B2m and Abb Targeted Mutation Mice
Abb/B2m Double Targeted Mutation Mice
In vivo Systems for Drug Discovery and Research

Absence of MHC Class I Molecules and Reduction of Single Positive CD 8+ Cells in B2m Mice

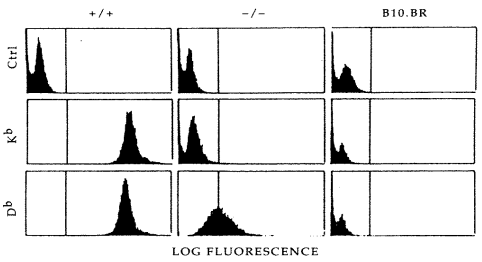

Figure 1. The absence of H-2K^b class I expression in B2m mice homozygous for the deficiency was demonstrated by FACS analysis after incubating purified CD4$^+$8$^-$ T cells with a panel of MHC class I specific antibodies. *(Courtesy of R. Jaenisch et al.)* [1]

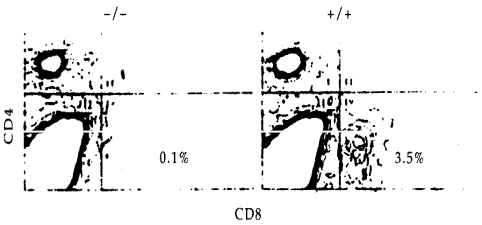

Figure 2. Two-color analysis of B2m mouse splenocytes indicated a severe reduction of mature CD4$^+$8$^-$ T cells in comparison to wild type, demonstrating that differentiation of CD4$^+$8$^-$ double positive cells into CD8+ single positive cells requires interaction with class I molecules. *(Courtesy of R. Jaenisch et al.)*

DEFICIENT IN MAJOR HISTOCOMPATIBILITY COMPLEX (MHC) CLASS I AND/OR CLASS II PROTEINS, Taconic B2m and Abb Targeted Mutation Mice are powerful laboratory models for research in transplantation, gene therapy and immunological diseases.

Applications of B2m and Abb and Abb/B2mDouble Targeted Mutation Mice include studies involving:

- The role of MHC antigens in transplant rejection and disease resistance.
- NK cell function in the absence of cytotoxic T cell function.
- The potential of transfecting vectors into MHC deficient donor cells for the production of specific proteins for gene therapy.
- The genetics of immunodeficient and MHC associated diseases.
- The role of CD4$^+$ and CD8$^+$ T cells in cell mediated immune responses.
- The role of compensatory mechanisms in severely immunocompromised animals.

Features of B2m, Abb and Abb/B2m Mice

B2m and Abb mice are available on two different backgrounds. One background is congenic B6.129 background (N12). The other is a congenic B6.SJL, which carries the *Ptprc*^{a} marker on hematopoietic cells allowing for their identification in immunological adoptive transfer experiments. The Abb/B2m Double Targeted Mutation is on a congenic B6.129 background.

B2m, Abb and Abb/B2m Targeted Mutation Mice Background Strains

Taconic Model #	Nomenclature	Background Strain	Genotype	Haplotype
#004020-M	B6.SJL-*Ptprc*^{a}/BoAiTac-*β2m*^{tm1Jae} N10	*B6.SJL	Homozygote	b
#004026-M	B6.SJL-*Ptprc*^{a}/BoAiTac-*H2-Ab1*^{m1Glm} N13	*B6.SJL	Homozygote/Homozygote	b
#004080-M	B6.129-*H2-Ab1*^{tm1Jae}-*B2m*^{tm1Glm} N17	B6.129	Homozygote	b
#ABBN12-M	B6.129-*H2-Ab1*^{tm1Glm} N12	B6.129	Homozygote	b
#B2MN12-M	B6.129-B2m^{tm1Jae} N12	B6.129	Homozygote	b

*B6.SJL carries the marker for *Ptprc*^{a}

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B2m Targeted Mutation Mice Display a Reduction of single positive $CD4^+8^-$ cells

