An Ear Pinnae Mutation in the Mouse on Chromosome Two

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Mutation Symbol: *lear*

Mutation Name: little ears

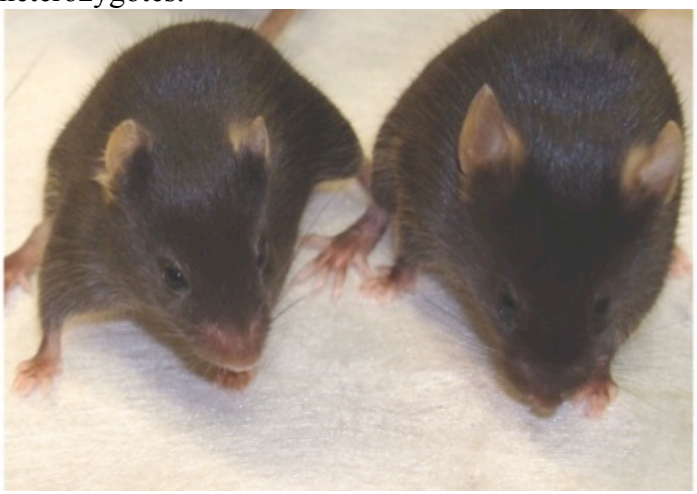
Current Strain Name: B6(CAST)-*Prkra*^{lear}/GrsrJ

Stock #008568 (jaxmice.jax.org)

Phenotype Category: Craniofacial, ear pinna, size

Origin and Description

Little ears (*lear*) was discovered in December 2007 in a C57BL/6J-derived sequence of a B6.CAST congenic research colony. This recessive spontaneous mutation causes mice to have smaller ear pinnae and smaller overall body size. The colony is maintained by mating heterozygotes to homozygotes and the reciprocal, but due to occasional poor breeding of homozygotes, the colony is sometimes maintained by intercrossing heterozygotes.



B6(CAST)-*Prkra*^{lear}/GrsrJ female littermates at nine weeks old. The homozygote is on the left and carrier is on the right

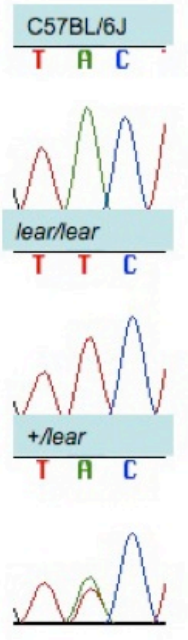
A second little ears mutation *lear-2J* was discovered at about the same time as *lear*. This second allele arose on a predominantly C57BL/6J background that carried two targeted mutations. The two *lear* strains were intercrossed to confirm that they are allelic. The *lear-2J* strain is now extinct.

Genetic Analysis

The little ears mutation was determined to be recessive by mating a mutant male to an unrelated C57BL/6J female; there were no mutants in the 16 F1 mice born. These unaffected F1 offspring were mated to produce an F2 generation in which 3 of 7 siblings were mutants.

To determine a genetic map position, a male homozygote (*lear*/*lear*) mouse was bred to a C3H/HeSnJ female mouse (Stock # 000661). Obligate heterozygotes produced from this mating were bred and sixty-seven F2 mutants produced were sent to the Fine

Mapping Laboratory at The Jackson Laboratory. The *lear* mutation maps to Chromosome 2 with flanks at markers *D2Mit418* at 74.9 Mb and *D2Mit474* at 79.9 Mb (Ensembl.org). A candidate gene *Prkra* maps at 76.4 Mb. Mice homozygous for the *Prkra*^{tm1Gsc} targeted mutation also exhibit reduced size of both the ear pinnae and body. Using the Primer3 design program, primers were designed to amplify all eight exons of the *Prkra* gene and were sequenced at The Jackson Laboratory core sequencing facility. Three *lear* homozygotes had a T to A transversion at Chromosome 2: 76,477,254 (Build 37) in intron 5, immediately adjacent to the conserved splice donor site. Three *lear* heterozygotes typed heterozygous for this substitution and a C57BL/6J wild type control matched the published NCBI sequence.



A single base change from A to T was detected in what may be a splice site. It is located three bases into the intron after exon 5 in the *Prkra* gene.

RT-PCR was done on *+/lear* and *lear/lear* mice using tail and spleen; the results were inconclusive.

Pathology

A standard pathology screen of a 13-week-old female mutant and heterozygote littermate revealed no lesions. Hearing was assessed by auditory brainstem response testing (ABR) on mice approximately two and a half months old. All three controls had normal hearing but the three mutants varied with one having normal hearing, the second having moderate hearing loss, and the third having severe hearing loss. A clinical eye exam on five mutants and four heterozygotes revealed that all had normal vision.

Discussion

lear is the first reported spontaneous mutation in the *Pkra* gene as of this writing.

Acknowledgements

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