Overview

This strain is commonly known as MRL-lpr or lpr mutant. Mice are homozygous for the lymphoproliferation spontaneous mutation (Fas\textsuperscript{lpr}), 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.

GENETIC OVERVIEW

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<th>Genetic Background</th>
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<th>Allele Type</th>
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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. Splenomegaly 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<sup>lpr</sup>/2J and is available as Stock No. 006825.

Detailed Description

Mice homozygous for the lymphoproliferation spontaneous mutation (Fas<sup>lpr</sup>) 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<sup>lpr</sup> gene is strain-dependent. For example, lymphoproliferation varies greatly with congenic strain C57BL/6J-Fas<sup>lpr</sup>/Fas<sup>lpr</sup> at a 24 fold increase over control lymph node weight, MRL/MpJ-Fas<sup>lpr</sup>/Fas<sup>lpr</sup> at 75 fold and congenic strain C3H/HeJ-Fas<sup>lpr</sup>/Fas<sup>lpr</sup> highest at 116 fold increase over control lymph node weight (Morse et al 1985). Variance in renal pathology ranks from extensive in
MRL/Mp-\textsuperscript{Fas}\textsuperscript{lt} \textstatus{lt}/\textstatus{lt}Fas\textsuperscript{lt}

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{lt} (Kelley and Roths 1985). Spontaneous production of anti-dsDNA autoantibodies is likewise affected with percentage binding of radiolabeled dsDNA in Fas\textsuperscript{lt}/Fas\textsuperscript{lt} 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{lt} 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{lt}/Fas\textsuperscript{lt} 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 0-0.4mm in MRL/MpJ mice but were still 1.2-1.6mm in C57BL/6J 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{lt} \times \textit{B6}

progeny McBrearty et al. identified wound healing QTLs: the heal\textsubscript{2} and heal\textsubscript{3} loci were identified on MRL/MpJ Chromosome 13 in the region of D13Mit15 and D13Mit129 respectively; the heal\textsubscript{5} locus was identified on MRL/MpJ chromosome 12 in the region of D12Mit233; the heal\textsubscript{1} locus was identified on chromosome 8 of C57BL/6 in the region of D8Mit211; 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 punch wounds of MRL/MpJ-Fas\textsuperscript{lt} versus C57BL/6. The changes in expression patterns suggest that in MRL/MpJ mice there is less of an inflammatory response and an earlier transition into tissue repair than is seen in C57BL/6. (Li et al., 2000 and 2001.)

Blankenhorn et al. found that MRL/MpJ females heal faster and more completely than males. Some heal QTL are sexually dimorphic with heal\textsubscript{2}, 3, 7, 8, 10, and 11 having greater effect in males and heal\textsubscript{4}, 5, and 9 having greater effect in females. Castration improves wound healing in MRL/MpJ males to nearly the degree seen in females, but ovariectomy does not improve the degree of healing seen in MRL/MpJ females. (Blankenhorn et al., 2003)

Relative to B10.D2nSnJ mice, MRL/MpJ mice have decreased Neutrophil accumulation in the bronchiolar lavage in response to LPS infusion and tests using bone marrow chimeras revealed that the pulmonary inflammatory response transfers with bone marrow. Transforming growth factor beta 1 autologous induction is reduced in MRL/MpJ splenocytes while macrophages show a reduction in the transforming growth factor beta 1 induction of interleukin 1 beta and tumor necrosis factor alpha production but no significant reduction in transforming growth factor beta 1 production. (Kench et al., 1999.) MRL-Fas\textsuperscript{lt} are also highly susceptible to Mycobacterium leprae (Yogi et al., 1989).
Genotyping Protocols
Standard PCR: Fas
Standard PCR: Fas MCA
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-lpr 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

- MP14 (Maximum)
- RB03 (Maximum)
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Domestic

Pricing effective for USA, Canada and Mexico shipping destinations

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