B6.129-Apoe<sup>tm3(APOE<sup>−</sup>)<sub>Lae</sub></sup> Ldlr<sup>tm1(LDLR<sup>−</sup>)<sub>Lae</sub></sup>/J

Stock No: 012307

Congenic Targeted Mutation

REQUEST CRYORECOVERY

Typically mice are recovered in 10-14 weeks. Contact Customer Service to place an order or for more information.
Overview

In “E4h” mice, the mouse apolipoprotein E is replaced with a human apoE4 isoform. Similarly, the mouse low density lipoprotein receptor is replaced with a transcript-stabilized human LDLR that expresses at three times that of wildtype endogenous levels. E4h mice may be useful in applications related to the study of lipoprotein metabolism-related genes in dyslipidemia, vascular complications and diet-induced atherosclerosis.

Donating Investigator

Dr. Nobuyo Maeda, University of North Carolina at Chapel Hill

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<table>
<thead>
<tr>
<th>Genetic Overview</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic Background</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ldlr&lt;sup&gt;Im1(LDLR)Mae&lt;/sup&gt;</th>
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<tr>
<td><strong>Allele Type</strong></td>
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<td><strong>Gene Symbol</strong></td>
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<td><strong>Gene Name</strong></td>
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<tr>
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RESEARCH APPLICATIONS

Neurobiology Research
Cardiovascular Research
Research Tools
Metabolism Research
Details

Detailed Description

ApoE<sup>−/−</sup> Ldlr<sup>−/−</sup> mice harbor two humanized knock-in mutations; the human APOE*4 replacement allele (ApoE<sup>−/−</sup> (APOE*4)) and the human LDLR replacement allele (Ldlr<sup>−/−</sup> (LDLR)). Unless noted otherwise, the phenotypes below are for mice maintained on regular chow (~5% fat; <0.1% cholesterol).

The human APOE*4 replacement allele (ApoE<sup>−/−</sup> or E4) expresses the human apoE4 isoform in place of the endogenous apoE protein. Under direction of the endogenous mouse apoE promoter/regulatory regions, human apoE4 expression is observed at physiological levels in the same temporal and spatial pattern observed in humans. Mice homozygous for human APOE*4 (ApoE<sup>−/−</sup>) are viable and fertile with normal plasma lipid and lipoprotein profiles. ApoE<sup>−/−</sup> show mild retinal changes with aging. When maintained on high fat/cholesterol diet mirroring that consumed by humans, ApoE<sup>−/−</sup> exhibit increased susceptibility to atherosclerosis, impaired glucose tolerance, fat overload, amyloid beta immunoreactivity, degenerative changes in the retina and other metabolic defects.

The human LDLR replacement allele (Ldlr<sup>−/−</sup>) has the promoter/regulatory regions and exon 1 (encoding only the signal peptide) from endogenous mouse Ldlr directing expression of a human LDLR sequence modified to have increased mRNA transcript stability; this results in expression of human LDLR protein in place of endogenous mouse Ldlr protein, with three-fold greater levels. Both homozygous human LDLR (Ldlr<sup>−/−</sup>) mice and heterozygous human LDLR (Ldlr<sup>+</sup>/−) mice are viable and fertile with a ~40% reduction in steady state plasma cholesterol. The reduction is primarily in the HDL cholesterol fraction, resulting in elevated non-HDL/HD cholesterol ratio. The HDL cholesterol of Ldlr<sup>−/−</sup> mice is ~50 mg/dL and is close to that normally seen in humans. Of note, because of the equivalency in protein expression and reduced HDL between heterozygotes and homozygotes, the Ldlr<sup>−/−</sup> genotype has been more extensively characterized.

Stock No. 012307: Mice homozygous for human APOE*4 and heterozygous for human LDLR (ApoE<sup>−/−</sup> Ldlr<sup>−/−</sup> (APOE*4/LDLR)) are called E4h mice. E4h mice are viable and fertile with low plasma cholesterol (normal non-HDL cholesterol) presumably due to increased Ldlr metabolism in the liver. E4h mice are highly sensitive to diet-induced dyslipidemia. Specifically, when maintained on high fat/cholesterol diet mirroring that consumed by humans, E4h animals develop hypercholesterolemia and atherosclerosis. The donating investigator reports mice homozygous for ApoE<sup>−/−</sup> and homozygous for Ldlr<sup>−/−</sup> are viable and fertile with no breeding problems.

