperm includes performing IVF and two embryo transfers. Typically, 10 or more pups are produced from each recovery attempt. The cost for the standard recovery attempt is \$1,095. Weaned (four-week old) pups are usually available 9-12

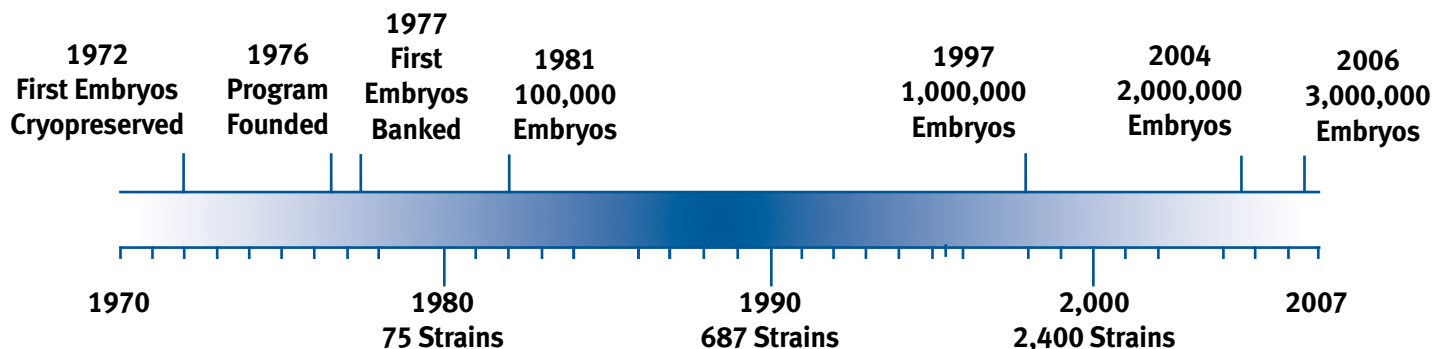
weeks after an order is placed. Larger quantities of mice can be produced to meet specific project requirements. Price will depend on fertilization and recovery rates for the background strain.

Rather than recovering live mice from cryopreserved sperm, two-cell embryos can be produced. If the strain has been previously recovered, the cost for this option is \$1,095 to produce approximately 60 embryos for the same standard background strains (other backgrounds will be priced upon request). More embryos can be produced. Price will depend on the quantity of embryos desired, strain background, and fertilization rate of the strain. If the strain has not been previously recovered, a test recovery to live born is required for an additional \$500.

The Jackson Laboratory's new service has been developed at a particularly appropriate time. In the last 20 years, the use of knockout and transgenic mice in biomedical research has risen sharply. Approximately 10,000 peer-reviewed scientific journal articles per year mention using such mice. The use of knockout and transgenic mice is expected to increase even more in the future (see the article describing the Knockout Mouse Project in this issue of JAX® NOTES). Keeping a genetically modified mouse strain in 'maintenance mode' on the shelf costs an average of \$6,000 to \$10,000 a year. The same strain can be maintained as cryopreserved sperm for a fraction of that cost, and, when needed, can be quickly and conveniently recovered at an SPF status.

In summary, the Jackson Laboratory's new Sperm Cryo Service is a reliable and cost-effective option for cryopreserving mice and managing colonies of transgenic and knockout mice. It saves money, time, resources, and is inexpensive insurance against catastrophic loss of a strain from disease, fire, flood, breeding mishaps, and other accidents.

For more information about The Jackson Laboratory's new Sperm Cryo Service, call 1-800-422-MICE (6423) or e-mail jaxservices@jax.org.



Evolution of The Jackson Laboratory's cryopreservation program. The Jackson Laboratory maintains the world's largest repository of genetically defined mice and has been a pioneer in the field of cryopreservation. Over 5,000 unique strains and 3,000,000 embryos are cryopreserved, and over 600 cryopreserved strains are recovered each year at its Bar Harbor facility.

New Alopecia Areata Service Developed at The Jackson Laboratory

The Jackson Laboratory is offering a new service to alopecia areata researchers. Alopecia areata (AA) is a T cell-mediated autoimmune skin disease resulting in hair loss from the scalp and elsewhere. It is a common disease, affecting approximately 1.7 percent of the population worldwide, including more than five million people in the United States. AA equally affects men and women of all races and ages, but onset often begins in childhood. Hair loss usually starts with one or more small, round, smooth bald patches on the scalp and may progress to the entire scalp (*alopecia totalis*) or body (*alopecia universalis*) (National Alopecia Areata Foundation, www.naaf.org).

The Jackson Laboratory's new service takes advantage of the AA-like symptoms that spontaneously develop in 0.25% of C3H mice by 18 months of age. Although, selective breeding can increase this incidence rate to 20%, the rate is still low and has restricted the use of C3H mice as an AA model. Dr. Sundberg

and his colleagues at The Jackson Laboratory have circumvented this problem. They demonstrated that AA-like symptoms in C3H mice can be surgically-induced by grafting a small piece of diseased skin from an older mouse onto a younger recipient. Patchy alopecia usually develops within 10 weeks, and generalized alopecia is evident at approximately 20 weeks (McElwee *et al.* 1998). The alopecia developed by these mice is a complex polygenic trait and is very similar to adult onset AA in humans.

With the support of the National Alopecia Areata Foundation, The Jackson Laboratory has developed the first large-scale pre-clinical program for producing and screening mice with surgically-induced alopecia. The Service includes the following features:

- Limited quantities of C3H/HeJ (000659) mice with generalized AA (mice are 28 weeks old or older and specific pathogen free).
- Larger quantities of mice available through JAX® Dedicated Supply Service.
- Highly qualified service personnel with extensive expertise in a variety of skin disorder models.
- Custom screening of candidate therapeutic compounds for AA available through JAX® *In Vivo* Research Services.
- Histopathological analysis available through JAX® *In Vivo* Research Services (staff includes a board-certified pathologist with extensive experience in skin disorders).

