T, B and NK Cell Deficient Targeted Mutation Animal Models

Potential Applications of the Pfp/Rag2, Pfp and Rag2 Targeted Mutation Models

- Evaluate and differentiate the role of perforin dependent and independent pathways in CTL and NK cell function.
- Evaluate function of lymphocyte specific genes in immune cell differentiation.
- Research the immune system's effect on tumorigenesis and metastasis.
- Explore the genetics of autoimmune or infectious diseases.

Pfp/Rag2 Double Targeted Mutation Mice exhibit a severe depletion of NK cell function through the disruption of the *Pfp* gene, and lack mature T and B lymphocytes through disruption of the *Rag2* gene. Homozygous for both the disrupted *Rag2* gene and *Pfp* gene, the Pfp/Rag2 Double Targeted Mutation Mouse offers an alternative model to traditional models bearing combinations of naturally occurring mutant genes such as scid-bg and bg-nu-xid.

Rag2 Targeted Mutation Mice lack mature T and B lymphocytes due to an ability to initiate V(D)J rearrangement. Otherwise, the mouse shows apparently normal hematopoiesis. Taconic's 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 indicates that the *Rag2* defect blocks T cell and B cell differentiation earlier and/or more completely than the *scid* defect. Mice heterozygous for the mutation were found to be normal compared with wild type littermates.[1]

Pfp Targeted Mutation Mice carry a germline disruption of the endogenous perforin (*Pfp*) genes achieved by homologous recombination in AB-1 embryonic stem cells. They express normal numbers of $CD8^+$ and NK cells and are viable and fertile. Analysis of mice homozygous for the gene disruption showed no detectable perforin levels when splenocyte populations were cultured and induced by T-cell growth factor(s) (TCGF) to express perforin.

Homozygous mutant mice thrive and the lymphoid organs and tissues appear normal. A distribution of CD4 and CD8 T-cell subsets is essentially identical in homozygote knockout mice and wild type mice.[2]

Origins of the Models

Rag2 - 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. Taconic has the Rag2 Targeted Mutation Model available on four backgrounds (models 000461, 000601, RAG2 and RAGN12).

Pfp - The Pfp mouse was developed by Craig M. Walsh *et al*. at UCLA and GenPharm International. The model was created by targeting the *Pfp* gene in AB-1 ES cells and injecting the targeted cells into C57BL/6 blastocysts. Resultant chimeras were backcrossed to C57BL/6. Taconic received stock in 1995. The line was backcrossed to C57BL/6NTac to N12, embryo transfer derived and intercrossed to homozygosity. The colony is maintained through incrossing of homozygous mice.

Pfp/Rag2 - The Pfp/Rag2 mouse was developed by crossbreeding the Pfp targeted mutation mouse (model PFPN12) and the Rag2 targeted mutation mouse (model RAGN12) at Taconic and breeding to homozygosity for both genes. This model was backcrossed twelve generations

(N12) to C57BL/6NTac. The colony is maintained through homozygous matings.

Ready for Your Experiments

Taconic's quality program assures that each of these T, B and NK cell deficient models are genotyped for homozygosity.

The Pfp Targeted Mutation Mouse and the Pfp/Rag2 Double Targeted Mutation Mouse are available on a hybrid background strain C57BL/6 x 129S6/SvEv. A B6129F1 mouse is available as a control. The Rag2 Targeted Mutation Mouse is available on several different inbred and congenic backgrounds; 129S6/SvEv, B6.SJL, B10.D2, BALB/c, and C3H.

This strain is on an inbred 129 background. Taconic mice are shipped in Taconic Transit Cages (TTC™) and come with an up-to-date health report documenting their Murine Pathogen Free (MPF™) health status. Barrier housing conditions are recommended for maintenance of Rag2, Pfp, and Pfp/Rag2 mice.

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Taconic Transgenic Models
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