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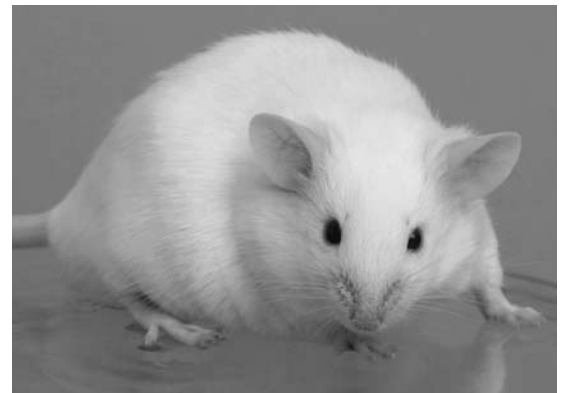
The Jackson Laboratory Expands Focus on Diabetes Research

Diabetes is one of the world's most serious diseases. In America alone, it affects 20.8 million people (seven percent of the population), burdening our economy with approximately \$132 billion a year in related health costs (The American Diabetes Association, www.diabetes.org). In some parts of the country, especially in large cities, diabetes has reached epidemic proportions. In recent years, research on diabetes and its risk factors (particularly obesity, smoking, and lack of exercise) has increased exponentially, prompting an intensive effort to develop better diabetes research tools. Our mouse models, services, online resources, publications, and educational offerings are among the best diabetes research tools available.

JAX[®] Mice Diabetes Models

We offer over 260 JAX[®] Mice models suitable for diabetes and obesity research (www.jax.org/jaxmice/research/diabetes_obesity). They include the classic "diabetes mouse" BKS.Cg-*m* +/- *Lepr^{db}/J* (000642) (see the profile of this mouse on page 7), the obese mouse B6.V-*Lep^{ob}/J* (000632), the NOD/ShiLtJ (001976) mouse, as well as some models developed by our scientists which are becoming increasingly popular:

- Dr. Ed Leiter, diabetes researcher for nearly 35 years, has developed numerous diabetes models, recognizable by the code "Lt" in their strain names. He brought the NOD/ShiLtJ (001976) strain to The Jackson Laboratory, and initiated the first set of MHC congenics on this substrain. He developed the NONcNZO10/LtJ (004456) mouse which exhibits many of the characteristics of human type 2 diabetes. Dr. Leiter also directs the Type 1 Diabetes Resource (T1DR, www.jax.org/t1dr), a repository dedicated to collecting and cryopreserving mouse strains for use in type 1 diabetes research.
- Dr. Leonard Shultz has developed several diabetes models, recognizable by the code "Sz" in their strain names. He developed the NOD.Cg-*Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ* (005557) model which is widely used in cancer and immunology research. Its utility in diabetes research stems from the fact that it does



NONcNZO10/LtJ (Stock number 004456, common name RCS-10) an albino (white) recombinant congenic laboratory mouse, commonly used for diabetes and obesity research.

not need to be irradiated when used as a recipient of diabetic T cells in diabetes transfer experiments.

- Dr. David Serreze has developed numerous diabetes models, recognizable by the code "Dvs" in their strain names. Four of these, NOD.129S7(B6)-*Ifng^{tm1Tb}/DvsJ* (002575), NOD.129P2(B6)-*Il4^{tm1Cgn}/DvsJ* (004222), NOD.Cg-*Il10^{tm1Cgn}/DvsJ* (004266), and NOD.Cg-Tg(TcraTcrbNY8.3)1Pesa/DvsJ (005868) are being used by Dr. Christophe Benoist of the Joslin Diabetes Center (see the feature article on page 6).
- Dr. Yaacov Barak has developed several JAX[®] Mice models, including B6.129-*Pparg^{tm2Rev}/J* (004584), a model suitable for researching the molecular

links between peroxisome proliferator activated receptor gamma (PPAR γ), fat cell function, and susceptibility to diabetes and metabolic disease.

- Dr. Jürgen Naggert and his colleagues have developed several diabetes models, recognizable by the code “Jng” in their strain names. The TALLYHO/JngJ (005314) mouse is a model of type 2 diabetes which is characterized by moderate obesity, hyperglycemia (males only), hyperlipidemia, hyperinsulinemia, glucose intolerance, and enlarged pancreatic islets.

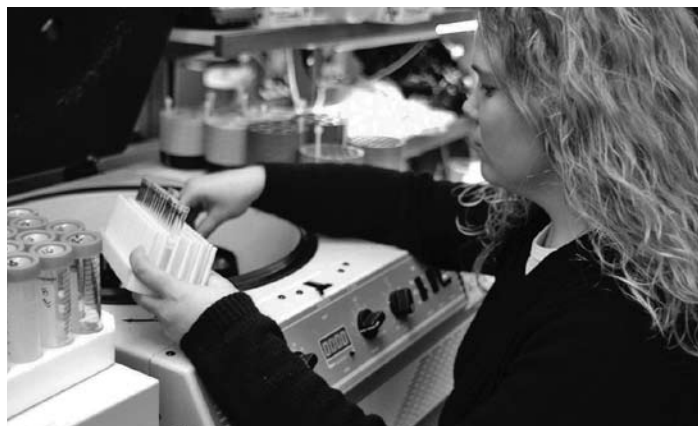
The diabetes phenotypes of these and other type 2 diabetes models are compared in our Type 2 Diabetes and Obesity Resource Manual (see Table 1, page 3) and described in detail in the JAX[®] Mice Database (www.jax.org/jaxmice). We are constantly acquiring new diabetes models. In the last six months, 23 new models have become available, and over 40 are currently under development.

JAX[®] Services for Diabetes Research

JAX[®] Services offers four highly successful services that facilitate diabetes research:

- **JAX[®] *In Vivo* Services.** We use a battery of high-throughput, non-invasive tests to evaluate novel compounds and clinically relevant disease endpoints in mouse models of diabetes and obesity.
- **STZ-induced Diabetes.** We use streptozotocin (STZ) to damage pancreatic islets and induce diabetes in males of several strains of mice, including C57BL/6J (moderately susceptible) and NOD/ShiLtJ (001976) and CBA/J (000656) (both highly susceptible. Strains FVB/NJ (001800), BALB/cJ (000651), and A/J (000646) are resistant.
- **JAX[®] Diet-induced Obesity (DIO) Services.** We use special diets to produce obese mice, including the most popular and well-characterized DIO model, the male C57BL/6J (B6, 000664) mouse. This service may be combined with *In Vivo* Services to evaluate novel compounds.
- **JAX[®] Services “study-ready” DIO mice.** We can deliver study-ready DIO C57BL/6J males from six to 26 weeks old to you or to JAX[®] *In Vivo* Services for studies conducted according to your specifications. Mice fed a control diet are also available.

For details about these and other JAX[®] Services, please visit our website, www.jax.org/jaxservices.



A Jackson Laboratory Research Assistant loads test tubes containing mouse serum into a centrifuge for an experiment in the laboratory of Dr. David Serreze.

The Type 1 Diabetes Resource

The Type 1 Diabetes Resource (T1DR, www.jax.org/t1dr) collects and cryopreserves mouse strains that may be used to research type 1 diabetes. Included are NOD strains carrying transgenes and targeted mutations and NOD and NOD-related strains congenic for chromosomal intervals containing type 1 diabetes susceptibility or resistance loci. The strains are either generated here at The Jackson Laboratory or donated by external investigators. Each strain is distributed live for a limited period of time, on a rotating basis, so check regularly.

