JAX™ MICE AND RESEARCH SERVICES PROVIDED THROUGH CHARLES RIVER

The Jackson Laboratory and Charles River, Inc. have a cooperative agreement to provide local supplies of JAX™ Mice to biomedical researchers in many European and Asian countries.

Through this agreement, Charles River serves as the exclusive, authorised, commercial distributor and breeder of JAX™ Mice strains in the countries listed below.

- Austria
- Belgium
- China
- Czech Republic
- Denmark
- Finland
- France
- Luxembourg
- Germany
- Netherlands Norway

Hundary

Ireland

Japan

Korea

Italy

Portugal • Spain

Poland

- Sweden
- Switzerland
- Taiwan
- United Kingdom
- JAX™ Mice are The Gold Standard for **Biomedical Research**

Used by researchers around the world, JAX[™] Mice are the most frequently cited strains in biomedical research publications and are supported by world-renowned scientific and technical staff. JAX™ Mice are produced according to the highest standards of animal health and genetic quality. Charles River provides researchers in Europe and Asia with expedited access to over 6,000 JAX™ Mice strains and hundreds of new mouse models each year. JAX™ Mice strains include commonly used inbred strains as well as thousands of specialised disease models and genetically engineered strains.

JAX™ Mice are The Most Published, Best **Characterised Mouse Models**

JAX™ Mice have been referenced in more than 30,000 peer reviewed publications. Over 11,000 PubMed references cite use of the authentic JAX™ Mice B6 strain (C57BL/6J, stock number 000664). The JAX[™] Mice B6 strain, along with many other JAX[™] Mice inbred strains have been fully sequenced as part of the Mouse Genome Project (see: www.sanger.ac.uk/resources/mouse/genomes). The genome sequence data of JAX™ Mice strains will remain relevant over time due to the rigorous genetic quality programs (including the JAX[™] patented Genetic Stability Program) used to breed JAX[™] Mice Strains. Additional genetic and phenotypic information about JAX[™] Mice is publicly available in data resources hosted by The Jackson Laboratory, including Mouse Genome Informatics (www.informatics.jax.org/) and The Mouse Phenome Database (www.jax.org/phenome).

Only JAX[™] Mice Strains bred by Charles River in Europe and Japan are equivalent in genetic quality to those bred by The Jackson Laboratory.



Charles River in Europe and Japan тм breed JAX™ Mice in strict adherence to The Jackson Laboratory's breeding protocols and genetic quality control guidelines. These protocols provide the following benefits:

• Minimise naturally occurring genetic drift by systematically reinfusing breeding colonies with pedigreed mice from The Jackson Laboratory.

· Assure genetic quality through routine use of state-of-the-art genetic quality monitoring methods such as SNP analysis.

Under these conditions, JAX[™] Mice strains bred by Charles River are:

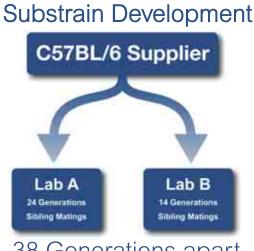
- Equivalent in genetic quality to those bred by The Jackson Laboratory
- Provide the genetic integrity and stable phenotypes needed to support research excellence.

"J" Substrains Differ from Authentic JAX™ Mice Strains due to Genetic Drift

Over the years, organisations around the world have been maintaining colonies of mouse substrains with JAX™ Mice ancestry ("J" substrains). These "J" substrains differ from JAX™ Mice strains due to the genetic mutations which spontaneously occur and accumulate in mouse breeding colonies over time.

Due to naturally occurring genetic drift, a mouse strain will diverge into a genetically distinct substrain if its breeding colony is separated from the parental breeding colony for more than 20 generations of breeding (i.e., 10 generations in the parent colony plus the 10 that simultaneously pass in the sub-colony*). This divergence can occur within only a few years. Genetic differences between a parental strain and a substrain accumulate with time and at a rate dependent upon the level of quality control at the facilities housing and breeding the mice. These genetic differences often result in phenotype differences between a parental strain and a substrain. Such differences confound interpretation of experimental results especially when comparing results to published research based on using JAX[™] Mice strains. IMPORTANT NOTE: JAX™ Mice strains bred by Charles River are authentic JAX™ Mice and are NOT genetically drifted "J" substrains.

* For more information on mouse nomenclature and substrain divergence, see http://www.informatics.jax.org/mgihome/nomen/strains.shtml#substrains.



