

Histological cross-section of skin following transplantation of human PBMCs in TTG mice. Detection of CD3+ human T cells in the skin.

HUMANIZED, TRIPLE TRANSGENIC MOUSE

Functional analyses with monoclonal antibodies (mAb) against human surface molecules *in vivo* are limited. *In vitro* effects cannot completely be transferred to the *in vivo* situation. The triple transgenic mouse model (on a stable C57Bl/6 genetic background) expresses human CD4- and MHC-II-molecules while murine CD4-molecules are knocked out (are not expressed). Thus it is possible to directly test anti-human CD4 and anti-human MHC-II antibodies *in vivo*. At the same time the interaction of the complete accessory T cell synapses is simulated and can be influenced by anti-human CD4 and MHC-II antibodies.

Unique Feature

This triple transgenic mouse model is unique in this form and allows investigation of anti-human CD4 and MHC-II antibodies regarding their effect on immune cells.

Methods

Following application of antibodies a variety of analyses can be carried out including analysis of optimal dose, potential for T cell depletion, detailed flow cytometric analysis of lymphocyte subpopulations with or without antigen-specific stimulation and studies of pharmacokinetics using ELISA. In addition, peripheral blood parameters can be determined and histological / immunohistochemical as well as molecular biological methods can be used.

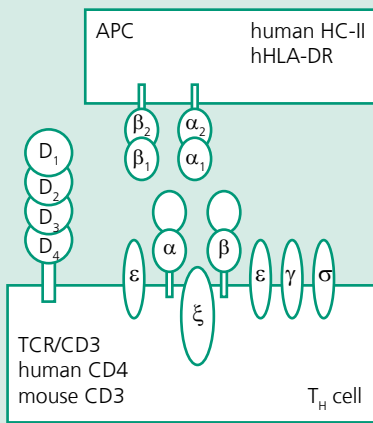
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Selected Applications

Using humanized, triple transgenic, mice newly developed anti-human CD4 and anti-human MHC class II antibodies can directly be analyzed *in vivo*. In this way immunosuppressive or -stimulating effects on immune cells or other cell types can be examined.

Reference Project

Tolerance towards tetanus toxoid was achieved in humanized mice following anti-human CD4 treatment (Laub R et al., Transplant Proc 2001; 33 (3): 2182-2183). Antibody conditioning protocols have been established at Fraunhofer IZI and transplantation experiments with TTG mice have been carried out.

In vitro studies in MLC-cultures demonstrate the therapeutic efficiency of applied monoclonal antibodies. CD4 mAb are produced in the institute and can be used for the experiments.

The animals for the model are bred in cooperation with the University of Leipzig (Translational Centre for Regenerative Medicine).

Description of the animal model – phenotype (schematic) of TTG mice.