For details, contact JAX® Services at 1-800.422.MICE (6423), 1-207-288-5845, or jaxservices@jax.org.

Reference

McElwee KJ, Boggess D, King LE Jr, Sundberg JP, 1998. Experimental induction of alopecia areata-like hair loss in C3H/HeJ mice using full-thickness skin grafts. *J Invest. Dermatol* 111:797-803.

Basketball Star with AA Recognized for Involvement with AA Families

The National Basketball Association awarded the Community Assist Award for February 2006 to Toronto Raptors forward, Charlie Villanueva. Villanueva received the award for his visits with families affected by AA at Raptors home and away games, and for his participation in a number of NBA Cares Community events. Villanueva was diagnosed with AA during his childhood, (www.naaf.org/CharlieTracker/Charlie.asp)

JAX® Mice: the Gold Standard Just Got Better

One of the most important reasons why biomedical researchers use JAX® Mice is that they are the most well-characterized laboratory mice in the world. The JAX® Mice Database is renowned for its wealth of genotypic and phenotypic information. The C57BL/6J strain was selected by the Mouse Genome Sequencing Initiative to be the first mouse strain to be sequenced. A set of 40 genetically-diverse and widely-used JAX® Mice strains were selected to be comprehensively characterized by the Mouse Phenome Project. More recently, with the construction of two new mouse bioinformatics resources, the characterization and utility of JAX® mice has expanded substantially. The National Institute of Environmental Health Sciences (NIEHS) recently announced the completion of their Resequencing Project involving 15 JAX® Mice strains, and a group of scientists (Shifman *et al.* 2006)

used JAX® Mice strains and strains derived from JAX® Mice to construct the most detailed genetic map of any mammal except humans. This article reviews these two recent events and explains why the Jackson Laboratory's Genetic Stability Program helps ensure the enduring value of JAX® Mice and the research tools derived from them.

The Completion of the NIEHS Resequencing Project

The NIEHS recently announced the completion of the Resequencing and SNP Discovery Project (NIH News 2006). This project involved identifying the single nucleotide polymorphisms (SNPs) among the following 15 JAX® Mice strains:

129S1/SvImJ (002448)	C3H/HeJ (000659)	MOLF/Eij (000550)
A/J (000646)	CAST/Eij (000928)	NOD/LtJ (001976)
AKR/J (000648)	DBA/2J (000671)	NZW/LacJ (001058)
BALB/cByJ (001026)	FVB/NJ (001800)	PWD/PhJ (004660)
BTBR T ^r tf/J (002282)	KK/HIJ (002106)	WSB/Eij (001145)

The Project members selected these strains because of their genetic diversity and routine use as research models (NIH News 2006). The SNPs were identified with the same high-density oligonucleotide array technology used to discover common DNA variation in the human genome.

The publication of the Resequencing Project data was greatly anticipated. More than 8.3 million SNPs were discovered among the resequenced strains. The polymorphisms will help researchers better understand the factors that affect susceptibility to and development of some 200 complex human diseases, including Parkinson's, cancer, diabetes, heart and lung diseases, reproductive diseases, and asthma. Says David A. Schwartz, M.D., NIEHS director (NIH News 2006): "Making this wealth of data freely available to the research community is a significant milestone. Each mouse strain is genetically unique. Now that we know the DNA variations for these mouse strains, we can compare the genetic makeup of one strain that acquires a certain disease to another strain that does not get the same disease. In this way researchers gain insight into the same processes that may cause one human to get a disease while another human in the same environment remains disease-free."

The SNP and other Resequencing Project data are publicly available at the National Center for Biotechnology Information Web site, www.ncbi.nlm.nih.gov/SNP, the Mouse Genome Informatics (MGI) Web site, www.informatics.jax.org, and the Mouse Phenome Database (MPD) Web site, www.jax.org/phenome. The MGI Web site, maintained at The Jackson Laboratory, is an indispensable storehouse of mouse genetic information. The MPD, also maintained at The Jackson Laboratory, is a repository for phenotypic and genotypic data on 40 commonly used and genetically diverse inbred JAX[®] Mice strains and a platform for data analysis and *in silico* hypothesis testing. It enables investigators to choose optimal strains for their research, including physiological studies, drug and toxicology testing, and modeling disease processes. The new SNP information in these two databases will greatly enhance their value as tools for genetic analysis.

New Genetic Maps of the Mouse Genome

Although the sequencing of the mouse genome and the discovery of millions of SNPs in the mouse genome have permitted the construction of high-resolution physical maps, these maps cannot be used to construct high-resolution genetic maps because recombination rates across the mouse genome are not constant. The genetic maps of the mouse genome recently constructed by Shifman *et al.* (2006) will give scientists some very powerful and much anticipated tools. Shifman and his colleagues used more than 10,000 single nucleotide polymorphisms (SNPs) evenly spaced across the mouse genome to construct two high-resolution sex-specific genetic maps of the mouse genome. One map

was constructed using eight recombinant inbred (RI) lines, AXB, BXA, CXB, BXD, BXH, AKXD, LXS, and SWXJ (all JAX[®] Mice strains except LXS); the second was constructed using genetically heterogeneous stocks descended from eight JAX[®] Mice inbred progenitors: A/J (000646), AKR/J (000648), BALB/cJ (000651), C3H/HeJ (000659), C57BL/6J (000664), CBA/J (000656), DBA/2J (000671), and LP/J (000676).