38 Generations apart

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24

Patented Genetic Stability Program



The JAX[™] patented Genetic Stability Program (GSP) effectively prevents cumulative genetic drift, including that caused by copy number variation, in the most popular strains of JAX[™] Mice.

The GSP program effectively limits cumulative genetic drift by refreshing The Jackson Laboratory's foundation stocks with cryopreserved pedigree embryos or gametes approximately every five generations (Figure 1). The program was initiated in 2003 (Taft et al. 2006) and is covered by 2010 US Patent 7,592,501 and 2012 US patent 8,110,721.

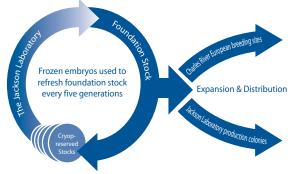


Figure 1: Foundation stocks of several broadly-used JAX™ Mice strains are refreshed with cryo-recovered stocks every five generations.

The Jackson Laboratory's unique, patented GSP has several components: 1) an extensive supply of cryopreserved stock for each strain; 2) isolated foundation colonies, maintained by inbreeding for only five generations before refreshing with cryo-recovered stock; 3) large, independent expansion and production colonies fed directly from pedigreed colonies for distribution through The Jackson Laboratory and through Charles River in Europe and Japan. Importantly, the generations between the cryopreserved stocks and mice produced for distribution are kept to a minimum to prevent the accumulation of mutations that result in genetic drift (see: http://www.jax.org/jaxmice/genetichealth/stability.html).

* The Jackson Laboratory's innovative Genetic Stability Program is covered by 2010 US Patent 7,592,501 and 2012 US patent 8,110,721.

Importance of Indicating Strain Lineage and History using Proper Strain Nomenclature

Proper mouse strain nomenclature, as established by the International Committee on Standardised Genetic Nomenclature for Mice, provides researchers with essential information about the lineage and history of inter-laboratory transfers of substrains over time.

Using proper strain nomenclature requires including in the strain name all Laboratory Codes (i.e., a unique 2-4 letter code assigned to each investigator or institution) as a means to identify all investigators or institutions which have maintained a strain or substrain.

For a complete list of Laboratory Codes, see: http://dels-old.nas.edu/ilar_n/ilarhome/search_lc.php

Research Services Using JAX[™] Mice

Charles River breeding facilities located in Europe and Japan also serve as The Jackson Laboratory's exclusive commercial providers of research services using JAX[™] Mice bred by Charles River. Services offered include:

Biospecimen provision

- Cross-breeding
- Custom breeding
- · Dedicated supply
- DIO (Diet Induced Obesity) studies
- Health monitoring
- Recovery of cryopreserved embryos
- Surgeries

Benefits to Researchers in Europe and Asia

The relationship between The Jackson Laboratory and Charles River provides researchers with the convenience of working with Charles River's numerous international sales offices, in their own time zones and in their native languages when ordering and importing JAX[™] Mice strains. Through this cooperative agreement, the worldwide research community has more convenient access to JAX[™] Mice and benefits from the expertise of both organisations.

Importing JAX[™] Mice strains

Please contact us to request a JAX[™] Mice order form. We are also pleased to assist customers with their search for a specific JAX[™] Mice strain. Once you select a JAX[™] Mice strain of interest, we can furnish you with an import price quotation - including details of availability. Charles River will take charge of all importation steps.

Charles River will not be responsible for any damages arising during the importation process whilst the mice are in the care of non-Charles River transport companies, e.g. airlines.

For Technical Support

Technical information is available by telephone :

- in France : +33 (0)4 74 01 69 66
- in Germany : +49 (0)9761/406 49
- in U.K. : 0845 6013160
- in Italy : +39 039 509915
- or on the web at: http://www.criver.com and askcharlesriver@crl.com

Educational Information on Mouse Genetics and Strain Nomenclature

Handbook on Genetically Standardized Mice See: http://jaxmice.jax.org/literature/handbook.html

JAX Mice Genetic Quality Control Programme. See: http://www.jax.org/jaxmice/genetichealth/GQCprogram

JAX Mice Genetic Stability Program. See: http://www.jax.org/jaxmice/genetichealth/stability

Interactive Tutorial on Mouse Strain Nomenclature. See: http://www.jax.org/jaxmice/nomenclature

Published Reference: Taft RA, Davisson M, Wiles MV. 2006 Know Thy Mouse. Trends Genet 22:649-53.