Also Known As: KKAy, KK-Ay
Mice homozygous for the yellow spontaneous mutation (A^y) die before implantation or shortly thereafter. Heterozygotes usually become obese and infertile within a few months after birth. Heterozygotes are more susceptible to several kinds of tumors than are normal mice. Further, spleen cells from heterozygotes cause a significantly lower graft vs. host reaction. Mice of the KK strain develop diabetes of polygenic origin, and KK.Cg-A^y/J heterozygotes develop hyperglycemia, hyperinsulinemia, glucose intolerance and obesity by eight weeks of age. Pancreatic islets are hypertrophied and the β-cells are degranulated. Both the fat and lean tissue mass are increased compared to non-obese mice, with fat accounting for 30-35% of total body weight.

**GENETIC OVERVIEW**

<table>
<thead>
<tr>
<th>Genetic Background</th>
<th>Generation</th>
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<tbody>
<tr>
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<table>
<thead>
<tr>
<th>Allele Type</th>
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<tbody>
<tr>
<td>Spontaneous</td>
<td>a</td>
<td>nonagouti</td>
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RESEARCH APPLICATIONS

Diabetes and Obesity Research
Dermatology Research
Endocrine Deficiency Research
Research Tools
Immunology, Inflammation and Autoimmunity Research
Internal/Organ Research
Reproductive Biology Research

Important Note

It has been reported that the KK strain is hemolytic complement deficient (Hc^0), however, our strains have not been tested to confirm this allele. (Cinader B, et al., 2004, J Exp Med, 120:897)

Detailed Description

A^y and other mutations at the a locus conferring a completely yellow coat color are dominant to all a alleles that produce a darker coat. Hair pigment of A^y heterozygotes is yellow, but eyes are black. Heterozygotes usually become obese and infertile within a few months after birth. Increased adipose tissue mass is due to fat cell hypertrophy, and it has been hypothesized that the obesity results from the observed reduction in hypothalamic norepinephrine and dopamine. Heterozygotes are more susceptible to several kinds of tumors than are normal mice, possibly due, at least in part, to a general increase in cell proliferation that also manifests as a slight increase in lean body mass and skeletal length. Further spleen cells from heterozygotes cause a significantly lower graft vs. host reaction. Mice homozygous for the yellow spontaneous mutation (A^y) die before implantation, or shortly thereafter. The time of death and type of abnormality is, in part, determined by the genetic background on which the mutation is placed. Mice of the KK strain develop diabetes of polygenic origin, and mice of other strains heterozygous for A^y become obese and mildly diabetic. KK.Cg-A^y/J heterozygotes develop hyperglycemia, hyperinsulinemia, glucose intolerance and obesity by eight weeks of age. Studies using isolated adipocytes indicate that tissue responsiveness to insulin is decreased. Histo- and immunocytochemical studies show that the pancreatic islets are hypertrophied and the β-cells are degranulated. These findings suggest that the principal cause of diabetes in these mice is insulin resistance. Body composition analysis shows that both the fat and lean tissue mass are increased.
compared to non-obese mice, with fat accounting for 30-35% of total body weight. The pleiotropic mutant phenotype of \( A^{y} / a \) mice is attributed to ectopic expression of the agouti protein, while the early embryonic lethality of the \( A^{y} \) mutation in the homozygous state is assumed to result from lack of expression of the \( Raly \) gene product (Bultman et al. 1992, Miller et al. 1993, Duhl et al. 1994, Michaud et al. 1993, 1994). That ectopic expression of the agouti protein is probably responsible for the non-lethal aspects of this mutation has been demonstrated by transgenic expression of the protein from a ubiquitous promoter (Klebig et al. 1995, Perry et al. 1995).

For further information, see Mouse Genome Informatics entries for \( a \) and for \( Raly \) and Michael F.W. Festing’s description of KK.
Genotyping Protocols
Separated PCR: A A A
Separated PCR: A A A Alternate2
Genotyping resources and troubleshooting

Coat color is used to determine genotypes of our KK.Cg-A^V/J colony. Black (a/a homozygous) females are bred to yellow (A^V/a) males. All offspring with the A^V/a mutation and phenotype are yellow, the wild-type mice are black.

Dietary Information
LabDiet® 5K52 formulation (6% fat)

Breeding Considerations

This strain is a challenging breeder.

All yellow (A^V/a) male breeders are confirmed to be diabetic at 13 weeks of age (non-fasting blood glucose exceeding 300 mg/dL) and weigh either 32 grams at 13 weeks of age or 33 grams at 14 weeks of age.

Additional Breeding and Husbandry Support
Mating System
+/+ sibling x Heterozygote
Appearance
yellow, affected
Related Genotype: A^V/a
black, unaffected
Related Genotype: a/a

Citation
When using the KK.Cg-A^V/J mouse strain in a publication, please cite the originating article(s) and include JAX stock #002468 in your Materials and Methods section.

Animal Health Reports
Facility Barrier Level Descriptions

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