The T1DR also serves as the Mouse Generation and Husbandry Core (MGHC) for the Animal Models of Diabetes Complications Consortium (AMDCC, www.amdcc.org), whose mission is to coordinate efforts to produce and/or improve and characterize animal models of human diabetic complications. The T1DR produces, maintains, expands, phenotypes, and distributes new strains established in cooperation with the AMDCC.

Types of Diabetes

There are two major types of diabetes, type 1 and type 2. Type 1 is characterized by the destruction of the pancreatic beta cells. Patients produce little or no insulin. It accounts for only 5-10% of diabetes cases in America. Type 2 is a combination of an inability to properly use and produce adequate amounts of insulin. It accounts for 90-95% of diabetes cases in America (American Diabetes Association, www.diabetes.org).

The Type 2 Diabetes and Obesity Resource Manual

Our updated Type 2 Diabetes and Obesity Resource Manual contains a wealth of useful information for diabetes researchers. It includes a chart comparing type 2 diabetes and obesity phenotypes among humans and selected JAX® Mice models (see Table 1 below for a modified version), and brief descriptions of selected JAX® Mice models and relevant JAX® Services, online resources, and courses and conferences. You can obtain

a complimentary copy of this manual and other JAX® Mice & Services literature by filling out the literature request form at www.jax.org/jaxmice/literature.

For more information about our diabetes resources, visit the JAX® Mice Database (www.jax.org/jaxmice), or contact one of our technical information support scientists at micetech@jax.org, 1-800-422-6423, or 1-207-288-5845.

Table 1. Comparison of diabetes phenotypes among humans and selected JAX® Mice models of type 2 diabetes (modified from the Type 2 Diabetes and Obesity Resource Manual).

Type 2 Diabetes Phenotypes

Humans and mouse models (stock number)	Induced or spontaneous	Genetics	Onset	Sex	Hyper-insulinemia	Glucose intolerance	Hyper-glycemia	Islet atrophy
Humans	Spontaneous	Polygenic	Mature (progressive)	M, F	Moderate	Yes	Yes	Variable
NONcNZO10/LtJ (004456)	Diet-induced	Polygenic	Mature	M, F	Moderate	Yes	Severe	Yes
C57BL/6J (000664)	Diet-induced	Polygenic	Mature	M	Mild	Yes	Moderate	No
KK.Cg-A ^y /J (002468)	Spontaneous	Polygenic	Mature	M, F	Severe	Yes	Yes	Hypertrophy
BKS.Cg-m +/+ <i>Lep^{ob}</i> /J (000642)	Spontaneous	Polygenic	Young	M, F	Severe	Yes	Severe	Yes
B6.V- <i>Lep^{ob}</i> /J (000632)	Spontaneous	Polygenic	Young	M, F	Severe	Yes	Moderate (transient)	No
BTBR.V(B6)- <i>Lep^{ob}</i> /WiscJ (004824)	Spontaneous	Polygenic	6 wks (M); 8 wks (F) (progressive)	M, F	Severe	Severe	Severe	Earlier in males
KK/HlJ (002106)	Spontaneous	Polygenic	Mature	M	Severe	Yes	Yes	Hypertrophy
NZL/LtJ (005067)	Spontaneous	Polygenic	Mature	M	Yes	Yes	Yes	ND
BKSC ^h pLt.HRS- <i>Cpe^{fat}</i> /J (002391)	Spontaneous	Polygenic	Mature	M	Yes	Yes	Yes	Hypertrophy
TALLYHO/JngJ (005314)	Spontaneous	Polygenic	Mature	M	Yes	Yes	Males	Hypertrophy (males)

The Scientist: Postdocs Rank The Jackson Laboratory Among Top Ten Best Places to Work

The life sciences magazine *The Scientist* recently released the results of a yearly international survey it conducts to determine which research institutions and universities provide the best experience for postdocs. In 2008, postdocs ranked The Jackson Laboratory as ninth among U.S. research institutions.

More than 2,400 U.S. postdocs participated in the survey, which measured a wide range of factors, from quality of training, facilities and infrastructure to funding for family and personal life. The postdocs gave particularly high marks to the Laboratory's training and travel opportunities, available research grants, and helpfulness of the staff managing the postdoc program.

In the article accompanying the survey results, Jackson Laboratory President and CEO Rick Woychik, Ph.D., noted that a lack of "departmental silos" at the Laboratory facilitates interaction among postdocs. The postdocs also have access to first-class scientific services, "enabling them to focus on their research projects instead of spending all their time setting up and operating scientific instruments."

You can find more information about the survey at www.the-scientist.com/bptw.

In Vivo Imaging Capabilities Expanded With Xenogen's IVIS[®] Lumina Imaging System

Imagine having the ability to monitor cellular events such as tumor progression and metastasis in live mice! Well, thanks to a newly installed image monitoring system at The Jackson Laboratory – West, that concept is now a reality. The Jackson Laboratory's *In Vivo* Services group has recently purchased and installed the IVIS[®] Lumina Imaging System from Xenogen, now part of Caliper Life Sciences. Located in Sacramento, California, JAX[®] *In Vivo* Services deliver target validation and efficacy testing in the context of mouse models of human disease. The addition of the IVIS[®] Lumina imaging system to the *In Vivo* Services group allows monitoring of cellular activity through bioluminescent or fluorescent reporters in live mice. The IVIS[®] Imaging System is physically calibrated and measures absolute light emitted from an animal. This enables meaningful comparisons of results obtained from different mice, experiments, or labs over the course of time.

By leveraging our cancer research experience and the extensive collection of immunodeficient mouse strains available at JAX, we have developed orthotopic transplant models

of human cancer incorporating the IVIS[®] Lumina imaging system. These models allow longitudinal evaluation of tumor development before, during and after treatment as well as the detection of small tumor and micrometastases, offering an excellent preclinical strategy to assess tumor response and recurrence. Our service is very customizable. We have the flexibility to import client-provided cancer cell lines to develop new orthotopic models. We can perform standard protocols, modify our routine procedures to match clients' requirements, and/or transfer protocols from the literature.

Still have questions? Want to get started? Contact JAX[®] Services at jaxservices@jax.org, 1-800-422-6423, or 1-207-288-5845.

The Jackson Laboratory Steps Up to Green Initiatives

In a world where "going green" is become an increasingly integral part of the collective consciousness, it is also one of the top priorities at The Jackson Laboratory.

We recently received the Northeast Energy Efficiency Partnership award for energy conservation leadership. The award is partly due to the following:

- Buildings completed since 2000 are extremely energy-efficient and inexpensive to maintain.
- Fans and pumps turn at the minimum speed.
- High-efficiency motors exceed the efficiency mandated by codes and standards.
- Steam System Maintenance Program minimizes heat loss.
- New high-efficiency fluorescent lights and ballast systems are tied to motion-detectors and timers, ensuring that lights are on only when needed.
- Boilers have precision controls for maximum fuel efficiency.
- New chillers have a non-HCFC (non-ozone depleting) refrigerant and are equipped with energy-efficient variable frequency drives.
- 100% outside-air economizers are used on all our HVAC systems, taking advantage of "free cooling" when ambient temperatures allow.

Reducing, Reusing, Recycling

- We recycle more than 60 tons of paper and cardboard a year.
- We recycle more than 3,000 lbs of glass each year.
- We use locally supplied wood shavings as mouse bedding and compost approximately 1,800 tons of used bedding a year.

