

MRL.CBAJms-Fas^{lpr-cg}/J

Stock No: 002983 | lpr^{cg}

◆ Congenic, Spontaneous Mutation

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GENETIC OVERVIEW

Genetic Background

Generation

000486 MRL/MpJ

Fas^{lpr-cg}

Alele Type

Gene Symbol

Gene Name

Spontaneous

Fas

Fas (TNF receptor superfamily member 6)

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Details

Detailed Description

Mice homozygous for the lymphoproliferation complementing *gld* spontaneous mutation (Fas^{lpr-cg}) are viable and fertile. Homozygous mutant mice are characterized by massive lymphadenopathy. Fas^{lpr-cg} complemented both Fas^{lpr} and the Fas^{gld} mutation in that double heterozygotes with either mutation had lymphadenopathy. However, further crosses showed the new mutation to be an allele at Fas^{lpr} . Like Fas^{lpr} and Fas^{gld} homozygotes, CBA/KJms- Fas^{lpr-cg} homozygotes (Stock No. 001876) produce antibodies to some nuclear antigens, such as dsDNA, ssDNA, and poly(ADP-ribose); however, they do not produce anti-erythrocyte antibodies. Although they exhibit lymphoid cell infiltration around blood vessels in lung, liver, and kidney, they lack the immune-complex glomerulonephritis, vasculitis, and interstitial pneumonia characteristic of Fas^{lpr} homozygotes. Fas^{lpr-cg} homozygotes on the MRL/MpJ genetic background developed glomerulonephritic lesions similar to those of MRL/MpJ- Fas^{lpr} mutants, but at a lower frequency, suggesting MRL/MpJ background genes control this aspect of the disease.

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/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- $Tnfrsf6^{lpr}$ 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 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- $Tnfrsf6^{lpr}$ 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 2, 3, 7, 8, 10,* and *11* having greater effect in males and *heal 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.)

Development

Control Suggestions

Genetics

+ *Fas^{lpr-cg}*

Disease/Phenotype

+ Disease Terms

+ Research Areas By Phenotype

+ Mammalian Phenotype Terms by Genotype

+ References

Technical Support

C O N T A C T T E C H N I C A L S U P P O R T

Genotyping Protocols

[Genotyping resources and troubleshooting](#)

Breeding Considerations

Due to the heightened healing which occurs in mice with the MRL genetic background, ear punch is not expected to be a good method for individual mouse identification in this strain.

[Additional Breeding and Husbandry Support](#)

Appearance

albino

Related Genotype: *a/a Tyr^c/Tyr^c*

Citation

When using the *lpr^{cg}* mouse strain in a publication, please [cite the originating article\(s\)](#) and include JAX stock #002983 in your Materials and Methods section.

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