**Overview**

BXSB mice develop a spontaneous autoimmune syndrome similar to lupus, which is accelerated in males (BXSB males have the mutant Yaa-containing Y chromosome). These mice may be useful in applications related to systemic lupus erythematosus.

**GENETIC OVERVIEW**

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<th>Genetic Background</th>
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**Yaa**
RESEARCH APPLICATIONS
Immunology, Inflammation and Autoimmunity Research

Details

Important Note
Males of this strain carry the BXSB-derived Yaa mutation on the Y chromosome.

Detailed Description
The Y-linked autoimmune accelerator locus (Yaa) on the Y chromosome of BXSB inbred male mice is the result of a duplication of an ~4 Mbp telomeric segment near the pseudoautosomal region of the X chromosome onto the Y chromosome. The duplicated segment contains 19 genes, including toll-like receptor 7 (Tlr7) and phosphoribosyl pyrophosphate synthetase 2 (Prps2). BXSB males have the mutant Yaa-containing Y chromosome, and are a model for a severe form of systemic lupus erythematosus (SLE). Their spontaneously arising autoimmune disease is characterized by the robust development of follicular T cells and germinal centers. Marginal zone B cells are depleted in BXSB-Yaa mice and a dramatic increase in number of peripheral monocytes is seen beginning at two months of age. Disease progression is characterized by lymph node and spleen enlargement, hemolytic anemia, hypergammaglobulinemia, anti-nuclear antibodies, and immune complex glomerulonephritis. This leads to morbidity on average of six months of age. BXSB females develop a greatly attenuated form of autoimmune disease; indicating that autoimmune disease acceleration is due to the presence of the Yaa mutation carried on the Y chromosome.

A duplicated copy of the Tlr7 gene is primarily responsible for the autoimmune phenotype attributed to the Yaa mutation. The BXSB-Yaa mouse therefore provides a model for investigating the effects copy number variation of Tlr7 on autoimmune disease. Therapeutic treatment of BXSB-Yaa mice with an anti-Type I interferon receptor antibody attenuates their autoimmune disease; indicating that Type I interferon signaling involved is in the pathogenesis of this disease.

The most suitable control animals are sex-matched, autoimmune disease-resistant BXSBB6-Yaa<sup>+</sup> consomic males carrying the C57BL/6-derived Y chromosome in place of the BXSB-derived mutant Yaa-containing Y chromosome. BXSB.B6-Yaa<sup>+</sup> consomic mice (backcrossed to BXSB/MpJ inbred females for at least 40 generations) are described and available at The Jackson Laboratory as Stock No. 021330.

A note on outcrossing BXSB males with other inbred females: similar autoimmune disease acceleration occurs in males (but not in females) from an outcross of BXSB males to NZB females. Acceleration does not occur in offspring of the reciprocal cross. The same effect of Yaa is seen in offspring of outcrosses to strains SJL, C57BL/6, and AKR.

In addition, BXSB males lacking the interleukin 21 receptor (BXSB-Yaa/Ii21<sup>−/−</sup> or BXSB-Yaa/Ii21<sup>+/−</sup>) are highly resistant to disease and are therefore a model for investigating the role of interleukin 21 in disease pathogenesis. Populations of regulatory CD8<sup>+</sup> and potentially natural killer cells are also actively retarding disease in this model; making them useful to investigate the roles of such regulatory cells in autoimmune disease.
Genotyping Protocols
Genotyping resources and troubleshooting

Dietary Information
LabDiet® 5K52 formulation (6% fat)

Breeding Considerations
This is an inbred strain. Males carry the BXSB-derived Yaa mutation on the Y chromosome. To maintain the live inbred colony, unaffected females (+/+) may be bred with affected males (Yaa/Y).
Additional Breeding and Husbandry Support

Mating System
+/+ sibling x Hemizygote

Appearance
white-bellied agouti, affected
Related Genotype: A^w/A^w X/Yaa (male)

white-bellied agouti, unaffected
Related Genotype: A^w/A^w X/X (female)
Leading the search for

TOMORROW'S CURES

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