The new genetic maps provide the high resolution needed to address many problems in biomedical research. For example, they will help researchers finely resolve quantitative trait loci (QTLs) to intervals of a few megabases, more easily identify QTL genes, investigate the effects of sex on recombination rates, determine why recombination rate constraints are seemingly different over long and short distances, explain why recombination hotspots rarely occur in the same positions in humans and chimpanzees, and define the features that induce and maintain recombination hotspots in mammals. The maps are available from http://gscan.well.ox.ac.uk/#genetic_map and as supporting information to the article by Shifman and his colleagues.

The Jackson Laboratory's Genetic Stability Program

Given the extensive characterization of JAX[®] Mice and the vast amount of public health research that depends on their genetic integrity, The Jackson Laboratory is taking a proactive approach to ensure that the JAX[®] Mice researchers use today will be the same tomorrow. In 2004, The Jackson Laboratory implemented an innovative Genetic Stability Program (GSP) (Fig. 1) designed to minimize genetic drift. Defined as a cumulative change in the genetic make-up of an organism over time (Silver 1995), genetic drift in inbred mouse colonies happens slowly, subtly, and can be difficult to detect and control. It is primarily due to three factors: 1) separation of a sub-colony from its parent colony for more than 20 generations (10 generations in the parent colony plus the 10 that simultaneously pass in the sub-colony); 2) undetected spontaneous mutations that become fixed in a colony; and 3) residual heterozygosity in or incomplete inbreeding of a colony before it is separated from its progenitors (Bailey 1977, 1982; Taft *et al.* 2006). To limit genetic drift, The Jackson Laboratory's GSP uses a three-pronged approach: 1) it minimizes the number of generations attained in its foundation and production stocks; 2) it uses highly skilled technicians to oversee breeding in those stocks, and 3) it uses a unique cryopreservation approach to nearly eliminate genetic drift in the most commonly used inbred strains.

The cryopreservation component entails cryopreserving 25-year supplies of embryos from widely-used strains and refreshing foundation stocks of those strains with frozen embryos about every five generations. Already, embryos from JAX[®] Mice strains 129S1/SvImJ (002448), C3H/HeJ (000659), C57BL/6J (000664), DBA/2J (000671), FVB/NJ (001800), NOD/LtJ (001976), and NOD.CB17-*Prkdc*^{scid}/J (001303) have been cryopreserved to use in this program (Taft *et al.* 2006). Limiting genetic drift in these strains is particularly important because all except NOD.CB17-*Prkdc*^{scid}/J were part of the Resequencing Project. Furthermore, some 300 congenic JAX[®] Mice strains constructed by backcrossing to these inbred strains are, by extension, included in the pro-

gram. The Jackson Laboratory Genetic Stability Program ensures that the genotypic and phenotypic characterization of some key JAX® Mice strains will be reliable over space and time.

The “J” at the end of a JAX® Mice strain names indicates that the strain originates from The Jackson Laboratory. It represents over 75 years of expertise in mouse husbandry and mouse-based genetic research, a vast resource of mouse bioinformatics, and a comprehensive genetic quality monitoring and stability program.

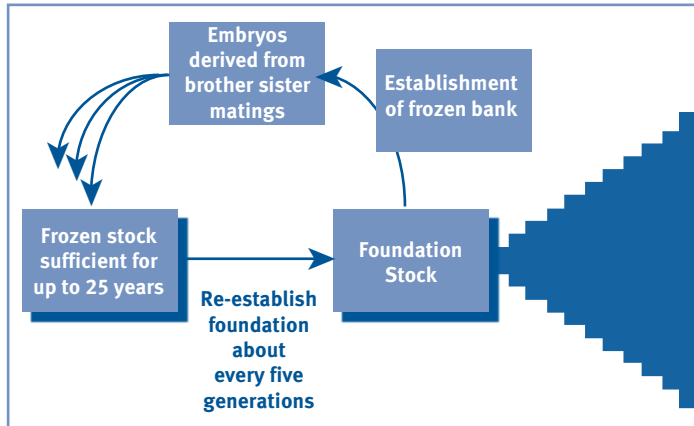


Figure 1. The Jackson Laboratory Genetic Stability Program. For more details, visit the following Web site: www.jax.org/geneticquality.

The use of JAX® Mice by many of the most published biomedical researchers and as the strains of choice for publically accessible bioinformatics tools are testaments to their importance and gold standard quality.

References

- Bailey DW. 1977. Genetic drift: the problem and its possible solution by frozen-embryo storage. *Ciba Found Symp* 291-303.
- Bailey DW. 1982. How pure are inbred strains of mice? *Immunology Today* 3:210-14.
- NIH News. 2006. Mouse DNA to Aid Biomedical Research. NIEHS PR #06-17, October 25 (www.niehs.nih.gov/oc/news/snp2.htm).
- Shifman S, Bell JT, Copley RR, Taylor MS, Williams RW, Mott R, Flint J. 2006. A high-resolution single nucleotide polymorphism genetic map of the mouse genome. *PLoS Biol* 4(12):e395.
- Silver L. 1995. *Mouse Genetics*. Oxford.
- Taft RA, Davisson M, Wiles MV. 2006. Know thy mouse. *Trends Genet* 22:649-53.

To learn more about The Jackson Laboratory's Genetic Integrity Program, visit this Web site: www.jax.org/jaxmice/geneticquality

JAX® Mice News

JAX® Ready Strains™: Ready When You Are

Some mouse strains are so critical to biomedical research that they must be available in large quantities at virtually a moment's notice. The Jackson Laboratory has designated the following eleven most commonly used strains as JAX® Ready Strains™: BALB/cJ (000651), BALB/cByJ (001026), B6.129P2-*ApoE*^{-tm1Unc}/J (002052), B6D2F1/J (100006), C3H/HeJ (000659), C57BL/6J (000664), CBA/J (000656), DBA/2J (000671), FVB/NJ (001800), NOD.CB17-*Prkdc*^{scid}/J (001303), and NOD/LtJ (001976). The inventories of these strains have been expanded to ensure that they are always readily available in the quantities you need.

