TACONIC

Transgenic HLA Models

MODELS DESIGNED TO TAKE
YOUR STUDY FURTHER

Transgenic HLA Models

In vivo investigations of human immune system function can be frustrating when you don't have the right tools. Transgenic mice that express human HLA molecules represent a unique *in vivo* experimental model for evaluating human immune system function.

These models have been used to study the role of the human class I or class II restricted T cell repertoire in autoimmune disease, infectious disease, and vaccine development.

They are also valued tools for evaluating human HLA restricted T cell-mediated vaccine efficacy in oncology applications.

Taconic's collection of transgenic mice that express human HLA molecules have helped advance the science related to human immune system function, as well as potential novel therapeutics.

Check out Taconic's transgenic HLA models at **Taconic.com/HLA**

EXCLUSIVELY FROM TACONIC BIOSCIENCES

MODEL NUMBER	MODEL NAME
9662	HLA-A1 Mouse
9659	HLA-A2.1 Mouse
9660	HLA-A11 Mouse
9663	HLA-A24 Mouse
9661	HLA-B7 Mouse
9664	HLA-B44 Mouse
4149	Abb Knockout / Transgenic HLA-DR4 Mouse

KEY APPLICATIONS OF THE TRANSGENIC HLA MODELS

VACCINE RESEARCH

Transgenic HLA mice are great tools to help identify epitopes or to test vaccine efficacy in challenge studies, and support rational vaccine design through epitope identification (Ishioka et al. 1999, Okochi et al. 2008). The models can be used to study T cell responses restricted by HLA molecules (Alexander et al. 2003, Alexander et al. 1997, Okochi et al. 2008, Vitiello et al. 1991), and given the range of HLA types offered in these models, this facilitates the development of vaccines targeted against specific ethnic/regional populations, as well as broad populations. Models in this portfolio have been used in research on immunogenicity and vaccines directed against human lymphocytic choriomeningitis virus (LCMV) infection (Botten et al. 2007), HIV (McKinney et al. 2004, Nanjundappa et al. 2012, Singh et al. 2002, Wilson et al. 2003), hepatitis B virus (Depla et al. 2008, Oseroff et al. 1998) and Lassa virus (Botten et al. 2006), among others (Cong et al. 2011, Cong et al., 2012, Kotturi et al. 2009, Tan et al. 2010, Weiskopf et al. 2011).

ONCOLOGY

Transgenic HLA mice are used for cancer immunotherapy research. Example applications include evaluation of HLA restricted CTL epitope responses *in vivo,* determining the immunogenicity of novel cancer vaccines (Casnici et al. 2012, Hospers et al. 2009, Kang et al. 2013, Men et al. 1999, Tomita et al. 2013), and to test expansion and response of chimeric antigen receptor T cells.

Custom crosses to immunodeficient models or other genetically modified strains are available. Please contact your Strategic Account Manager for more information.

AUTOIMMUNE DISEASES

HLA models have proven to be important tools in the study of autoimmune disease, since certain HLA types are associated with autoimmune diseases. For example:

- HLA-DR4 is associated with rheumatoid arthritis and multiple sclerosis. The Abb Knockout/Transgenic HLA-DR4 Mouse expresses hybrid class II molecules with the peptide binding domains of human HLA-DRA and HLA-DRB*0401 and the membrane proximal domains of mouse I-E on an H2-Ab1 knockout background. These mice are susceptible to experimentally allergic encephalomyelitis (EAE) (Ito et al. 1996, Kawamura et al. 2008), as well as arthritis (Walker et al. 2012), and induced connective tissue disease (Greidinger et al. 2008).

INFECTIOUS DISEASES AND BIOTERROR AGENTS

Transgenic HLA models may be used to study human T cell response to infections to help elucidate if, and how, a protective response is initiated. For highly pathogenic emerging infections and bioterror agents, access to infected or immune human patients is sometimes not possible. Transgenic HLA models fill this important need. Use of predictive algorithms in combination with *in vivo* experiments in transgenic HLA mice permits epitope identification without having to manipulate dangerous pathogens, or having access to human donors. The models have been used in the study of arenaviruses (including Lassa, lymphocytic choriomeningitis, Guanarito, Junin, Machupo, Sabia and Whitewater Arroyo viruses) (Botten et al. 2010, Kotturi et al. 2009), HIV (McKinney et al. 2004, Nanjundappa et al. 2012, Singh et al. 2002, Wilson et al. 2003), poxviruses (Pasquetto et al. 2005), and hepatitis B (Oseroff et al. 1998).

IMMUNOGENICITY TESTING AND SAFETY ASSESSMENT

Transgenic HLA models might be exactly what you need when you are looking for a tool to screen immunogenicity of biologic drugs.

RELATED MODELS

Taconic offers other models which can be useful for these research applications.

Immunodeficient mice reconstituted with a human immune system via engraftment of human hematopoietic stem cells can be a complementary model to the transgenic HLA mice.

The CIEA NOG mouse® is the premier model for this type of reconstitution experiment and can be easily engrafted via a simple tail vein injection of CD34+ cord blood cells. Taconic now offers NOG mice which have been engrafted with human PBMCs or hematopoietic stem cells.

To learn more about the CIEA NOG mouse®, visit **Taconic.com/NOG**

TRANSGENIC HLA MOUSE MODELS

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