Also Known As: FcRn<sup>−/−</sup> hFcRn (32) T, FcRn<sup>−/−</sup> hFcRn (32) Tg, hFcRn Tg32, Tg32

Tg32 mice (also called hFcRn Tg32 or FcRn<sup>−/−</sup> hFcRn line 32 Tg) carry a knock-out mutation for the mouse Fcgrt (Fc receptor, IgG, alpha chain transporter) gene and a transgene expressing the human FCGRT gene under the control of its own native promoter (hTg32). Useful in evaluating the pharmacokinetics and pharmacodynamics of human immunoglobulin G (IgG) and Fc-domain based therapeutics, homozygous Tg32 mice have the highest, most human-like protection of humanized IgG and are the best model for use when maximum half-life data is required.

Need assistance evaluating antibodies in FcRn mice? Human preclinical pharmacokinetic (PK) analysis is available. See our FcRn full service platform.

Donating Investigator

Dr. Derry Roopenian, The Jackson Laboratory
There are several challenges facing researchers who are developing antibody-based therapeutics, including assessing half-life, selecting efficacious variants, and determining dosage for clinical trials. The mechanism behind IgG’s extended half-life lies in the interaction between IgG and the neonatal Fc receptor (FcRn), encoded by *Fcgrt*, Fc receptor, IgG, alpha chain transporter.
transporter (Roopenian et al., 2003; Challa et al., 2014). Standard rodent models are problematic in that mouse and rat FcRn do not bind human IgG with the same affinity as human FcRn, leading to inaccurate half-life data (Ober et al., 2001).

Tg32 (Stock No. 014565) and Tg276 (Stock No. 004919) are humanized mouse models that can be used to predict the pharmacokinetics (PK) of IgG antibodies in humans with an accuracy comparable to non-human primates (NHPs). Both carry a knock-out mutation for the mouse Fcgrt gene (Stock No. 003982) in addition to a transgene expressing the human FCGRT gene either under the control of its own native promoter (Stock No. 014565) or under the control of the more broadly-expressed CAG promoter (human cytomegalovirus (CMV) enhancer fused to the chicken beta-actin; Stock No. 004919). Each line has its unique attributes and optimal applications.

Tg32 mice (also called hFcRn Tg32 or FcRn-/- hFcRn line 32 Tg; Stock No. 014565) express the human FCGRT transgene from the native human promoter, and have the highest, most human-like protection of humanized IgG and are the best model for use when maximum half-life data is required. The transgene, integrated on mouse Chromosome 2, displays a physiological human FCGRT expression pattern (Latvala et al., 2017). Experimental variability between the mice is minimal, enabling a small number of animals per study. Using this model and human PK-predictive allometric scaling (Bets et al., 2018), clinicians can estimate the minimum dose to achieve therapeutic serum concentrations, reducing the need for potentially risky dose-escalation treatments during clinical trials. Avery et al., 2016 show that monoclonal antibody clearance in homozygous mice correlates with human pharmacokinetics better than non-human primates. In this line, serum albumin levels are slightly above those seen in C57BL/6J mice, while mouse IgG levels are low due to the species-specific activity of human FCGRT.

Immunodeficient FCGRT-humanized models carrying the Tg32 transgene are also available to evaluate Fc-domain based therapeutics that are potentially immunogenic or involve xenografts - see B6.Cg-Fcgrt^tm1Dcr Prkdc^sca^tm1Wjl Prkdc^sca^tm1Dcrjson;Tg(FCGRT)32DcrDcrJ (Stock No. 018441), and NOD.Cg-Fcgrt^tm1Dcr Prkdc^sca^tm1Wjl Prkdc^sca^tm1Dcrjson; Tg(FCGRT)32DcrJ (Stock No. 028615).

Tg276 mice (Stock No. 004919) express the human FCGRT transgene from the broadly-expressed CAG promoter (human cytomegalovirus (CMV) enhancer fused to the chicken beta-actin). Plasma albumin levels are similar to wild-type mice, however the serum IgG levels remain low due to the species-specific behavior of human FCGRT. These mice are best suited to detect subtle differences in antibody persistence in vivo. Tg276 model lies in its ability to allow fine distinctions in half-life between several candidate molecules. Longer IgG half-lives are observed in homozygotes, as compared to hemizygotes. Petkova et al., 2006 demonstrate that antibody half-life in Tg32 hemizygotes (Stock No. 014565) is comparable to that of Tg276 (Stock No. 004919) homozygotes.
Genotyping Protocols
Standard PCR: Fcgrt
Standard PCR: Fcgrt Alternate1
QPCR: Tg(FCGRT)-qPCR
Genotyping resources and troubleshooting
Dietary Information
LabDiet® 5K52 formulation (6% fat)
Breeding Considerations

When maintaining a live colony, mice homozygous for the Fcgrtm1Dcr allele and homozygous for the Tg(FCGRT)32Dcr transgene can be bred together.

Additional Breeding and Husbandry Support
Mating System
See "Breeding Considerations"

Citation
When using the FcRn/- hFcRn (32) Tg, hFcRn Tg32, Tg32 mouse strain in a publication, please cite the originating article(s) and include JAX stock #014565 in your Materials and Methods section.

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**Frozen Mouse Embryo**

B6.Cg-Fcgrt<tm1Dcr> Tg(FCGRT)32Dcr/DcrJ

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