**C57BL/6-Ins2 Akita/J**

**Stock No:** 003548 | Akita

- Spontaneous Mutation

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**Also Known As: Akita**

The Akita strain is a monogenic model for phenotypes associated with type 1 diabetes. A spontaneous mutation in the insulin 2 gene leads to incorrect folding of the insulin protein producing toxicity in pancreatic β cells, reduced β cell mass and reduced insulin secretion. Heterozygous Ins2<sup>Akita</sup> mice develop insulin dependent diabetes, including hyperglycemia, hypoinsulinemia, polydipsia, and polyuria by 3-4 weeks. The phenotype is more severe in males than females. Obesity and insulitis do not accompany diabetes. Akita mice may be useful for testing islet transplantation and studying diabetic complications such as nephropathy, sympathetic autonomic neuropathy, and macrovascular disease.

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**GENETIC OVERVIEW**

<table>
<thead>
<tr>
<th>Genetic Background</th>
<th>Generation</th>
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<tbody>
<tr>
<td>N25pN8</td>
<td>(2017-10-25 00:00:00)</td>
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</table>
Mice heterozygous for the Akita spontaneous mutation (Ins2\textsuperscript{Akita}) are viable and fertile. Symptoms in heterozygous mutant mice include hyperglycemia, hypoinsulinemia, polydipsia, and polyuria, beginning around 3-4 weeks of age. The diabetic phenotype is more severe and progressive in the male than in the female. Obesity or insulinitis does not accompany diabetes.

Expression of glutathione S-transferase mRNA is increased in epithelial cells in proximal tubules of hyperglycemic mutants (Fujita et al., 2001). As well, plasma concentrations of valine, leucine, isoleucine, as well as the total branched chain amino acids, alanine, citrulline and proline, were significantly higher in the Akita mice (Mochida et al., 2011). Sphingosine-1-phosphate is elevated and diabetic animals demonstrated reductions in plasma levels of omega-9 24:1 ( nervonic acid)-containing ceramide, sphingomyelin, and cerebrosides. Reduction of 24:1-esterfied sphingolipids was also observed in liver and heart (Fox et al., 2011).

Aged mice exhibit gait disturbance and decreased sensory nerve conduction velocity, but do not exhibit learning or memory deficits (Choeiri C et al., 2005). They do, however, exhibit hyperphagia and anxiety behavior (Asakawa et al., 2007).

Progressive retinal abnormalities begin as early as 12 weeks after the onset of hyperglycemia. Retinal complications include increased vascular permeability, alterations in the morphology of astrocytes and microglia, increased apoptosis and thinning of the inner layers of the retina (Barber AJ, et al., 2005).

The mean lifespan of diabetic male mice on the C57BL/6Jc background (305 days) was significantly shorter than that of nondiabetic males in another colony of the same strain (690 days). Mortality rates of diabetic and nondiabetic female mice of this
strain did not differ significantly. Islets from Ins2\textsuperscript{Akita} mice are depleted of beta cells and those remaining release very little mature insulin. This, and the finding that mutant mice respond to exogenously administered insulin, indicate that Ins2\textsuperscript{Akita} mice will serve as an excellent substitute for mice made insulin dependent diabetic by treatment with alloxan or streptozotocin. Heterozygous Ins2\textsuperscript{Akita} mice are also ideally suited to allogeneic or xenogeneic islet transplantation protocols because the investigator does not need to treat the mice with a diabetogen to induce the hyperglycemic state. Untreated homozygotes rarely survive beyond 12 weeks of age.

Metabolic phenotype data may be found on the Diabetic Complications Consortium (DiAComp) website.

Genotyping Protocols
Restriction Enzyme Digest: Ins2\textsuperscript{Akita}
Pyrosequencing: Ins2\textsuperscript{Akita}
End Point Analysis: Ins2\textsuperscript{Akita}
Genotyping resources and troubleshooting

Dietary Information
LabDiet\textsuperscript{®} 5K52 formulation (6% fat)

Breeding Considerations
Mice are currently maintained by breeding a C57BL/6J inbred female with a heterozygous male. After onset of diabetes, when cages become very wet (due to diabetes-associated polyuria), the health of heterozygotes is best maintained by housing them individually in cages containing a mixture of regular litter and Alpha-Dri, changed twice weekly.

Additional Breeding and Husbandry Support
Mating System
C57BL/6J (000664) x Heterozygote
Breeding Summary: C57BL/6J (000664) female x Heterozygous male

Appearance
black
Related Genotype: a/a

Citation
When using this stock, please cite the originating article(s) and include JAX stock #003548 in your
Materials and Methods section.
Facility Barrier Level Descriptions
AX12 (Maximum)

Pricing & Availability
0–2 week average lead time for 10 or more mice with age range

<table>
<thead>
<tr>
<th>AGE</th>
<th>SEX</th>
<th>GENOTYPE</th>
<th>PRICE</th>
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</thead>
</table>
| 4 weeks | Female | Heterozygous for Ins2
| 4 weeks | Male | Heterozygous for Ins2
| 5 weeks | Female | Heterozygous for Ins2
| 5 weeks | Male | Heterozygous for Ins2
| 6 weeks | Female | Heterozygous for Ins2
| 6 weeks | Male | Heterozygous for Ins2
| 7 weeks | Female | Heterozygous for Ins2
| 7 weeks | Male | Heterozygous for Ins2
| 8 weeks | Female | Heterozygous for Ins2
| 8 weeks | Male | Heterozygous for Ins2
<table>
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<tr>
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<tbody>
<tr>
<td></td>
<td>Female</td>
<td>C57BL/6J (000664)</td>
<td>$244.05</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Heterozygous for Ins2&lt;sub&gt;α&lt;/sub&gt;</td>
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