- Our Shipping and Receiving Department provides battery and ink cartridge recycling depositories.
- We ship our mice in re-usable shipping containers.
- We recycle all non-functioning or outdated computers.
- Our dining facility, Roscoe's, recycles coffee grounds as compost for local gardens, composts food scraps for local pigs, uses biodegradable paper plates and napkins made of recycled paper, and turns kitchen grease into Biodiesel.
- Our new trade show booth was constructed primarily of recycled styrofoam packing peanuts.
- Most of the documents we distribute externally are printed on Forest Stewardship Council-certified and mainly recycled paper, using soy-based inks, by a printing company that is 100% wind-powered.

Environmentally-Sound Landscaping and Maintenance

- We use organic fertilizer and pest and disease control products, and natural alternative ice melt.
- We compost all leaves and grass clippings and use them for plantings.
- We mulch planting beds, reducing the need for water and fertilizer.
- We have reduced lawn areas and introduced native plantings to cut maintenance costs, equipment use, fuel emissions, and provide an attractive, natural appearance.
- We have replaced harsh chemical-based cleaning products with green cleaning products.

- Our Custodial Department uses trash bags made of at least 30% post-consumer waste, and uses "Echo Mops" made of 30% post-consumer waste, 67% post-industrial waste, and free from post-recycling dyes.
- We use Leadership in Energy and Environmental Design (LEED) standards to select renewable building materials (stone, brick, aluminum, steel, copper, cork, and wood).

Reducing the Number of Cars on the Road

- We operate a carpool and busing program, reducing the number of vehicles traveling to and from MDI each day by more than 200.
- Our JAXfit program encourages local employees to walk or ride a bicycle to work.
- We minimize travel miles by teleconferencing and videoconferencing.
- We facilitate distance learning with the University of Maine, high school students in North Carolina, and the Maine School of Science and Mathematics.

Keeping MDI Beautiful

- In keeping with the Dark Sky initiative, our shielded lighting protects the night skies.
- Our campus is designed to blend into its natural surroundings.
- We installed paths and benches to encourage employees to take lunchtime and other breaks outdoors.



As long as this list of green initiatives is, we realize that it is but one step in many more that we and others must take to make the earth a cleaner, better place. Please join us in our commitment and send us your suggestions for making the biomedical research community greener.

Pictured at left is The Jackson Laboratory's new, flexible, trade show booth, which utilizes the lite system developed in Europe (www.thatlithing.com). The booth is composed of 27 inch square curved lightweight panels, which can be modified to suit various configurations. Composed of recycled Styrofoam packing peanuts, each panel weighs less than four pounds, so it truly is a "light" system.

The Joslin Foundation and JAX[®] Services

A Sample Diabetes Breeding Project

The Joslin Diabetes Research Foundation (JDRF) Center for Immune Tolerance in Diabetes at Harvard (CITDH), a collaborative group of eight laboratories based at Harvard Medical School is working with JAX[®] Services on an innovative breeding project which supports diabetes research.

We began working with Dr. Christophe Benoist, Director of the CITDH Mouse Lines Core, in 2002, when we initially setup dedicated colonies of JAX[®] Mice along with colonies of Dr. Benoist's own research strains. The CITDH performs basic immunological research to understand the fundamental mechanisms of immune tolerance, and how these mechanisms go awry in mouse models of the disease and in humans with type 1 (autoimmune) diabetes. CITDH studies range from explorations of transcription factors that control the activation of autoimmune T lymphocytes to pre-clinical trials of treatments to reduce pancreatic inflammation, and thus potentially reverse diabetes.

Research at the CITDH makes use of the powerful approaches offered by transgenic and knockout manipulations in the NOD mouse. The CITDH Mouse Lines Core supports CITDH investigators by constructing transgenic and knockout mice on the NOD background, providing the investigators with rapid access to a range of experimental mice. The CITDH also makes its strains available to diabetes researchers worldwide, which is greatly facilitated by our shipping logistics.

Initially, we managed about 15 colonies for CITDH, but the projects grew, and we now manage some 40 colonies, most of which were imported from CITDH colonies at Harvard. Nine of the colonies are JAX[®] Mice or variants thereof, including NOD/ShiLtJ (001976), NOD.129P2(B6)-*B2m*^{tm1Unc}/J (002309), NOD.129S7(B6)-*Ifng*^{tm1Ts}/DvsJ (002575), NOD.129P2(B6)-*Il4*^{tm1Cgn}/DvsJ (004222), NOD.Cg-*Il10*^{tm1Cgn}/DvsJ (004266), NOD.B6-(*D6Mit254-D6Mit339*)/CarJ (004482), NOD.129S2(B6)-*Igh*-*γ*^{tm1Cgn}/DoiJ (004639), NOD.129(B6)-*Tnfrsf4*^{tm1Shr}/DoiJ (005075), and NOD.Cg-Tg(TcraTcrbNY8.3)1Pesa/DvsJ (005868). A few of these strains were donated by the Harvard researchers to our Type 1 Diabetes Resource, with which the CITDH works closely.

The CITDH's project comprises several hundred cages. Each week, 30–50 mice are shipped to CITDH researchers, and, several times a month, mice are shipped from these colonies to collaborating diabetes researchers all over the world, including Australia, Germany, Japan, and France.

Managing these colonies is a full time job for one of our technicians, Jody Morse. In fact, to manage these colonies, Jody routinely enlists the help of other technicians. And, Diana Heckman, the JAX[®] Services Project Specialists dedicated to this



NOD/ShiLtJ (Stock number 001976) Non-obese diabetic inbred strain

project, communicates almost daily with CITDH line managers, Kimie Hattori or Susan Vitolo, and oversees the invoicing and shipments of mice. (Ms. Hattori offers a unique perspective to this program: She or members of her family have been involved with research using NOD mice almost since their inception.)

Not only is this project large, it is unique in that CITDH researchers are very involved in managing it – remotely from their laboratory. The Harvard researchers provided a computer and customized colony management software that CITDH technician in charge of the colonies can access. This close cooperation illustrates the flexibility and customization possible with JAX[®] Breeding Services and how we ensure that CITDH researchers have the mice they need for their critical research.

Dr. Benoist chose JAX[®] to manage CITDH's mouse colonies for several reasons. First, because of our expertise at raising, managing, and shipping laboratory mice. We've been at it for nearly 80 years, we have excellent facilities, and our animal caretakers are experienced with managing mouse strains with special needs. For example, having NOD backgrounds, the

For information on how JAX[®] Services can help with your research, please contact us today at:

jaxservices@jax.org,

1-800-422-6423, or 1-207-288-5845,

or visit us on the web at

www.jax.org/jaxservices.

Additionally, if you are interested in obtaining mouse strains from the CITDH, see **www.citdh.org/mice_available.html**

CITDH mice can be affected by diabetes. Consequently, they require particular monitoring and may need extra water and frequent bedding changes. Second, we maintain our mouse colonies at the highest possible health status. This guarantees that CITDH researchers and the international community receive mice at a health and safety status that is difficult to match in University facilities. The health status of our mice allows them to be shipped all over the world and readily imported into most research facilities.

Our work with CITDH staff has been a rewarding experience. We wish them continued success in their important research and hope that our joint effort will ultimately improve the lives of people with diabetes.