Development

Expression Data

Control Suggestions

Selected References

Genetics
Genotyping Protocols
MELT: Ldlr<sup>tm1(LDLR)Mae</sup> Alternate1
High Resolution Melting: Apoe<sup>tm3(APOE*4)Mae</sup>
Genotyping resources and troubleshooting

Breeding Considerations
Apoε<sup>+</sup> Ldr<sup>h</sup> mice harbor two mutations that segregate independently; the human APOE*4 replacement allele (Apoe<sup>tm3(APOE*4)Mae</sup>) on chromosome 7 and the human LDLR replacement allele (Ldlr<sup>tm1(LDLR)Mae</sup>) on chromosome 9. The donating investigator reports mice homozygous for Apoe<sup>+</sup> and homozygous for Ldlr<sup>h</sup> are viable and fertile with no breeding problems. Of note, because of the equivalency in hLDLR protein expression and reduced HDL between heterozygotes (Ldlr<sup>−/−</sup>) and homozygotes (Ldlr<sup>−/−</sup>), the Ldlr<sup>h</sup> genotype has been more extensively characterized. Therefore, when maintaining our live colony, mice homozygous for Apoe<sup>+</sup> and heterozygous for Ldlr<sup>h</sup> are bred to mice homozygous for Apoe<sup>+</sup> and wildtype at the Ldlr locus. Alternatively, breeding mice homozygous for Apoe<sup>+</sup> and homozygous for Ldlr<sup>h</sup> is possible.

Additional Breeding and Husbandry Support

Citation
When using the B6-129-Apoε<sup>tm3(APOE*4)Mae</sup> Ldlr<sup>tm1(LDLR)Mae</sup> <J mouse strain in a publication, please cite the originating article(s) and include JAX stock #012307 in your Materials and Methods section.
Facility Barrier Level Descriptions
Production of mice from cryopreserved embryos or sperm occurs in a maximum barrier room, G200

Pricing & Availability
Typically mice are recovered in 10-14 weeks. Contact Customer Service to place an order or for more information.

<table>
<thead>
<tr>
<th>Domestic Pricing</th>
<th>International Pricing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cryorecovery</strong></td>
<td><strong>Pricing effective for USA, Canada and Mexico shipping destinations</strong></td>
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<td><strong>SERVICE</strong></td>
<td><strong>GENOTYPE</strong></td>
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<tr>
<td>Cryo Recovery</td>
<td>Heterozygous for Apoe&lt;tm3(APOE*4)Mae&gt;, Heterozygous or wildtype for Ldlr&lt;tm1(LDLR)Mae&gt;</td>
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</table>

We will fulfill your order by providing at least two carriers for each strain ordered. The total number, sex, and genotypes provided will vary, although typically 8 or more animals are provided. **Please check genotypes which will be recovered.** While the genotypes of all animals produced will be communicated to you prior to scheduling shipment, the genotypes of animals provided may not reflect the mating scheme and genotypes described in the strain description. **Animals are typically ready to ship in 11-14 weeks.** If a second recovery is required to produce the minimum number of animals, then delivery time would increase to approximately 25 weeks. If we fail to produce animals of the correct genotype, you will not be charged. We cannot guarantee the reproductive success of mice shipped to your facility. If the mice are lost after the first three days (post-arrival) or do not produce progeny at your facility, a new order and fee will be necessary.

Cryorecovery to establish a **Dedicated Supply** for greater quantities of mice. Mice recovered can be used to establish a dedicated colony to contractually supply you mice according to your requirements. Price by quotation.

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<tr>
<th>Related Products and Services</th>
<th>Price</th>
</tr>
</thead>
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<tr>
<td>Frozen Mouse Embryo</td>
<td>$2,595.00 per straw or vial</td>
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**Payment Terms and Conditions**
Terms are granted by individual review and stated on the customer invoice(s) and account statement. These transactions are payable in U.S. currency within the granted terms. Payment for services, products, shipping containers, and shipping costs that are rendered are expected within the payment terms indicated on the invoice or stated by contract. Invoices and account balances in arrears of stated terms may result in The Jackson Laboratory pursuing collection activities including but not limited to outside agencies and court filings.

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