Rag2 Targeted Mutation Mice from Taconic

**In vivo Immunology Model for Drug Discovery and Toxicology**

### The Taconic Rag2 Targeted Mutation Mouse

- Lacks mature T and B lymphocytes due to an inability to initiate V(D)J rearrangement. Otherwise, the mouse exhibits apparently normal hematopoiesis.

### Potential Applications of the Rag2 Targeted Mutation Mouse

- Evaluate function of lymphocyte specific genes in immune cell differentiation (Figure 1).
- Reconstitute with human hematopoietic cells for research in AIDS and other immune cell disorders.
- Model human hematopoiesis for studying experimental therapeutics or developing vaccines.
- Research the immune system's effect on tumorigenesis and metastasis.
- Investigate somatic cell therapy in vivo.
- Explore the genetics of autoimmune or infectious diseases.

### Scientific Profile of the Rag2 Targeted Mutation Mouse

The Taconic Rag2 Targeted Mutation Mice carry a germline mutation in which a large portion of the Rag2 coding region is deleted. Mice homozygous for the mutation are observed to lack mature T and B lymphocytes. Analysis of these mice indicate that the Rag2 defect blocks T cell and B cell differentiation earlier and/or more completely than the scid defect.

Homozygous mutant mice were found to appear normal except for immunological defects. Spleens, thymuses, and lymph nodes were small and hypoplastic. No detectable alterations were observed in other tissues tested.

Mice heterozygous for the mutation were found to be normal compared with their wild type littermates.

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**Figure 1: RAG2 deficient blastocyst complementation assay.** Chen, J., Lansford, R., Stewart, V., Young, F., Alt, F. Proceedings of the National Academy of Science 90, 4528–4532. 1993. (Diagram courtesy of Dr. Chen and Dr. Alt.)
Taconic Rag2 Mice Background Strains

<table>
<thead>
<tr>
<th>Taconic Model #</th>
<th>Nomenclature</th>
<th>Background Strain</th>
<th>Inbred/ Congenic</th>
<th>Haplotype</th>
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<tbody>
<tr>
<td>RAG2-M</td>
<td>129S6/SvEvTac-Rag2&lt;sup&gt;2&lt;sub&gt;mut&lt;/sub&gt;Fwa&lt;/sup&gt;</td>
<td>129/SvEv</td>
<td>Inbred</td>
<td>b</td>
</tr>
<tr>
<td>461-M</td>
<td>B6.SJL(129S6)-&lt;sub&gt;Ptprc&lt;/sub&gt;B6.SJL(129S6)</td>
<td>B6.SJL(129S6)</td>
<td>Congenic</td>
<td>b</td>
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<tr>
<td>601-M</td>
<td>C.129S6(B6)-Rag2&lt;sup&gt;2&lt;sub&gt;mut&lt;/sub&gt;Fwa&lt;/sup&gt; N12</td>
<td>C.129S6(B6)</td>
<td>Congenic</td>
<td>d</td>
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<tr>
<td>RAGN12-M</td>
<td>B6.129S6-Rag2&lt;sup&gt;2&lt;sub&gt;mut&lt;/sub&gt;Fwa&lt;/sup&gt; N12</td>
<td>B6.129S6</td>
<td>Congenic</td>
<td>b</td>
</tr>
</tbody>
</table>

**Genetic Background**

The Taconic Rag2 line is maintained on several different genetic backgrounds to meet your particular research needs (see table). The Rag2 mutant mouse on the 129/SvEv background is on the inbred strain used to create the embryonic stem cells for the initial gene targeting experiments done in the laboratory of Dr. Fred Alt. The Rag2 Targeted Mutation Mouse on the congenic B6.SJL(129S6) background makes this line useful for their identification in immunological adoptive transfer experiments. It is similar to a C57BL/6 background except that it carries the ptprc<sup>a</sup> and the pep 3<sup>b</sup> genes from the SJL strain of mice. This marker is also sometimes referred to as Ly5.1.<sup>3,4</sup>

The Rag2 mouse is also available on C57BL/6 and BALB/c congenic backgrounds. (See above table for haplotypes.)

**Origin of Models**

The Rag2 mouse was developed in the laboratory of Frederick W. Alt at Columbia University. The model was created by targeting the Rag2 gene in CCE ES cells and injecting the targeted cells into blastocysts. Ellis Reinherz of the Dana Farber Cancer Institute received Rag2 mice from the Alt lab on a mixed background. The mice were then backcrossed by S. Koyasu for 10 generations (N10) to B6.SJL-<sub>Ptprc</sub><sup>a</sup> (from Cancer Research). Taconic received stock in 1996. The mice were derived by embryo transfer, and the colony is maintained by mating homozygous mice.

