MRL/MpJ-Fas<sup>lpr</sup>/J

Stock No: 000485 | MRL-lpr

Spontaneous Mutation

READILY AVAILABLE

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Overview
Also Known As: lymphoproliferation, MRL-lpr

This strain is commonly known as MRL-lpr or lpr mutant. Mice are homozygous for the lymphoproliferation spontaneous mutation (Faslpr), and show systemic autoimmunity, massive lymphadenopathy associated with proliferation of aberrant T cells, arthritis, and immune complex glomerulonephrosis. Mice are useful as a model to determine the etiology of systemic lupus erythematosus (SLE) and Sjögren (Sicca) syndrome and to evaluate therapies. Information about lupus disease phenotypes in MRL-lpr is available here.

Our preclinical efficacy testing services offer scientific expertise and an array of target-based and phenotype-based outcome measures, both in vivo and at endpoint, for flexible study designs and assay development in mouse models of Lupus. See our full service platform.

<table>
<thead>
<tr>
<th>GENETIC OVERVIEW</th>
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<tbody>
<tr>
<td><strong>Genetic Background</strong></td>
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<table>
<thead>
<tr>
<th>Faslpr</th>
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<tr>
<td><strong>Allele Type</strong></td>
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<td>Spontaneous (Hypomorph)</td>
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RESEARCH APPLICATIONS
Immunology, Inflammation and Autoimmunity Research
Internal/Organ Research
Apoptosis Research
Cancer Research
Important Note

July 2007: This strain has been recovered from cryopreservation and the original phenotype was observed: The sixteen-week old mice have lymph nodes that were 4.5 (females) to 10.1 times (male) larger than age and sex matched individuals from the former colony. Spleenomegaly is 3 to 6 times greater and their life spans were also greatly reduced. The former version of this line, which displayed a loss of lymphoproliferative phenotype, has been renamed MRL/MpJ-Fas\textsuperscript{ipr}/2J and is available as Stock No. 006825.

Detailed Description

Mice homozygous for the lymphoproliferative spontaneous mutation (Fas\textsuperscript{ipr}) show systemic autoimmunity, massive lymphadenopathy associated with proliferation of aberrant T cells, arthritis, and immune complex glomerulonephrosis. Starting at about three months of age, levels of circulating immune complexes rise greatly in the MRL-lpr/lpr mouse but not the MRL normal (Hewicker 1990). Onset and severity of symptoms associated with the Fas\textsuperscript{ipr} gene is strain-dependent. For example, lymphoproliferation varies greatly with congenic strain C57BL/6J-Fas\textsuperscript{ipr}/Fas\textsuperscript{ipr} at a 24 fold increase over control lymph node weight, MRL/Mp-Fas\textsuperscript{ipr}/Fas\textsuperscript{ipr} at 75 fold and congenic strain C3H/HeJ-Fas\textsuperscript{ipr}/Fas\textsuperscript{ipr} highest at 116 fold increase over control lymph node weight (Morse et al 1985). Variance in renal pathology ranks from extensive in MRL/Mp-Fas\textsuperscript{ipr}/Fas\textsuperscript{ipr} at 4 to 7 months to negligible at 14 to 16 months in mice with C57BL/6J and C3H/HeJ backgrounds and homozygous for the Fas\textsuperscript{ipr} (Kelley and Roths 1985). Spontaneous production of anti-dsDNA autoantibodies is likewise affected with percentage binding of radiolabeled dsDNA in Fas\textsuperscript{ipr}/Fas\textsuperscript{ipr} mice varying from 5 percent on C57BL/6J to 26 percent on C3H/HeJ to as high as 49 percent on MRL/Mp (izui et al 1984). Female MRL/Mp-Fas\textsuperscript{ipr} mice die at an average age of 17 weeks of age and males at 22 weeks. This compares to between 42 and 52 weeks in females on the C57BL/6J or C3H/HeJ background (Roths 1987). Embryonic stem cell lines have been established with MRL/Mp-Fas\textsuperscript{ipr}/Fas\textsuperscript{ipr} mouse strains (Kawase et al 1994). This mouse is a model for systemic lupus erythematosus-like autoimmune syndromes.

MRL/MpJ and one of its ancestral strains LG/J display heightened wound healing relative to a panel of other inbred strains. At 4 weeks post-injury, 2mm ear punch wounds healed to 0.0-0.4mm in MRL/MpJ mice but were still 1.2-1.6mm in C57BL/6 mice. At 15 days post-injury C57BL/6 showed a maximal closure of 30% reduction in ear hole size while MRL showed 85% reduction. The process of healing in MRL/MpJ mice was faster, more complete, showed increased swelling, angiogenesis, fibroblast migration, extracellular matrix deposition, and decreased scarring and fibrosis. Additionally, hair follicles and accompanying sebaceous glands were regenerated to a much greater degree. The other ancestral strains of MRL/MpJ (C3H, C57BL/6, and AKR) do not display this enhanced healing. Bone marrow transplantation showed that the MRL/MpJ healing phenotype did not readily transfer with bone marrow and did remain in the irradiated host tissues. Enhanced healing of cardiac wounds has also been reported in MRL/MpJ mice. In this model a very high mitotic index (10-20%) was found, similar to that seen in non-mammalian tissue regeneration. Using F2 and backcross mapping of MRL/MpJ-Fas\textsuperscript{ipr} x B6 progeny McBrearty et al. identified wound healing QTLs: the heal2 and heal3 loci were identified on MRL/MpJ Chromosome 13 in the region of D13Mit115 and D13Mit129 respectively; the heal5 locus was identified on MRL/MpJ chromosome 12 in the region of D12Mit233; the heal1 locus was identified on chromosome 8 of C57BL/6 in the region of DBMit211; and a highly suggestive locus was found on MRL/MpJ Chromosome 7 in the region of D7Mit220. (Clark et al., 1998; Leferovich et al., 2001; Kench et al., 1999; McBrearty et al., 1998.)

Microarray analysis and SELDI ProteinChip analysis have identified multiple genes and proteins that have varied expression in the ear...
Genotyping Protocols

Melt Curve Analysis: Fas<sup>lpr</sup> MCA

Standard PCR: Fas<sup>lpr</sup>

Genotyping resources and troubleshooting
Dietary Information
LabDiet® 5K52 formulation (6% fat)

Breeding Considerations

This strain is a challenging breeder.
Due to the heightened healing which occurs in mice with the MRL genetic background, ear punch is not a good method for individual mouse identification in this strain. Mice may have only 2 litters before developing phenotype.

Additional Breeding and Husbandry Support

Mating System
Homozygote x Homozygote

Appearance
albino
Related Genotype: a/a Tyr<sup>c</sup>/Tyr<sup>c</sup>

Citation
When using the MRL for a mouse strain in a publication, please cite the originating article(s) and include JAX stock #000485 in your Materials and Methods section.

Animal Health Reports
Facility Barrier Level Descriptions

Pricing & Availability

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<th>AGE</th>
<th>SEX</th>
<th>GENOTYPE</th>
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<td>10 weeks</td>
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