BKS.Cg-m +/+ *Lepr^{db}*/J (000642), One of the Most Widely-used Diabetes Models at JAX

Who would have thought that a black mouse with a chance mutation would one day become one of the most requested mice in diabetes and obesity research? Such is the case with BKS.Cg-m +/+ *Lepr^{db}*/J (000642), a JAX[®] Mice strain harboring the spontaneous diabetes mutation (*db*) in the leptin receptor (*Lepr*) gene. The JAX[®] Mice Database lists over 300 journal articles with this mouse as a main character. It has played a key role in many research areas, including type 2 diabetes, obesity, endocrine defects, fertility, immunodeficiency, metabolism, cardiovascular, thermoregulation, and wound healing. Its popularity as a research tool has resulted in its extensive characterization. Some of its more notable features include the following:

- Diabetes phenotypes: hyperinsulinemia, insulin resistance, hyperglycemia, glucose intolerance, abnormal islet morphology (Hummel et al. 1966. *Science* 153:1127-8; Uchida et al. 2005. *Nat Med* 11:175-82; Yamauchi et al. 2007. *Nat Med* 13: 332-9); peripheral neuropathy (Raizada et al. 1980. *J Biol Chem* 255:9149-55; Robertson and Smith. 1980. *Diabetes* 29:60-7)
- Exogenous insulin fails to control blood glucose levels (Robertson and Smith. 1980. *Diabetes* 29:60-7)
- Renal defects: increased creatinine clearance, decreased albumin secretion (Wendt et al. 2003. *Am J Pathol* 162:1123-37)
- Obese by three to four weeks of age (Hummel et al. 1966. *Science* 153:1127-8; Greer. 2006. *Am J Physiol Heart Circ Physiol* 290 H146-53)
- Abnormal lipid levels: high HDL, LDL, VLDL, and triglyceride levels (Nishina et al. 1994. *Metabolism* 43:549-53)



Since *Lepr^{db}* homozygotes are sterile, we have incorporated the misty coat color mutation (*m*) into our BKS.Cg-m +/+ *Lepr^{db}*/J colonies. Homozygotes, with the coupling double heterozygous genotype (*m Lepr^{db}/++*), are black (upper left); heterozygotes, with the repulsion double heterozygous genotype (*m +/+ Lepr^{db}*), are misty (lower right) and used for breeding.

- Polyphagic (Uchida et al. 2005. *Nat Med* 11:175-82)
- Severe liver steatosis (Kanda et al. 2006. *J Clin Invest* 116:1494-505)
- Low body temperature (Trayhurn. 1979. *Pflugers Arch* 380:227-32; Uchida et al. 2005. *Nat Med* 11:175-82)
- Increased gluconeogenic enzyme activity (Leiter et al. 1979. *In Vitro* 15:507-21)
- Cardiovascular defects (Greer et al. 2006. *Am J Physiol Heart Circ Physiol* 290:H146-53; How et al. *Diabetes* 55:466-73)
- Reproductive defects: sterile, low uterine and ovarian weights, low ovarian hormone production and hypercytolipidemia in follicular granulosa and endometrial epithelial tissue layers (Garris. 2004. *Tissue Cell* 36:19-28)
- Increased metabolic efficiency (Trayhurn. 1979. *Pflugers Arch* 380:227-32)
- Delayed wound healing (Werner et al. 1994. *J Invest Dermatol* 103:469-73; Brem et al. 2007. *Exp Gerontol* 42:523-31)

To find out more, start with the JAX[®] Mice Database (www.jax.org/jaxmice/strain/000642), or the Mouse Phenome Database (www.jax.org/phenome). Maybe you'll decide that this is the mouse you've been looking for, or maybe you'll find another JAX[®] Mice strain that is more appropriate. In either case, you can order JAX[®] Mice by contacting Customer Service at orderquest@jax.org, 1-800-422-6423, or 1-207-288-5845.

Investigator Finds Lost Mouse – 30 Years Later

We all know how it feels to lose something – a favorite book, CD, tool, reference publication, data - and find it again. The thing may pop up in the most unusual and unexpected place and time, sometimes a week, a year, or, as was recently the case with Dr. Yash Kanwar of Northwestern University in Chicago, over 30 years later and half a continent away. Dr. Kanwar's lost item was a mouse, and he recently found it in one of our freezers. And now, here's the rest of the story.

In the early and mid 1970's Dr. Kanwar wrote his Ph.D. thesis and published several scientific journal articles on a mouse strain named PRO/Re. He obtained a pair of the mice, along with a few mice of the parental strains, C57BL/6J and 129/Re, from Dr. Elizabeth "Tibby" Russell of The Jackson Laboratory and produced a colony large enough to meet his research needs. Blake and Russell (1972) had already characterized the PRO/Re mouse as the only known mouse model of hyperprolinemia (high concentrations of proline in the plasma) and prolinuria (high concentrations of proline in the urine). In his thesis and other publications (Kanwar et al. 1975, 1977), Dr. Kanwar further described the morphological, biochemical, and pedigree characteristics of the mouse and established it as a unique model of chemically-induced renal disease, the characteristics of which are very similar to those of human nephrosis.

When Dr. Kanwar completed his studies, he sent the remaining mice to The Jackson Laboratory. Several times since, he has thought that he or someone else should resume research

In humans, hyperprolinemia is of two types. Type 1 hyperprolinemia is a rare inborn autosomal recessive disorder due to a deficiency in proline oxidase. Although the disease is generally believed to be benign, it has been reported to be associated with many abnormalities, including seizures, epilepsy, nerve deafness, mental retardation, and familial nephritis (Jaquet 2005; Kanwar 1975). Type 2 hyperprolinemia is characterized by a deficiency of delta-pyrroline-5-carboxylic acid. It is sometimes associated with convulsive disorders and mental retardation (Kanwar 1975).

with the mouse. As he stated in an interview, "There are very few mice models of hyperprolinemia and proteinuria. The PRO/Re mouse is the only mouse model in which nephrosis can be induced chemically, as is traditionally done in the rat model, to study the pathogenesis of proteinuria. In the past decade, the extensive characterization of the mouse genome and phenome, along with the development of sophisticated technologies to produce genetically-engineered mice, make the PRO/Re mouse a superior model for discovering the genetic bases of hyperprolinemia and proteinuria in humans." However, up until a few months ago, Dr. Kanwar did not know if the PRO/Re mouse was still available. It was then that two of our field representatives, Laura Lockwood and Ray Tritch, met Dr. Kanwar in his laboratory at Northwestern University. Dr. Kanwar brought up the subject of the PRO/Re mouse as a model of human proteinuria and wondered if the mouse was still available from The Jackson Laboratory. The two representatives made a few phone calls to our Bar Harbor facility and learned that the mouse was indeed available – in one of our freezers. It had been cryopreserved as strain PRO/ReJ (000059) in 1981 and could be easily recovered.

After over 30 years, Dr. Kanwar was back in touch with his mouse.

Our records show that since the PRO/ReJ mouse was cryopreserved, it has been recovered for about a dozen customers. Due to time and funding constraints, Dr. Kanwar does not intend to resume his studies with the mouse, but he hopes that someone else will. By cross-breeding the PRO/ReJ strain with genetically-engineered strains that do not show any phenotype, researchers may discover the genetic bases of glomerular diseases such as proteinuria and Alport's syndrome. And, we are excited about this unique story illustrating the value of cryopreserving little-used but potentially very valuable strains of mice for future researchers.