By choosing JAX® Ready Strains™, you gain access to a wealth of mouse genetic, phenotypic, and disease informatics resources. Of the 15 JAX® Mice Strains surveyed in the Resequencing Project (see article titled “JAX® Mice: the Gold Stan-

dard Just Got Better” in this issue of JAX® NOTES), six are JAX® Ready Strains™. These are the best characterized and most widely published JAX® Mice Strains, and their enduring value for future research is protected by our unsurpassed animal health and genetic quality programs. To order JAX® Ready Strains™, call 1-800-422-MICE (6423) or 1-207-288-5845.

AXB and BXA RI Strains Reclassified

After analyzing AXB and BXA recombinant inbred (RI) strains with high-density single nucleotide polymorphic (SNP) markers, Jackson Laboratory staff concluded that some of the strains were genetically similar. Thus, the following strains have been reclassified:

BXA8/PgnJ (001697) and BXA17/PgnJ (001704). Strain BXA17/PgnJ, shown to be a replica of BXA8/PgnJ, was discarded and is now listed as extinct. The original

and unique BXA17/PgnJ strain was lost between 1989 and 1990. Literature before then refers to the original strain; literature since then refers to strain BXA8/PgnJ.

AXB13/PgnJ (001826) and AXB14/PgnJ (001684). These strains were shown to be “sister” strains: isogenic except for large regions of chromosomes 11, 12, and 13, and smaller regions of a few other chromosomes. They are therefore “near congenics.” Thus, AXB13/PgnJ retained its name, and AXB14/PgnJ was renamed AXB13a/PgnJ.

AXB18/PgnJ (001686), AXB19/PgnJ (001687), and AXB20/PgnJ (001688). These three strains were also shown to be sister strains, but with significant regions of some chromosomes differing between them. Two of these strains were renamed: AXB18/PgnJ is now AXB19a/PgnJ; AXB20/PgnJ is now AXB19b/PgnJ. AXB19/PgnJ was considered the primary strain because it has the best traceable

history, and its name was retained.

In general, the sister strains should not be used for primary screening or QTL mapping. However, if a QTL is located in a region of difference between sister RI strains, the strains may be used as near congenics for additional analysis.

JAX[®] Mice Strain Sleeps While Standing

At the very moment when Jackson Laboratory biologist Peter Reifsnyder was in the doctor's office being diagnosed with sleep apnea, a sleep disorder that troubles roughly 12 million Americans, some animal technicians in one of the Laboratory's mouse rooms were curiously observing a very odd behavior by individuals of a mouse strain called New Zealand Obese (NZO/HILtJ, 002105). The mice were standing vertically upright on their hind legs – while sleeping. When Reifsnyder himself observed this behavior, he immediately suspected that it was a kind of sleep apnea. The discovery of this unusual behavior in mice is a significant breakthrough because, until then, the only known animal model of sleep apnea was the English bulldog (Hendricks *et al.* 1987).

Although apparently rare in other animals, in humans, sleep apnea, clinically called obstructive sleep apnea (OSA), is as common as adult diabetes. It may affect people of any age and sex, but it is more prevalent in males, people who are overweight, and people who are over 40. Due to a general lack of awareness of the disease by health care professionals, the vast majority of people with sleep apnea are undiagnosed and untreated.

In Greek, the word apnea means “without breath.” While sleeping, people with sleep apnea repeatedly stop breathing, wake up, and fall back asleep, sometimes several hundred times a night. As a result, they are exhausted the next day, and may nod off at work, at traffic signals, and while driving.

Sleep apnea is increasingly recognized as a risk factor for hypertension,

cardiovascular disease, and metabolic syndrome, and it has been implicated in memory loss, obesity, impotence, and headaches.

Fortunately, sleep apnea can be treated. Treatments include sleeping in a semi-prone position, losing weight, wearing a pressurized mask that keeps the airway open during sleep, surgery to modify the airway, and a dental device that pulls the jaws forward.

Reifsnyder's sleep apnea and that of the NZO mice have different causes. Whereas Reifsnyder's apnea is due to his jaws being located farther back than normal, allowing his tongue to repeatedly interfere with breathing during his sleep, the NZO apnea is hypothesized to be due to airway compression by unusually large neck fat pads when the mice are prone. Researchers are testing this hypothesis by analyzing magnetic resonance images (MRIs) and the behaviors of some NZO mice temporarily housed in a sophisticated Comprehensive Cage Monitoring System (CCMS), which, among other things, assesses sleep patterns. The sleep-assessment component of the CCMS was developed in cooperation with the University of Pennsylvania's Dr. Allan Pack, a collaborator in The Jackson Laboratory's Center for New Mouse Models of Heart, Lung, Blood, and Sleep (HLBS) Disorders (featured in the last issue of JAX[®] NOTES). One of the goals of the HLBS Center is to identify and/or produce new mouse models of sleep disorders.

The discovery of the unusual sleep behavior of NZO mice prompted some Jackson Laboratory staff to examine other mouse strains for similar behavior. They soon discovered that two other strains of obese mice and two strains of lean mice exhibit fragmented sleep – though none of these strains were observed standing while sleeping.

Research indicates that the cause of sleep apnea is at least partly genetic. Identifying the alleles responsible for sleep disorders in mouse models could help researchers find the fundamental cause

of and better treatments for sleep apnea. Comments Dr. Luanne Peters, Senior Staff Scientist at The Jackson Laboratory and principal investigator of the HLBS project: “For the first time, this gives us genetically defined mice in which we can start to look for the genes that cause this disorder. More research must correlate the mouse's sleepiness with blood chemistry to see if it mimics the blood-oxygen changes in the human disorder. But we have made progress toward monitoring blood oxygen levels reliably in the sleepy mice, and we'll be measuring them as soon as we can.”

