MT-PSX transgenic line 23-3 mice (also called Tg[MT-1,HBV]Bri28) have the zinc-inducible mouse metallothionein I promoter sequences directing expression of the envelope/surface antigen coding region (HBsAg) of the hepatitis B virus (HBV). This results in high serum HBsAg before zinc treatment, and hepatocellular retention of HBsAg following zinc treatment. These mice are a model for studying the impact of secreted HBsAg on induction of HBsAg-specific adaptive immune responses during infection or to therapeutic vaccination. They are also useful in studying the immunopathogenesis of acute T cell mediated hepatitis, chronic T cell mediated hepatitis, and the downstream consequences of chronic hepatitis, especially hepatocellular carcinoma.

Donating Investigator

Dr. Francis (Frank) V Chisari, The Scripps Research Institute
MT-PSX transgenic line 23-3 mice (also called Tg[MT-1,HBV]Bri28) have zinc-inducible expression of nontoxic quantities of the three hepatitis B virus envelope/surface antigen proteins (large, middle, and small; all containing hepatitis B surface antigen (HBsAg) determinants) in their hepatocytes, and are immunologically tolerant to HBsAg at the T cell level. Independent of zinc activation, these mice display no evidence of spontaneous liver disease nor hepatocellular carcinoma during their lifetime.

During the normal HBV replication cycle, the middle and small envelope proteins assemble to form the HBV major envelope polypeptide (a 22 nm spherical subviral particle containing HBsAg) that is rapidly-secreted secreted by the hepatocyte into the circulation. However, the ability of the hepatocytes to secrete these HBsAg subviral particles is inversely proportional to the abundance of the large envelope protein which, when coexpressed with the middle and small envelope proteins, forms long non-secretable filamentous particles that accumulate in the endoplasmic reticulum (where they are readily detectable immunohistochemically), thus precluding secretion of the 22 nm spherical forms.

The MT-PSX transgene is designed to have the zinc-inducible mouse metallothionein I promoter sequences directing expression of the HBV large envelope protein, but expression of the middle and small envelope proteins are regulated by a constitutively active internal promoter located within the envelope coding region on the transgene. Therefore, in the absence of dietary zinc supplementation, expression of the middle and small envelope proteins, but not the large envelope protein, is observed; this results in high serum HBsAg levels and very low hepatocellular HBsAg levels (barely detectable immunohistochemically).

Activation of the metallothionein I promoter by oral zinc administration leads to expression of the large envelope polypeptide by the hepatocyte; this results in the formation and retention of the non-secretable filamentous HBsAg particle in the hepatocyte endoplasmic reticulum (where it is detectable principally as cytoplasmic HBsAg in periportal hepatocytes close to the point of entry of the circulation into the hepatic lobule) and gives the hepatocytes a "ground glass" appearance. This renders the hepatocytes highly susceptible to destruction (MHC class I-restricted necro-inflammatory liver disease) after immune system ablation with subsequent adoptive transfer of HBsAg-specific cytotoxic T lymphocytes (CTLs).

MT-PSX transgenic line 23-3 mice exhibit no detectable liver expression (RNA or protein) from the transgenic HBV X gene. Hemizygous mice are viable, fertile and healthy. To date (July 2015), it has not been attempted to make this strain homozygous.

Importantly, the donating investigator confirms that the MT-PSX transgenic line 23-3 mice do not produce the infectious HBV particle (hepatitis B virion aka Dane particle), independent of zinc administration. This is because the MT-PSX transgene does not have the sequences encoding the viral DNA polymerase (P gene) or the HBV core protein (pre-C [HBeAg] and C gene [HBcAg]).
Genotyping Protocols
Standard PCR: Tg(Mt1-HBV)28Bri-alternate1
Genotyping resources and troubleshooting

Breeding Considerations
When maintaining a live colony, hemizygous mice may be bred to wildtype (noncarrier) siblings or to C57BL/6J inbred mice (Stock No. 000664). To date (July 2015), it has not been attempted to make this strain homozygous.

Additional Breeding and Husbandry Support
Citation
When using the MT-PSX transgenic line 23-3 mouse strain in a publication, please cite the originating article(s) and include JAX stock #027527 in your Materials and Methods section.

Animal Health Reports
Facility Barrier Level Descriptions
Production of mice from cryopreserved embryos or sperm occurs in a maximum barrier room, G200

Pricing & Availability

Typically mice are recovered in 10-14 weeks. Contact Customer Service to place an order or for more information.

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<th>SERVICE/PRODUCT</th>
<th>DESCRIPTION</th>
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<td>Cryo Recovery</td>
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RELATED PRODUCTS AND SERVICES

Frozen Mouse Embryo B6;SJL-Tg(Mt1-HBV)28Bri/ChiJ Frozen Embryo $2,595.00

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