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New MGI Web Interface

The Mouse Genome Informatics website (MGI, www.informatics.jax.org) has been recently redesigned to enhance navigation. Most web pages offer a Quick Search field that searches mouse gene and marker symbols, names, and many types of accession IDs. In addition to supporting searches by MGI IDs, the website also supports searches by nucleotide, protein, SNP, or gene trap sequence IDs, and identifiers from PubMed (PMID:), Ensembl, EntrezGene, OMIM, and other resources.

For more sophisticated searches, use the MGI search forms. These support multiple search parameters and take advantage of the extensive data integration of MGI. A horizontal navigation bar found near the top of MGI web pages now provides drop-down access to most search forms and MGI resources. With these search forms, you can simultaneously search molecular function, genome location, expression, phenotypes, and disease.

Also new to this release are content pages that organize the help documents and resources associated with topical sections of MGI. There are content pages for the following:

- Genes, Genome Features & Maps
- Phenotypes, Alleles & Disease Models
- The Gene Expression Database (GXD)
- Functional Annotation using the Gene Ontology (GO)
- Biochemical Pathways (MouseCyc)
- Strains, SNPs & Polymorphisms
- Mammalian Orthology
- Mouse Tumor Biology (MTB)

These sections are featured prominently on the MGI Home Page and can be accessed easily by tabs on other MGI web pages.

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

Courses and Conferences

We offer several courses that are applicable to diabetes and related research. For titles, dates offered, details on registration, course sizes, lodging, etc., visit our Courses and Conferences website at

www.jax.org/courses/events.

New Type 2 Diabetes and Obesity Therapeutic Discussion Area Online Web Forums Planned

As we mentioned in the Spring issue of JAX[®] NOTES, plans are underway for two interactive therapeutic area discussion forums to encourage researchers to share their experiences using JAX[®] Mice in disease research.

The first forum will cover the topic of JAX[®] Mice strain NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ (005557), an immunodeficient model becoming increasingly popular in cancer, autoimmune, HIV-AIDS and other infectious disease research.

The second forum will focus on type 2 diabetes and obesity and the mouse models used to study these problems. If you wish to join one of these forums you will need to register, select a username and password, and agree to terms of usage.

If your interest is the JAX[®] Mice strain NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ (005557), you can register by accessing www.jax.org/jaxmice/research/immunology/005557. When the type 2 diabetes and obesity forum debuts later this summer, you can register at www.jax.org/jaxmice/research/diabetes/type2.

Future discussion topics will include widely-used JAX[®] Mice strains in cardiovascular, cancer, and other disease research.

New Autoimmune Disease Resources Manual Available

In June, JAX[®] Mice & Services is releasing a new Autoimmune Disease Resources Manual. This resource manual briefly describes the following:

- Autoimmune disease research conducted at The Jackson Laboratory
- Common autoimmune diseases and recent mouse-based research of these diseases
- Over 70 JAX[®] Mice models appropriate for autoimmune disease research
- JAX[®] Services for autoimmune disease research
- Jackson Laboratory courses and conferences relevant to autoimmune disease research
- Online resources useful for autoimmune disease research

You may obtain a complimentary copy of this manual and other JAX[®] Mice & Services literature by filling out the literature request form at www.jax.org/jaxmice/literature.

A Guide to Unpacking and Working with C57BL/6J Diet-induced Obesity (DIO) Mice

JAX[®] Mice and Services provide both “DIO-on-Demand” inventory and custom DIO mice. For “DIO-on-Demand” inventory mice, C57BL/6J males are started on 60 kcal% fat diet (Research Diets, D12492i) at six weeks of age and are maintained on that diet for up to 26 weeks of age. Control mice, fed 10 kcal% fat diets (Research Diets, D12450Bi) from 6 up to 26 weeks of



age, are also available from inventory. “DIO-on-Demand” mice are available from our Bar Harbor facility. For more information on our DIO mice, see our webpage www.jax.org/jaxservices/dio. To sign up for our “DIO-on-Demand” inventory report email go to www.jax.org/jaxmice/news/dio.

The following information contains a few observations on the condition of DIO-on-Demand mice and suggestions for handling and using them:

Appearance

Mice fed 60 kcal% diet may appear “greasy” or “wet” on arrival. This is normal. We have observed that mice fed high fat diets have greasy or wet coats from rubbing against the diet in their cages or shipping boxes and, potentially, from metabolizing the extra fat in their diets. Control mice, fed 10 kcal% diet, have a normal coat appearance.

Effect of Shipping

All mice can experience some stress and concomitant weight loss during shipment. Although DIO-on-Demand mice are shipped with a gel-based water source and appropriate food, they may lose weight in transit. Therefore, we recommend that you acclimate these mice in your vivarium for a week to 10 days before using them. During that time, they should be fed the appropriate diet (60 or 10 kcal% diet) and have access to water *ad libitum*. In our experience, acclimation ensures both that the mice regain any lost weight and that their physiological parameters adjust to their new environment.

Assigning Mice To Study Cohorts

Throughout the diet preconditioning, DIO-on-demand mice are housed in 10-mouse cohorts, which are maintained during shipping. We strongly encourage you to maintain the integrity of these cohorts. In our experience, mixing established groups of male mice can result in fighting or other dominance behaviors that can negatively impact weight gain and general condition. We recommend that the 10-mouse cohorts are maintained, or that each cohort is divided into smaller groups, such as five males per cage, for housing and studies.

Managing the Mice

To keep stresses of DIO mice to a minimum, we recommend the following:

- Position cage racks a couple of inches away from a wall that transmits disturbing vibrations (e.g., from equipment such as air exchangers).
- Place cages away from a door or sink where there may be heavy traffic or loud noises.
- Remind caretakers to work gently, slowly and quietly when handling the mice.
- Change cage bedding only once a week.
- Resist the temptation to check on the mice too frequently.
- Handle the mice with gloves (a fresh pair for each cage) or forceps.
- Try using nestlets or kimwipes for nesting material.

To sign up for our “DIO-on-Demand”
inventory report email go to
www.jax.org/jaxmice/news/dio.

Newly Available JAX[®] Mice Strains

Below is a partial list of newly available JAX[®] Mice strains. For a complete list, see www.jax.org/jaxmice/newstrains

To search for a mouse model from over 4,000 JAX[®] Mice strains, see www.jax.org/jaxmice.
To order, contact Customer Service at orderquest@jax.org, 1-800-422-6423, or 1-207-288-5845.

CByJ.B6-Tg(UBC-GFP)30Scha/J 007076

This transgenic strain expresses enhanced green fluorescent protein (EGFP) under the direction of the human ubiquitin C promoter. EGFP is expressed in all tissues examined. Certain hematopoietic cell types display distinct expression levels, allowing researchers to identify different cell types by FACS analysis. This strain may be used to research hematopoietic cell differentiation and for tracking leukocytes *in vivo*.

B6.129S2(C)-Il8rb^{tm1Mwm}/J 006848

This strain harbors a targeted mutation of the interleukin 8 receptor, beta (*Il8rb*) gene. Homozygotes have several abnormalities, including neurological defects, impaired wound healing, impaired angiogenesis, and altered growth of induced implanted tumors. Homozygotes may also exhibit splenomegaly, lymphadenopathy, and increased susceptibility to various pathogens due to impaired neutrophil recruitment and decreased pathogen clearance during innate immune responses. This strain may be used to research inflammation, immunology, and cancer biology.