References

- Cooke, Robert. 2006. Odd mice in apnea study. *Newsday.com* (www.newsday.com/news/health/ny-hsdrug4896788sep19,0,2821465.story?coll=ny-health-print). Sep. 16.
- JAX[®] NOTES. 2006. The Jackson Laboratory's Center for New Mouse Models of Heart, Lung, Blood, and Sleep Disorders. *JAX[®] NOTES* 503:1-3.
- Hendricks JC, Kline LR, Kovalski RJ, O'Brien JA, Morrison AR, Pack AI. 1987. The English bulldog: a natural model of sleep-disordered breathing. *J Appl Physiol* 63:1344-50. The American Sleep Apnea Association (www.sleepapnea.org)

Clarification: Are C57BL/6J Male Mice Really Glucose Intolerant?

Many of our customers use C57BL/6J (B6, 000664) mice as normoglycemic and glucose tolerant controls for certain obesity/diabetes and genetically engineered mouse mutants with a B6 background. We therefore wish to clarify a potentially confusing article in the last issue of JAX[®] NOTES (JAX[®] NOTES 2006). The article reported that United Kingdom researchers (Freeman *et al.* 2006) demonstrated that a spontaneous mutation in the nicotinamide nucleotide transhydrogenase (*Nnt*) gene partly explains why, in response to a bolus injection of glucose, B6 males secrete less insulin and clear glucose more slowly than do C3H/HeH males. Although B6 males fed a chow diet clear glucose slower over a two-hour span than do certain other strains (Goren *et al.* 2004), they clear it much faster than

do males from truly glucose-intolerant strains, such as KK/HlJ (002106), NZO/HlLtJ (002105), and NON/LtJ (002423), the latter reportedly expressing the wild-type *Nnt* allele (online supplement to Freeman *et al.* 2006). The Mouse Phenome Database (www.jax.org/phenome) indicates that though plasma glucose levels in B6 mice before and after being fed a high fat diet are higher than those in many other comparably fed

inbred strains, they are within the normal range for inbred strains. Thus, as applied to B6 mice, glucose intolerance is a relative term: due to diminished glucose-stimulated insulin secretion, B6 clearance rates for injected glucose are slower than for some inbred strains. However, B6 males are very insulin sensitive and, following a glucose injection, restore their glucose levels to within a normal range over a two-hour period.

References

Freeman HC, Huggill A, Dear NT, Ashcroft FM, Cox RD. 2006. Deletion of nicotinamide nucleotide transhydrogenase: a new quantitative trait locus accounting for glucose intolerance in C57BL/6J mice. *Diabetes* 55:2153-6.

Goren JH, Kulkarni RN, Kahn CR. 2004. Glucose Homeostasis and Tissue Transcript Content of Insulin Signaling Intermediates in Four Inbred Strains of Mice: C57BL/6, C57BLKS/6, DBA/2, and 129X1. *Endocrinology* 145:3307-23

JAX® NOTES. 2006. Cause of glucose intolerance in C57BL/6J mice discovered. *JAX® NOTES* 403:7.

Newly Available JAX® GEMM® Strains

We are pleased to announce that The Jackson Laboratory is now distributing the following JAX® GEMM® (Genetically Engineered and Mutant Mice) strains. For more general information on JAX® GEMM® strains, visit www.jax.org/jaxmice/info/gemm.

For ordering information, please contact Customer Service by e-mail at orderquest@jax.org or call 800.422.MICE (6423) or 207.288.5845. Please see our Web site for more detailed strain data sheets (www.jax.org/jaxmice).

B6.129S2-Thbs1^{tm1Hyn}/J (006141)

Homozygotes for this targeted mutation of the thrombospondin 1 (*Thbs1*) gene are viable and fertile. Approximately 20% of the embryos and neonates have an obvious, mild, and variable lordotic curvature of the spine and are not viable. Homozygotes produce an abnormal and shortened protein transcript in multiple tissues. Western analysis confirms the absence of the protein in platelets. Homozygotes have an abnormally high number of circulating white blood cells. During the first four to ten weeks of life, they exhibit patches of acute and organizing pneumonia. With age, various epithelial cell lineages exhibit considerable hyperplasia. Mutants also have an abnormally high number of retinal endothelial cells and, after injury, retinal vasculature exhibits inappropriate remodeling and maturation. Mutants with an FVB/N background have significantly more spontaneous tumor growth and vasculature than do wild-type controls. This strain may be used to research inflammatory responses in the lungs, eyes, and skin, angiogenesis and vascular pathophysiology, cancer, chemotherapy, apoptosis, and cell differentiation and migration.

STOCK Pten^{tm1Hwu}/J (006068)

This strain possesses loxP sites on either side of exon 5 of the targeted phosphatase and tensin homolog (*Pten*) gene. Homozygotes are viable, and look and behave normally. When used in conjunction with a Cre recombinase-expressing strain, this strain may be used to generate tissue-specific mutants of the floxed allele.

NOD/LtJ-Tg(Ins1-EGFP/GH1)14Hara/HaraJ (005282)

This transgenic strain expresses enhanced green fluorescent

protein (EGFP) fused to a 2.1kb fragment of human growth hormone under the control of mouse insulin promoter 1. The donating investigator reports that mice of this strain develop normally and have normal glucose tolerance and pancreatic insulin content. Histology confirms that the islets of these mice have a normal architecture and express both insulin and EGFP. The EGFP reporter allows the beta cells to be easily identified and purified for further studies.