**Ready for Your Experiments**

Taconic's quality program assures that each Rag2 Targeted Mutation Mouse is bred for homozygosity. Taconic mice are shipped in Taconic Transport Cages (TTC<sup>TM</sup>) and come with an up-to-date health report documenting their Murine Pathogen Free (MPF<sup>TM</sup>) health status. Barrier housing conditions are recommended for maintenance of Rag2 homozygous mice.

**Related Mouse Models**

**Pfp/Rag2 (model 001177)** - This double targeted mutation exhibits a severe depletion of NK cell function through the disruption of the Pfp gene and lacks mature T or B lymphocytes through disruption of the Rag2 gene. It can be used to study overall regulation of the immune system or specific areas such as NK or CTL activity, immune suppression and transplantation. This mouse is homozygous for both the disrupted Pfp gene and Rag2 gene. It is an alternative to traditional models bearing combinations of naturally occurring mutant genes such as the scid-bg (Prkdc<sup>scid</sup>-Foxn1<sup>nu</sup>) and bg-nu-xid (Lyst<sup>bg</sup>-Foxn1<sup>nu</sup>-Btk<sup>-xid</sup>).

**Rag2-HY (model 004079)** - The Rag2 gene in this model has been inactivated by homologous recombination therefore no V(D)J rearrangements can occur. The result of this manipulation allows no maturing endogenous T or B cells. This provides a background to examine the phenotypic expression of the antigen HY transgene. This transgene results in a large fraction of T-cells expressing an a b
TCR specific for a minor histocompatibility antigen (H-Y) which is present on male but not female cells in the context of MHC Class I (H-2D<sup>b</sup>). These mice carry an H<sup>2</sup>d haplotype which is a non-selecting background for conventional T-cells. Therefore on a B10.D2 background(H<sup>2</sup>d), thymocyte development is arrested at the double positive stage in both male and female Rag<sup>2</sup>/HY mice. These mice can be useful for studying mechanisms of self-tolerance and lineage commitment and the role of CD4 and CD8 molecules in the deletion process of autospecific cells.

References Cited:

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Taconic Transgenic Models
Publication Reference List
Rag2 Targeted Mutation Mice


Reuther, T., Kuhler, A.C., Staff, C.J., Flechtmacher, C.,
glomeruli but are only pathogenic in combination with
Daha MR. (2004) Anti-C1q autoantibodies deposit in
IM, Prins FA, Kishore U, Salant DJ, Verbeek JS, van Kooten C,
Trouw LA, Groeneveld TWL, Seelen MA, Duijs JMGJ, Bajema
IM, Prins FA, Kishore U, Salant DJ, Verbeek JS, van Kooten C,
Daha MR. (2004) Anti-C1q autoantibodies deposit in
glomerular C1q-containing immune complexes; J Clin Invest,
114(5):679-88.

explanation for the association of Trousseau syndrome with

Wayne, J., Suh, H., Sokol, K.A., Petrie, H.T., Witmer-Pack, M.,
Edelhoff, S., Distech, C.M., Nussenzweig, M.C. (1994) TCR
Selection and Allelic Exclusion in Rag Transgenic Mice that
Exhibit Abnormal T Cell Localization in Lymph Nodes and
5491-5502.

Witt, C.M., Raychaudhuri, S., Schaefer, B., Chakraborty, A.K.,
Thymocytes Visualized in Real Time. PloS Biology, Vol. 3,
No. 6, pp. e160.

Xiao, H., Heeringa, P., Hu, P., Liu, Z., Zhao, M., Aratani, Y.,
cytoplasmic autoantibodies specific for myeloperoxidase
cause glomerulonephritis and vasculitis in mice. Journal of

lentiviral vectors to specific cell types in vivo. Proceedings of
the National Academy of Science, Vol. 103, No. 31, pp. 11479-
84.

Yang, J., Ertl, H.C., Wilson, J. (1994) MHC Class I-Restricted
Cytotoxic T Lymphocytes to Viral Antigens Destroy
Hepatocytes in Mice Infected with E1-Deleted Recombinant

Zhang, K., Wong, H.N., Song, B., Miller, C.N., Scheunir, D.,
IRE1α is required at 2 distinct steps in B cell lymphopoiesis.

Zuniga-Pflucker, J.C., Jiang, D., Schwartzberg, P.L., and
Differentiation of CD4<sup>+</sup>/CD8<sup>+</sup> into CD4<sup>+</sup>/CD8<sup>+</sup>
Thymocytes Without T Cell Receptor Beta Rearrangement in
Recombinase Activation Gene 2 -/- Mice, Journal of
Experimental Medicine, Vol. 189, pp. 1517-1521.