B6.Cg-Cebpa^{tm1Dgt}Tg(Mx1-cre)1Cgn/J 006230

Mice homozygous for this floxed allele of the CAAT/enhancer binding protein (C/EBP), alpha gene and hemizygous for the Mx1-cre transgene are viable, fertile, and have a normal hematopoietic system. Mx1-Cre expression can be induced by administering either interferon (alpha or beta) or synthetic double-stranded RNA (such as poly I:C), which deletes the floxed gene. Following 3-4.5 weeks of poly I:C treatment, deletion efficiency is greater than 95% in hematopoietic tissues, and C/EBPalpha protein is undetectable in bone marrow. Poly I:C-treated, *Cebpa*-deleted, Mx1-cre mice have defective myeloid cell development, increased hematopoietic stem cell repopulating activity, and a significantly increased myeloblast population in the bone marrow compartment. This strain may be used to research hematopoietic cell (e.g. myeloid and basophil progenitor cell) development and function, cancer (e.g. acute myeloid leukemia), and alveolar cell differentiation.

B6;129-Gt(ROSA)26Sor^{tm1(rtTA*M2)lac}Col1a1^{tm2(tetO-Pou5f1)lac}/J 006911

Mice heterozygous for both targeted mutations (R26-rtTA and *Col1a1::tetO-Oct4*) are viable and fertile. They express rtTA-M2, an optimized form of reverse tetracycline-controlled transactivator (rtTA) protein, in multiple tissues. In the absence of the tetracycline analog doxycycline (dox), Oct4 (*Pou5f1*) expression from the *Col1a1* locus is not detected. Following dox administration, high Oct4 expression is induced in liver, bone marrow, stomach, intestine, and skin, with lower levels in the heart, lungs, kidney, spleen, and thymus. No expression was detected in the brain and testes. Dox-induced activation of Oct4 results in dysplasia in epithelial tissues. This strain may be used to research tumorigenesis and pluripotent cells.

CB6-Tg(Gad1-EGFP)G42Zjh/J 007677

Hemizygotes for this GAD67-GFP transgene express enhanced green fluorescent protein (EGFP) in the calcium-binding protein parvalbumin (Pv)-expressing subclass of basket interneurons (soma, dendrites, and axons) and also in putative presynaptic boutons. This strain may be useful for fluorescent labeling of the Pv-expressing subset of GABAergic neurons, allowing reliable and efficient characterization of perisomatic innervation *in vivo*.

B6.Cg-Park7^{tm1Shn}/J 006577

Homozygotes for this targeted mutation of the Parkinson disease (autosomal recessive, early onset) 7 (*Park7*) gene are viable and fertile. Homozygotes exhibit hypokinesia and nigrostriatal dopaminergic deficits: evoked dopamine overflow in the striatum is reduced (primarily as a result of increased dopamine uptake); nigral neurons (dopaminergic neurons) have abnormal action potential characteristics; and long term depression is absent in medium spiny neurons. Dopaminergic neurons from *substantia nigra pars compacta* (SNpc) of homozygotes exhibit significantly higher sensitivity to energy metabolism impairment, and nigral dopaminergic neurons are particularly sensitive to Na⁺/K⁺ ATPase impairment. This strain may be used to research Parkinson's disease, dopaminergic physiology, nigrostriatal function, locomotor inactivity, and other neurobiological phenotypes.

B6.129-Gt(ROSA)26^{Sorm3Luo}/J 006075

This strain is designed for MADM (mosaic analysis with double markers) and must be crossed to one harboring a reciprocal mutation at the same locus (see Stock No. 006067 or Stock No. 006080, MADM-R (Dsred2/EGFP)). The resulting offspring have one copy of each reciprocal mutation on homologous chromosomes ("transheterozygous") and must next be bred to a cre-expressing strain for fluorescent protein expression. Using this MADM system, a researcher can generate genetic mosaics in which an individual organism contains somatic cells of different genotypes. This allows the researcher to ascertain lineal relationships and pleiotropic gene function in multicellular organisms. These mice may also be useful in studies of cell differentiation and mitosis.

B6;129S4-Mc4r^{tm1Lowl}/J 006414

The mice of this strain have a *loxP*-flanked transcriptional blocking (*loxTB*) sequence that prevents normal transcription and translation of the endogenous melanocortin 4 receptor (*Mc4r*) gene. They exhibit severe early-onset obesity, accompanied by hyperphagia, increased body length, and hyperinsulinemia. *Mcr4* function can be restored by the enzymatic activity of Cre-recombinase. This strain may be used to research neurobiology, obesity, diabetes, hunger/appetite, and fat and energy metabolism.

B6.Cg-Tg(Sp7-tTA,tetO-EGFP/cre)1Amc/J 006361

Homozygotes for this *Osx1*-GFP::Cre transgene are viable and fertile. The transgene carries both tTA under the regulation of the osterix (*Sp7*) promoter and, just downstream, a tetracycline responsive element (TRE; tetO)-controlled GFP/Cre fusion protein. In the absence of the tetracycline analog doxycycline, EGFP-Cre fusion protein expression is restricted to the osteoblast lineage throughout embryonic and early postnatal development. When this strain is mated to transgenic strains with *loxP*-flanked (floxed) conditional alleles, doxycycline-induced double mutant offspring will have no conditional deletion and no fusion protein expression; removal of doxycycline results in deletion of the floxed allele as well as fusion protein expression. The donating investigator suggests that this strain be maintained on dox treated water to avoid incidental effects of tTA expression. This strain may be used to research bone development, osteoblast lineage, and Hedgehog/Wnt signaling.

STOCK Gt(ROSA)26Sor^{tm4(ACTB-tdTomato,-EGFP)Luo}/J 007576

The mT/mG strain possesses *loxP* sites on either side of a membrane-targeted tdTomato (mT) cassette and express red fluorescence in all tissues and cell types examined. When bred to Cre recombinase expressing mice, the mT cassette is deleted in the *cre* expressing tissue(s), allowing expression

of the membrane-targeted EGFP (mG) cassette located just downstream. This double-fluorescent system allows direct live visualization of both recombined and non-recombined cells at single cell resolution, offering an internal control for phenotypic analysis of Cre-induced mosaic mutants and providing a second marker for lineage tracing applications. In addition, the localization of fluorescent proteins to membrane structures outlines cell morphology and allows resolution of fine cellular processes. This strain may be used as a Cre reporter strain, expressing red fluorescence before, and green fluorescence after, Cre-mediated recombination in widespread cell and tissue types.

FVB/N-Tg(Tagln-rtTA)E1Jwst/J 006875

This strain expresses the reverse tetracycline-controlled transactivator (rtTA) protein under the control of the murine SM22-alpha (SM22α or transgelin) promoter. When hemizygotes are mated to a transgenic strain carrying a gene of interest under the regulatory control of a tetracycline-responsive promoter element (TRE; tetO), they produce offspring in which expression of the target gene is inducible in smooth muscle cells by administering the tetracycline analog, doxycycline. This strain is a "Tet-On" tool that allows the inducible expression of genes in smooth muscle cells.

Brainbow Mice: a Rainbow of Colors in the Brain

Brainbow mice are an exciting new tool for color-identifying subsets of neurons involved in the brain's circuitry. The architects of Brainbow mice (Livet et al. 2007) used them to identify hundreds of neighboring axons and multiple synaptic contacts in a small part of a cerebellar lobe in which approximately 90 colors were distinguishable.