129-Gt(ROSA)26Sor^{tm1(EGFP)Luo}/J (006053)

These mutant mice are viable and look and behave normally. Regardless of Cre-recombination, these mice express enhanced green fluorescent protein (EGFP) because the beta-actin intron in-frame that interrupts the N- and C-terminals of the EGFP coding sequences splices EGFP together. EGFP expression is high in every cell and can be visualized in vivo and in fixed samples. This is a control EGFP-expressing strain to be used with MADM (mosaic analysis with double markers) strains 129-Gt(ROSA)26Sor^{tm3Luo}/J (006041) and 129-Gt(ROSA)26Sor^{tm2Luo}/J (006067). The three strains will be available as a set. By using the MADM system, researchers can generate genetic mosaics containing somatic cells of different genotypes and thereby determine lineal relationships and pleiotropic gene functions in multicellular organisms. This strain may also be used to research cell differentiation and mitosis.

B6.129X1-Gt(ROSA)26Sor^{tm1(EYFP)Cos}/J (006148)

This transgenic strain contains an enhanced yellow fluorescent protein (EYFP, Clontech) gene inserted into the Gt(ROSA)26Sor locus. Homozygotes are viable, fertile, and look and behave normally. EYFP expression is blocked by an upstream loxP-flanked STOP sequence. In the offspring produced when

this strain is bred to a strain containing the cre recombinase gene under the control of a promoter of interest, the STOP sequence of the targeted gene in the tissue of interest is deleted, and EYFP is expressed. This strain may be used to monitor Cre expression and trace the lineage of Cre-expressing cells in embryonic, young, and adult mice.

B10.Cg-H2^k Tg(NFkB/Fos-luc)26Rinc/J (006100)

This transgenic strain expresses the luciferase gene driven by two copies of the NF-kappaB (NF-kB or NFkB) regulatory element, now called v-rel reticuloendotheliosis viral oncogene homolog A (avian) (Rela). Hemizygotes for the transgene are viable, fertile, and look and behave normally. The presence of nuclear NF-kB DNA binding activity (as detected by electrophoretic mobility shift assay [EMSA]) is consistent with luciferase reporter activity. NF-kB transcriptional activity can be identified in any tissue. This strain may be used for immunology, cellular signaling, signal transduction, apoptosis, and transcription factor research.

B6.129S-Shh^{tm2(cre/ESR1)Cjt/J} (005623)

This strain expresses a fusion product involving Cre recombinase and a mutant form of the human estrogen receptor ligand binding domain from the endogenous sonic hedgehog (*Shh*) locus. The mutant human estrogen receptor does not bind natural ligand at physiological concentrations but does bind the synthetic ligand, 4-hydroxytamoxifen. Restricted to the cytoplasm, the Cre/ESR1 protein can only gain access to the nuclear compartment after exposure to tamoxifen. Tamoxifen administration induces Cre recombinase expression in all cells that express the endogenous gene, resulting in the deletion of the first 35 base pairs following the ATG. Homozygous mice are neither viable nor fertile. Heterozygotes are viable, fertile, and look and behave normally. This strain may be used to research limb patterning and development.

STOCK Tg(ACTA1-cre)79Jme/J (005936)

This transgenic strain expresses the cre recombinase gene driven by the human alpha-skeletal actin promoter. Hemizygotes are viable, fertile, and look and behave normally. Cre-mediated recombination in the offspring produced when this strain is bred to a strain containing a loxP-flanked sequence of interest deletes the flanked genome in striated muscle. Cre activity is restricted to adult striated muscle fibers and embryonic striated muscle cells of the somites and heart. Along with strains B6;129-Smn1^{tm1Jme/J} (005935) and STOCK Tg(Eno2-cre)39Jme/J (005938), this strain may be used to research spinal muscular atrophy (SMA).

STOCK Tg(Cp-EGFP)25Gaia/J (005854)

During development and adulthood, this strain expresses enhanced green fluorescent protein (EGFP) in a wide variety

of cell/tissue types, including enriched hematopoietic stem cell (HSC) populations. Homozygotes are viable, fertile, and look and behave normally. The location of EGFP expression is consistent with Notch signaling pathway elements/genes and faithfully reflects Notch activity. Expression is low in fully differentiated cells of the peripheral lymphoid organs (blood and spleen). Isolated HSCs retain their ability to differentiate. This strain may be used to research HSC populations and other cell types using the Notch, CBF1, or Wnt signaling pathways. Additionally, because immature (double negative [DN]) thymocytes have differential expression patterns as they progress from DN1-DN4, this strain may be used to research thymocyte maturation.

Discovery Strategies Conference:

The Laboratory Mouse in the Development of New Therapeutic Approaches to the Treatment of Neurological Disease

This meeting is designed for academic and pharmaceutical researchers with interests in the underlying biology and pathology of complex neurological and neuropsychiatric disorders.

Date(s): June 11, 2007 - June 13, 2007

Location: Bar Harbor, ME

Tony Yaksh, Ph.D., University of California, San Diego

Edward Bilsky, Ph.D., University of New England

Richard Hargreaves, Ph.D., Merck & Co. Inc.

Richard Smeyne, Ph.D., St. Jude Children's Research Hospital

Sheryl Moy, Ph.D., The University of North Carolina at Chapel Hill

Akira Sawa, M.D. Ph.D., Johns Hopkins University

E. David Leonardo, M.D., Ph.D., Columbia University

Guoping Feng, Ph.D., Duke University

Adron Harris, Ph.D., Waggoner Center for Alcohol Research
University of Texas Austin

Luis de Lecea, Ph.D., Stanford University School of Medicine

Hans Rollema, Ph.D., Pfizer Global Research and Development

Selena Bartlett, Ph.D., Gallo Center at University of California,
San Francisco

David R Borchelt, Ph.D., Evelyn F. & William L. McKnight
Brain Institute of the University of Florida

Frank M LaFerla, Ph.D., University of California, Irvine

Sue Ackerman, Ph.D., The Jackson Laboratory

Distinguished Speaker

Wayne N. Frankel, Ph.D., The Jackson Laboratory

Keynote Speaker

Story Landis, Ph.D., NINDS (invited but not confirmed)

For more information, please visit

<http://www.jax.org/pharma/discovery>, or

Contact Laura Lelansky at laura.lelansky@jax.org.