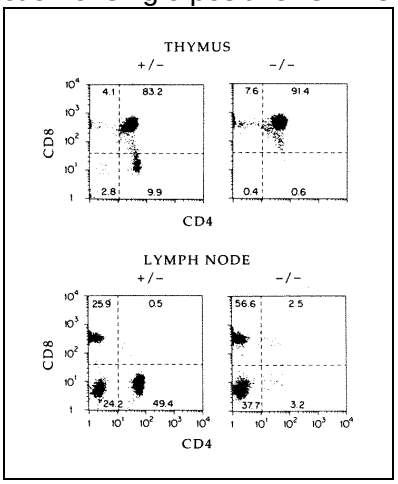

Figure 3. FACS analysis of thymocyte subsets in mutant mice revealed a reduction in the number of single positive $CD4^+8^-$ cells, while the number of double positive $CD4^+8^-$ cells was equivalent to that of control mice. Peripheral T cells from lymph nodes were severely depleted of single positive $CD4^+$ cells. Expression of CD4 during T cells maturation apparently does not require I-A and I-E class II molecules, but further progression to the single positive $CD4^+$ stage does. *(Courtesy of M. J. Grusby et al.)* [2]

Scientific Profile of B2m Targeted Mutation Mice

B2m mice are deficient in the expression of functional MHC class I molecules on the cell surface, resulting from inactivation of the B2-microglobulin gene *(β2m).* The lack of MHC class I molecules disrupts the development of cytotoxic T cells such that peripheral lymphoid organs of B2m mice are severely deficient in $CD4^-8^+$ T cells. In addition, class I deficient NK cells have reduced cytotoxic activity against NK sensitive YAC-1 tumor cells and allogeneic bone marrow.

Scientific Profile of Abb Targeted Mutation Mice

Abb mice lack functional MHC class II expression, resulting in the failure of antigen presentation to developing T cells. Consequently, these mice are largely deficient in mature $CD4^+$ T cells and mimic the human disease, Bare Lymphocyte Syndrome (BLS), found in a subset of SCID patients. This model contains a disrupted *H2-Ab1* gene. An intact *H2-Ab1* gene is necessary to form a functional class II molecule in this strain of mice.

Scientific Profile of Abb/B2m Transgenic Mice

B2m Targeted Mutation and Abb Targeted Mutation Mice have been mated to generate mice that are deficient in the expression of both classes of MHC antigens. Mice deficient in both MHC antigens combine the characteristics of the two individual targeted mutant models: low levels of class I heavy chain expression, no detectable class II expression and reduced levels of $CD4^+$ and $CD8^+$ T cells.[3] Although the resulting mice exhibit deficiency in both MHC classes they appear healthy and survive for many months. Phenotypically, MHC-deficient mice are depleted of $CD4^+$ and $CD8^+$ T cells in peripheral lymphoid organs due to a lack of appropriate restricting elements. In contrast, the B-cell compartment of these animals appears intact.[4]

Allotransplantation experiments with these animals have suggested that different mechanisms of graft rejection predominate and this depends on the specific target organ involved. This provides evidence for the role of the indirect pathway of antigen recognition in graft rejection.[3]

Origins of the Models

Abb Targeted Mutation Mice

The Abb mouse was developed in the laboratory of Michael J. Grusby *et al.* of the Harvard School of Public Health. The model was created by targeting the *H2-Ab1* gene in ES-D3 cells and injecting the targeted ES cells into C57BL/6 blastocysts. Resultant chimeras were backcrossed to C57BL/6 for 4 generations (N4). Taconic received stock from Tufts University in December 1991, and the mice were backcrossed eight additional generations (N12) to C57BL/6NTac. The mice were derived by

embryo transfer and intercrossed to homozygosity.

B2m Targeted Mutation Mice

The B2m mouse was developed in the laboratory of Rudolf Jaenisch at the Whitehead Institute. The model was created by targeting the *B2m* gene in D3 ES cells and injecting the targeted cells into C57BL/6J blastocysts. Resultant chimeras were backcrossed to C57BL/6 for five generations (N5). GenPharm International received stock from the Jaenisch lab in 1991. Taconic received stock in February 1994. The mice were then backcrossed seven generations (N12) to C57BL/6NTac and derived by embryo transfer. Heterozygotes were intercrossed to homozygosity. The colony is maintained through incrossing of homozygotes.