We offer the following four founder lines of Brainbow mice:

B6.Cg-Tg(Thy1-Brainbow1.1)MLich/J 007901

Cells labeled: peripheral and central neurons

B6;CBA-Tg(Thy1-Brainbow1.0)LLich/J 007910

Cells labeled: same as line H, and a few cerebellar Purkinje neurons

B6.Cg-Tg(Thy1-Brainbow1.1)MLich/J 007911

Cells labeled: astrocytes of all areas of the brain and spinal cord, dentate gyrus granule cells

B6.Cg-Tg(Thy1-Brainbow2.1)RLich/J 007921

Cells labeled: same as line H, plus a few cerebellar Purkinje neurons; expression is observed in the nucleus of these cells

More information and award-winning images:
www.jax.org/jaxmice/findmice/brainbow

Reference

Livet J, Weissman TA, Kang H, Draft RW, Lu J, Bennis R. 2007. Transgenic strategies for combinatorial expression of fluorescent proteins in the nervous system. *Nature* 450:56-62.

Dr. Ed Leiter — Nearly 35 Years Devoted to Diabetes Research

Contributions to diabetes research by Jackson Laboratory scientist Dr. Ed Leiter are universally recognized. Below, Dr. Leiter offers us a glimpse of his research career.



Dr. Ed Leiter

Early Influences

Dr. Leiter's interest in diabetes research was set in motion very early in his career: "Diabetes has always been my focus. My grandfather had type 2 diabetes, and one of my uncles on my grandpa's side has been a type 1 diabetic since 1942. So I had a personal 'stake' in this complex set of diseases. I began training for diabetes research when I learned how to culture pancreatic beta cells in Jackson Laboratory scientist Dr. Charity Waymouth's lab; she was a pioneer in the growth of mammalian cells in chemically-defined media. My arrival at the Laboratory coincided with the publication by Laboratory staff of the 'diabetes' mouse (subsequently found to become obese because of a mutation in its leptin receptor and diabetic because of additional genes in the inbred strain background on which the mutation occurred). In my first few years at The Jackson Laboratory, I was fortunate to be able to study diabetes pathogenesis of this intriguing new mouse model with Dr. Douglas Coleman, senior author of a well recognized diabetes mouse paper."

Unanswered Questions

When Dr. Leiter began his career, little was known about the nature of insulin, how it was produced, and the genetic and environmental factors that influenced diabetes susceptibility: "In the early 60's, when I was a graduate student, the chemistry of insulin and the biochemistry of insulin production in pancreatic beta cells were just beginning to be understood." Dr. Leiter explains that investigation into what causes beta cell failure in both type 1 and type 2 diabetes was only in its infancy.

"Researchers were beginning to ask if there were different sets of genes associated with each major diabetes form. In the case of type 2 diabetes, were the 'diabetes' genes really common variants, which, earlier in evolution, when food sources were limiting, conferred a more efficient metabolism? If so, such 'thrifty' genes would be deleterious in our modern 'Coke and bun' environment by promoting obesity-induced diabetes (diabesity). In the case of type 1 diabetes, why was the major genetic risk factor, the major histocompatibility complex (MHC) linked to diabetes, so common in Caucasians? Why would one

identical twin develop the disease and the other not? What was the role of the environment?" These questions are still being debated today.

Critical Breakthroughs

Looking back over his 35 years in the field, Dr. Leiter comments, "There have been many technological 'breakthroughs' since I entered diabetes research, not the least of which was gene cloning (with insulin being the first gene cloned, resulting in recombinant human insulin available for treatment of type 1 diabetic patients). However, the most notable breakthroughs have been in our understanding that most cases of type 1 diabetes represent an immune-mediated disease."

Dr. Leiter also feels that scientists are making significant inroads in understanding the genetics of diabetes: "Because of the genetic heterogeneity and outbred nature of human populations, diabetes was previously referred to as a 'geneticist's nightmare'. Now, with the advent of the human genome sequence and the ability to do high-throughput screening at many thousands of genetic variants marked by single nucleotide polymorphisms, this complex disease is more of a 'headache' than a 'nightmare'. Nevertheless, understanding the complex interaction between genes in multiple combinations and the physical environment in which they express has remained a major challenge."

Persistent Challenges

Despite all the progress made in diabetes research, Dr. Leiter feels that preventing diabetes is of utmost importance: "Given the high prevalence of type 2 diabetes worldwide, and the relatively high prevalence of type 1 diabetes in Caucasians, disease prevention remains a most pressing problem. The most prevalent 'garden variety' forms of type 2 diabetes can be prevented by lifestyle modifications, but this is not the case for type 1 diabetes. The big challenge for type 1 diabetes patients is the development of a 'cure'. Current efforts focus on disease reversal if treatment begins shortly after onset. For both forms of diabetes, prevention of diabetic complications like heart disease, nephropathy, neuropathy, and retinopathy remains a major challenge. Some diabetic individuals are more likely to develop these life-shortening complications than others. We need to understand the genetic basis for the increased risk of development of complications. The Jackson Laboratory is working with the Animal Models of Diabetic Complications Consortium to assist in this discovery effort."

The Mouse and Diabetes Research

Dr. Leiter comments: "The availability of diverse models has shown us the incredible genetic diversity that can underlie a complex disease. The MHC requirement underlying susceptibility to type 1 diabetes is common to both the rat

model and the NOD mouse, but the non-MHC genes required for a diabetogenic interaction are different in both. Yet, these divergent non-MHC genes in both rodent genera work in common immune networks to control T cell tolerance. The differences are fascinating: the NOD mouse is the 'poster mouse' for the hygiene hypothesis, positing that immune tolerance is not learned if individuals are not sufficiently exposed to natural enteric microbial challenges when juveniles. The NOD mouse develops a high incidence of type 1 diabetes if raised in high barrier specific pathogen-free (SPF) environments. By contrast, there is a genetically-predisposed rat model which remains type 1 diabetes-free unless one uses either a virus to trigger disease, or simulates a virus infection by injecting double stranded RNA."

Dr. Leiter readily admits that animal models cannot answer all our diabetes questions: "There are critical differences among the genera (mice, rats, humans) at multiple levels. For example, rodent beta cells are much more sensitive to killing by certain toxic insults than are human beta cells, and further differ in terms of the sets of protein antigens expressed in beta cells. Given such differences, when a diabetes prevention therapy works well in an inbred mouse model (where genetic homogeneity is assured and treatments can be initiated in early, prodromal stages), it is important that the protocol be tested in another animal genus before assuming that it will be efficacious in the human clinical setting. Jackson Laboratory researchers have been at the forefront of attempts to 'humanize' the NOD mouse model of type 1 diabetes. Drs. Lenny Shultz and Dave Serreze have been developing severely immunodeficient NOD stocks to both allow constitution with a human immune system and express key beta cell components not expressed in mouse pancreatic islets."

The Jackson Laboratory Difference

Having spent his career at The Jackson Laboratory, Dr. Leiter is clear about what differentiates the facility from other world-class biomedical institutions: "The Jackson Laboratory's most important resources are the community spirit of the Research Staff and its support team at JAX® Mice & Services. The Type 1 Diabetes Resource (T1DR) is but one manifestation of this, as is the Animal Models of Diabetes Complications Consortium. The Jackson Laboratory maintains a Phenome Database which, along with bioinformatics resources, and an incredible collection of induced mutant stocks of critical importance to diabetes research, collectively makes the mouse the pre-eminent mammalian resource for diabetes research."