Surgical Services Tissue Order Forms Revised

In addition to performing over 60 types of standard and custom surgical procedures, our Surgical Services group distributes biological specimens such as serum, plasma, whole blood, tissues, and organs. These can be ordered directly from the Surgical Services Web site, www.jax.org/jaxmice/services/surgical_pricing. So that orders are submitted directly to our Customer Service staff, the following Web forms have been revised:

- Request Organs/Tissues from JAX® Mice
- Request Mouse Whole Blood
- Request Mouse Plasma
- Request Mouse Serum

Note. Shipping surgically-altered mice to some geographical locations is subject to restrictions. Please check with the animal health and importation authorities within your organization for relevant regulations.

MGI Releases Version 3.51

Mouse Genome Informatics (MGI, www.informatics.jax.org) is pleased to announce its release of version 3.51. This new version has the following features:

- Genome coordinates updated to NCBI Mouse Build 36 and dbSNP Build 126, dbSNP is the official source of SNP based mouse genomic variation in MGI and serves as a central repository for single nucleotide polymorphisms (SNPs), multiple nucleotide polymorphisms (MNP), and short insertion/deletion polymorphisms (IN-DELS);
- Computational genome annotations from Ensembl and NCBI;
- Manually curated gene models from the Vertebrate Genome Annotation (VEGA) group at the Sanger Institute;

- MGI's Mouse GBrowse updated to Build 36;
- Mouse genome annotations from VEGA, NCBI, and Ensembl integrated into a unified catalog of mousegenome features;
- 6,496 additional genes (a 5% increase) and 4,615 additional pseudogenes (a 400% increase);
- Genome coordinate data for microRNAs (from mirBASE)
- Genome coordinates for many mouse QTL regions;
- SNPs that map to the Y chromosome; and
- More refSNPs (from 1.8 to 6.5 million).

For example, to sample the new VEGA data for the Opa interacting protein 5 (*Oip5*) gene, see the MGI gene detail page at www.informatics.jax.org/javawi2/servlet/WIFetch?page=markerDetail&key=54625. In the Sequence Map section, click the link to the VEGA ContigView. In the Sequences section, click the VEGA Gene Model link to a VEGA Mouse GeneView curated locus report. To find this (or similar) information yourself, enter a gene name on the MGI Genes and Markers Query Form at www.informatics.jax.org/javawi2/servlet/WIFetch?page=markerQF. You can also enter a gene's VEGA accession ID (for *Oip5*, it is OTTMUSG0000015949) or a gene's name in the Search box on the MGI home page (click Accession IDs for the former or Gene symbols/names for the latter search).

To see a summary of all microRNA data in MGI, set the Type field on the Genes and Markers Query Form at www.informatics.jax.org/javawi2/servlet/WIFetch?page=markerQF to microRNA. To find details, click any of the symbols on the microRNA Summary page that appears. The following Web site is an example of an MGI detail page with microRNA coordinates: www.informatics.jax.org/javawi2/servlet/WIFetch?page=markerDetail&key=170816.

Please send questions and comments to User Support, mgi-help@informatics.jax.org.

The Jackson Laboratory

- The world's largest private genetics research institute.
- The world's leading provider of genetically defined mice and related services.
- Has facilities in Bar Harbor, ME, and West Sacramento, Calif.
- Hosts nearly 40 research groups, comprising over 450 research staff, including over 175 Ph.D, M.D, and D.V.M scientists.
- Employs nearly 1,300 people.
- Has nearly 150 active research grants.
- The repository for over 3,000 mouse models (JAX® Mice are referenced in about 100 new publications per week).
- Ships over 2 million mice a year to 12,000 labs in 63 countries.

Jackson Laboratory Research News

The Jackson Laboratory to Play a Key Role in the Knockout Mouse Project

In early September, the National Institutes of Health (NIH) formally launched its Knockout Mouse Project (KOMP, www.nih.gov/science/models/mouse/knockout/). The goal of the project is to build a comprehensive and publicly available resource of approximately 20,000 knockout mouse strains, each with a mutation completely disrupting a different gene among the estimated 20,000 in the mouse genome. To date, researchers around the world have produced mouse knockouts for about 5,000 of the 20,000 genes. The Jackson Laboratory will play a major role in the project. It was awarded a five-year \$2.5 million cooperative agreement to establish KOMP's Data Coordination Center. Under the leadership of Dr. Martin Ringwald, the Center will collect information allowing researchers to track the scheduling and progress of knockout production. The Center will also serve as a central information resource for all publicly available knockout mutants and will integrate with other databases that contain information on the physical and biochemical characteristics of the knockout mice, mouse DNA sequence, and mouse genetics.

The agreement with The Jackson Laboratory was part of \$52 million awarded to other collaborating institutions. Projects at these institutions include producing thousands of mouse embryonic stem (ES) cell lines (each with a different gene knocked out), producing ES cell lines suitable for high-throughput gene targeting or trapping in C57BL/6, and optimizing an existing C57BL/6 strain ES cell line and growth medium.

During KOMP's initial stages, researchers will be able to obtain the ES cells and the targeting vectors used to produce them from the grantees, allowing them to swiftly and efficiently produce live lines of knockout mice. Later, all these materials will be available to the entire scientific community from a central KOMP repository.

The resources produced by KOMP will be extremely useful for researching human disease. Each knockout will allow researchers to closely study and determine the role of a different gene in the 20,000-gene mouse genome. More importantly, the KOMP resources will allow biomedical researchers to develop better models of inherited human diseases, such as cancer, heart disease, neurological disorders, diabetes, and obesity. Says NIH Director Elias A. Zerhouni, M.D., "Knockout mice are powerful tools for exploring the function of genes and creating animal models of human disease. By enabling more researchers to study these knockouts, this trans-NIH initiative will accelerate our efforts to translate basic research findings into new strategies for improving human health. . . . This is scientific teamwork at its best (www.genome.gov/19517927)."