Abb/B2m Double Targeted Mutation Mice

The Abb/B2m multiple targeted mutation model was generated through the mating of B2m and Abb lines from the Jaenisch laboratory at the Whitehead Institute and the Glimcher lab at Harvard University, respectively. Abb mice at three backcrosses (N3) onto C57BL/6 were mated to B2m at eight backcrosses (N8) onto C57BL/6 in 1992 by Laurie Glimcher. The mice were then backcrossed to N17. Taconic received stock through the NIAID repository and embryo transfer derived the line in 1996. The line is maintained through mating of double homozygotes.

Ready for Your Experiments

Taconic mice are shipped in Taconic Transport Cages (TTC™) and come with health reports documenting their Murine Pathogen Free (MPF™) health status. They are easy to handle and maintain.

Related Mouse Models from Taconic

Taconic provides a number of mouse models relevant to immune system function, including spontaneous mutants, targeted mutants, and microinjected models on a variety of backgrounds. Call or fax to inquire about the following additional models:

- **Nude (models B6NU, B6NBO, BALBNU, BLBANU, NCRNU, NSWNU and NMRINU)** – heterozygous or homozygous for the nude mutation, conferring in homozygous mice a T-lymphocyte deficiency due to absence of a functional thymus, but no altered T-cell immunity in heterozygous mice
- **Scid (models CB17SCRF, CB17SC, ICRSC and NODSC) –** homozygous for the *scid* (severe combined immunodeficiency) mutation, lacking both T- and B-lymphocytes, serves as a model for immunity research and a host for xenotransplanation studies
- **scid-beige (model CBSCBG)** – homozygous for the *scid* (severe combined immunodeficiency) and *beige* mutations, lacking both T- and B-lymphocytes and exhibiting impaired macrophage and NK cell function; serves as a model for immunity research and a host in xenotransplantation studies
- **beige-nude-xid (model NIHBNX)** – homozygous for *nude* and *beige* mutations, and carrying an X-linked *xid* mutation; lacking normal thymic development and T-lymphocytes, exhibiting impaired function of macrophages, NK cells, and B-lymphocytes; serves as a model for immunity research and a host in xenotransplantation studies
- **Fcer1g (FcRγ) Targeted Mutation (models 000584 and 000583)** – exhibiting impaired function of macrophages, neutrophils, mast cells, basophils, and NK cells due to lack of the gene encoding the γ subunit of the cell surface receptor proteins, FcγRIII and FcεRIγ
- **Fcgr2b (FcγRII) Targeted Mutation Mouse (models 000579 and 000580)** – exhibiting dysfunctional immune inhibitory pathways due to lack of the gene encoding FcγRIIβ, a low affinity IgG receptor

- **J_H Targeted Mutation Mouse (model 001147)** – carries a deletion of the endogenous murine J segments of the Ig heavy chain locus and exhibits a complete absence of mature B cells in the spleen and bone marrow and have no detectable IgM or IgG in the sera
- **Pfp Targeted Mutation (model PFPN12)** – exhibiting a deficiency in perforin, a protein essential for cytotoxic activities of NK cells; useful for studies of immune suppression and transplantation
- **Rag2 Targeted Mutation (models 000461, 000601, RAG2 and RAGN12)** – lacking mature B- and T-lymphocytes, due to inactivation of the *Rag2* (recombination activating 2) gene required for V(D)J rearrangement; useful for vaccine development, transplantation studies, and hematopoiesis research
- **Pfp/Rag2 Double Targeted Mutation (model 001177)** – lacking both *Pfp* and *Rag2* genes, exhibiting a severe depletion of functional NK cells and of B- and T-lymphocytes; useful for vaccine development, transplantation studies, and studies of the immune system
- **Rag2 Targeted Mutation-HY Micro-injected Mouse (model 004079)** – lacking endogenously derived mature B- and T-lymphocytes but with expression of receptors for the HY antigen, which rescues $CD8^+$ cell development in females

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