Sharing Knowledge — A Top Priority

Throughout his career, Dr. Leiter has never forgotten that people come first and that knowledge must be shared: "My most important contributions have been generating both human and mouse resources for diabetes research. The human resources are the students who have come through my laboratory and

now are making important contributions to diabetes research. One, Dr. David Serreze, is now a staff member advancing understanding of autoimmune diabetes in the NOD mouse model. The NOD/ShiLtJ mouse is one of many useful mouse resources for diabetes research that I have helped to bring to the Laboratory. One of the attributes that I learned from my mentor, Doug Coleman, and passed on to my students, is that an animal model of any disease or a reagent derived from it gains value when it is openly shared and not kept 'private' or unduly saddled with intellectual property issues. The story behind the NOD mouse emphasizes this point. Originally, in the 1980s, the NOD mouse was distributed primarily to Japan. Its promise was realized only after the international research community had access. Today, the Type 1 Diabetes Resource at The Jackson Laboratory serves as an international repository for over 150 genetically manipulated stocks of NOD mice important to advance type 1 diabetes prevention, treatment, and cures."

Although Dr. Leiter is in the process of closing his active research career, he continues to be involved with diabetes resources development and management at the Laboratory under the aegis of the Type 1 Diabetes Resource (T1DR, www.jax.org/t1dr). Through this resource, Dr. Leiter will undoubtedly inspire future diabetes researchers to continue the quest he began long ago — to search for a cure.

Cancer and Aging Research Specialist Dr. Rick Maser Joins The Jackson Laboratory

Rick Maser, Ph.D., a geneticist specializing in cancer and aging, will soon be the latest addition to The Jackson Laboratory's scientific staff. Dr. Maser's appointment as Assistant Professor will begin in late June, as he fulfills a postdoctoral fellowship in the laboratory of Dr. Ron DePinho, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School.



Dr. Rick Maser

Dr. Maser focuses on telomeres, structures that cap the ends of chromosomes and help prevent damage to them during mitosis. However, in a process that may define aging, telomeres themselves erode during mitosis, increasing the likelihood of chromosomal damage with each nuclear division. Cells with damaged chromosomes either die, potentially causing tissue or organ damage, or proliferate uncontrollably and become cancerous. Dr. Maser is investigating the genes involved in telomere erosion and its impact on human cancer, degenerative

disease, chronic inflammation, and aging. As a post-doc, while studying a mouse model of telomere dysfunction, Dr. Maser and his colleagues uncovered scores of cancer-relevant genomic alterations that are also found in a broad range of human tumors.

Jackson Laboratory President and CEO Rick Woychik, Ph.D., notes that Dr. Maser's work "will be a valuable contribution to two major collaborative research programs funded by the National Institutes of Health." Dr. Maser's work will contribute to The Jackson Laboratory's mission as a National Cancer Institute-designated Cancer Center: to study the genetic basis for all kinds of cancers. Also, it will enhance the mission of the Jackson Aging Center (one of five Nathan Shock Centers of Excellence, funded by the National Institute on Aging): to provide leadership in basic aging research.

Dr. Maser earned a Ph.D. in genetics from the University of Wisconsin-Madison in 2001. He has co-authored more than 20 publications (nine as first or co-first author) in peer-reviewed journals, including *Nature*, *Nature Genetics*, *Science*, and *Cell*. He is also the co-holder of three patents involving DNA repair mechanisms. Among his honors is a Damon Runyon Cancer Research Foundation fellowship (2002-2005), awarded to "extraordinary young scientists across the nation who are committed to discovering the causes and cures for cancer."

In choosing The Jackson Laboratory to begin his career as a principal investigator, Dr. Maser said, "This is the place to be to understand both the genetics and physiology of the laboratory mouse. The colleagues I will be working with are among the best in the world for using the mouse as model for human disease."

(This article was adapted from a Jackson Laboratory press release.)

The Jackson Laboratory Adopts New Titles for Research Faculty

The Jackson Laboratory is changing its research faculty titles to better align them with those of comparable research institutions.

Senior Staff Scientists will become Professors, Staff Scientists will become Associate Professors, and Associate Staff Scientists will become Assistant Professors.

These new titles, approved by faculty vote, will clarify the faculty's scientific roles on grant applications, in published papers and in other communications, said Robert Braun, Ph.D., associate director and chair for research.

One More Piece of the Type 1 Diabetes Puzzle Solved

Preventing diabetes is one of today's most pressing medical challenges. Thanks to Jackson Laboratory researchers Drs. David Serreze and Yi-Guang Chen, along with collaborators at Albert Einstein College of Medicine of Yeshiva University in Bronx, N.Y., and Rockefeller University in New York, N.Y., medical science is one step closer to meeting that challenge. In an exciting new development, this research team has shown that it's possible to destroy a type of rogue T cell that attacks the insulin-producing pancreatic beta cells, leading to type 1 diabetes (Mukhopadhyaya et al. 2008).



Dr. Dave Serreze

Dr. Serreze and his Jackson Laboratory research group identified the rogue T cells and named them "AI4" several years ago. As is the case with other killer T cells, AI4 cells are not activated until antigen-presenting cells (APCs) "teach" them what to attack. In patients with type 1 diabetes, the APCs teach the AI4 cells to recognize the pancreatic beta cells by their cell surface antigens and attack them. Dr. Serreze's collaborators at Yeshiva and Rockefeller Universities then made an important discovery: the way an antigen is introduced to the APCs determines whether or not the AI4 cells are activated. Once this was known, the team found a way to introduce beta cell antigens in diabetes-susceptible mice in such a way as to delete the AI4 cells.

Type 1 diabetes is a complex disease, and other cell types may be involved in its pathogenesis. As Dr. Serreze ponders, "Are other kinds also implicated in diabetes, and, if so, how many of them can we kill off? The next step will be to see whether we can use this method to actually prevent diabetes in the mouse model."

(This article was adapted from a Jackson Laboratory press release.)

Reference

(Authors in bold are Jackson Laboratory scientists.)

Mukhopadhyaya A, Hanafusa T, Jarchum I, **Chen YG**, Iwai Y, **Serreze DV**, Steinman RM, Tarbell KV, DiLorenzo TP. 2008. Selective delivery of beta cell antigen to dendritic cells in vivo leads to deletion and tolerance of autoreactive CD8+ T cells in NOD mice. *Proc Natl Acad Sci U S A* 105:6374-9.

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Research Affiliates Program

Teresa Chu, Ph.D. (Scientific Liaison)
Email: teresa.chu@jax.org
Tel: 1-207-288-6775
Web: www.jax.org/jaxmice/affiliates

Websites

The Jackson Laboratory
www.jax.org
International Mouse Strain Resource
www.informatics.jax.org/imsr
Mouse Genome Informatics
www.informatics.jax.org
The Mouse Phenome Database
www.jax.org/phenome

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Courses and Conferences

Sep 2 - Sep 4

Genetic Basis of Work-Related Disease: Science and Public Policy

Sep 15 - Sep 19

Phenotyping Mouse Models of Human Lung Disease

Sep 18 - Sep 21

The Mouse as an Instrument for Ear Research III

Oct 14 - Oct 18

Methods in Human Embryonic Stem Cell Research

Oct 26 - Oct 31

Workshop on Surgical Techniques in the Laboratory Mouse

For more information (content, registration, etc.) about these and other Jackson Laboratory courses, conferences, and workshops, please visit our website, www.jax.org/courses.

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