Jackson Laboratory Scientists Help Crack the Egg's Secrets

Drs. Alexei Evsikov, Barbara Knowles, and colleagues at The Jackson Laboratory recently published the results of their extensive investigation of the genetic mechanisms governing the development of a fully-grown oocyte into an embryo (Evsikov *et al.* 2006). By analyzing 19,000 expressed sequence tags in the cDNA library of fully-grown oocytes from the mouse (*Mus musculus*), the researchers found that the oocytes express 5,400 genes and transposable elements. Homologs for a majority of these genes were found to be expressed in the eggs of Zebra fish (*Xenopus laevis*) or Sea squirts (*Ciona intestinalis*), indicating that the genes are evolutionarily conserved in chordates. A large proportion of the genes unique to mammals belong to several gene families expressed only in oocytes. The transition between egg and embryo is accomplished by proteins and mRNA transcripts in the fully-grown oocyte. These proteins can be modified as a result of signal transduction processes and are eliminated at various times during the transition to an embryo. The research team was able to distinguish between transcripts of genes necessary for oogenesis and those necessary for the development of an embryo, and they identified motifs in maternal mRNAs associated with transcript stability and translation. Through this work, they identified an oocyte-specific mammalian form of eukaryotic translation initiation factor 4E, a gene important in translation. The results of this study reveal that, in the course of chordate evolution, pathways responsible for the initiation of a new life have been conserved, but that genes involved in female reproduction can diversify rapidly, leading to potential mechanisms for reproductive isolation.

Reference

Evsikov AV, Graber JH, Brockman JM, Hampl A, Holbrook AE, Singh P, Eppig JJ, Solter D, Knowles BB. 2006. Cracking the egg: molecular dynamics and evolutionary aspects of the transition from the fully grown oocyte to embryo. *Genes Dev* 20:2713-27.

Jackson Laboratory Scientists Discover Mutation Causing Charcot-Marie-Tooth-Like Disease in Mice

Drs. Robert Burgess, Kevin Seburn, and Gregory Cox (all at The Jackson Laboratory) and colleagues recently identified a dominantly inherited mutation that causes overt neuromuscular dysfunction and dramatically shortens lifespan in mice (Seburn *et al.* 2006). The mutation, designated Nmf249 because it was identified in a mutant mouse (C57BL/6J-*Gars*^{Nmf249}/J, 005013) produced at The Jackson Laboratory's Neuroscience Mutagenesis Facility in 2004, was found to be an amino acid alteration in the glycyl tRNA synthetase (*Gars*) gene, the mouse ortholog of the gene affected in human Charcot-Marie-Tooth type 2D (CMT2D) peripheral neuropathy.

CMTs are the most commonly inherited peripheral nerve-

diseases. They affect approximately 150,000 Americans and are found world-wide in all races and ethnic groups. They were discovered in 1886 by three physicians, Jean-Martin-Charcot, Pierre Marie, and Howard Henry Tooth (Charcot-Marie-Tooth Association, www.charcot-marie-tooth.org). CMT patients slowly lose the use of their feet, legs, hands, and arms because the nerves there degenerate and the muscles weaken.

The *Gars* gene mutation discovered by the scientists is unusual because it does not affect the normal enzymatic function of the gene's encoded protein, glycyl tRNA synthetase. Rather, the mutation confers an additional role to the protein, a novel pathogenic role that specifically affects motor and sensory nerves.

Reference

Seburn KL, Nangle LA, Cox GA, Schimmel P, Burgess RW. 2006. An active dominant mutation of glycyl-tRNA synthetase causes neuropathy in a Charcot-Marie-Tooth 2D mouse model. *Neuron* 51:715-26.

JAX® Mice Literature

Revised Resource Manuals Available

The Jackson Laboratory is pleased to announce that revised editions of the Cancer Resources Manual and the Genetic Background (formerly Genetic Resources) Resource Manual are now available.

The Cancer Resources Manual showcases over 30 JAX® Mice cancer models, describes publicly accessible databases such as the Mouse Tumor Biology (MTB) database, lists courses and conferences related to cancer research, and briefly summarizes the cancer research conducted by Jackson Laboratory scientists.

The Genetic Background Resources Manual explains the importance of using genetically well-defined mice for biomedical research, describes The Jackson Laboratory's resources for helping researchers choose those mice, encourages researchers to clearly communicate the genetic make-up of their models by using proper nomenclature, and summarizes The Jackson Laboratory's programs to ensure that JAX® Mice are genetically well-defined.

These and other Jackson Laboratory Resource Manuals are available in printed and electronic formats. To request them, simply fill out the literature request form at the JAX® Mice Web site, www.jax.org/jaxmice/literature.

New Jackson Laboratory Research Building Opens

In mid-August, The Jackson Laboratory celebrated the opening of its new \$26 million three-story, 50,000 square-foot, East Research Building. Attending the event were Maine Governor John Baldacci, U.S. Senators Olympia Snowe and Susan Collins, First District Congressman Tom Allen, and more than 100 Laboratory staff, board members, donors, and local public officials.

Director Dr. Rick Woychik said the building would be very instrumental in advancing "a new paradigm for doing genetics. We call it systems genetics, where we study traits not one gene at a time but by looking at all the genes in entire genomes." The new building and associated research will help create about 125 high-paying, high-quality jobs. Woychick said that "Ph.D. scientists, bachelor's level scientists, as well as individuals with high school educations will come and help make some fantastic science happen here." Several Jackson Laboratory research groups that study neurological diseases, including epilepsy, Alzheimer's, and Parkinson's, have already moved into the building.

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