

Histological analysis of the skin of GvHD mice.

GVHD-MODEL IN MICE

Graft-versus-Host-Disease (GvHD) is still the main complication following allogeneic transplantation of hematopoietic stem cells. For treatment of GvHD the development of new therapeutic options is required. Therapeutic and / or preventive effects of new drug candidates for treatment of GvHD can be tested in vivo through an allogeneic GvHD model. Depending on the question, allogeneic GvHD can be induced in transgenic or wild type mice (transplantation model C57Bl/6 → Balb/c) via transplantation of splenocyte enriched bone marrow cells following chemotherapy. Mice can be treated prior to or after induction of GvHD in order to investigate potential candidate drugs.

the same time the results are transferable to other humanized mice and can be offered as whole package.

Methods

Depending on the question the drug candidate to be tested can be applied prior to and after induction of allogeneic GvHD in different doses. Clinical scores, peripheral blood parameters, histological / immunohistochemical and molecular biological methods can be used to diagnose therapeutic effect. Furthermore cells can be labelled in order to visualize and evaluate them by means of immunofluorescence microscopy or bioluminescence imaging and serologic markers (e. g. interleukins).

Unique Feature

In Germany only a few centers exist, which can provide adequate GvHD models. The allogeneic model used at Fraunhofer IZI is comparably simple and cost effective as there are only few special requirements to be considered during breeding of mice. At

Selected Applications

The model is suitable for evaluation of drug candidates for therapy or prevention of GvHD.

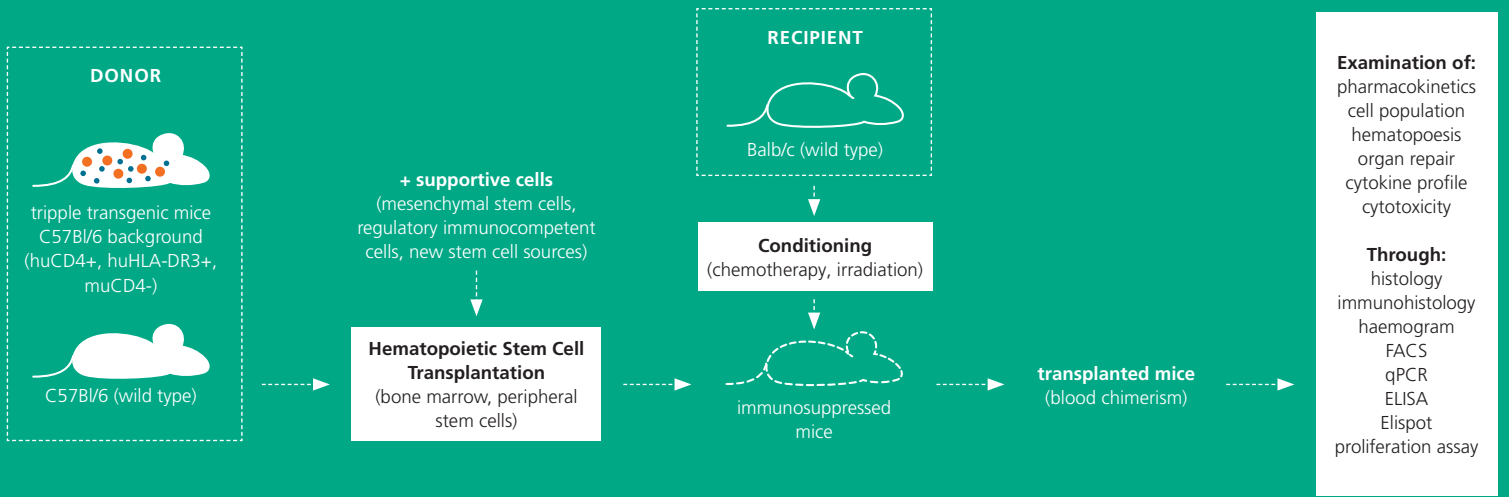
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Equipment available at Fraunhofer IZI

- Access to animal facilities and surgery
- Access to irradiation facility
- FACS (8 channels)
- Cell sorter / AutoMACS for cell separations
- Fluorescence microscope (automated)
- Histology:
 - Automated infiltration system for dehydration automated staining system
 - Embedding center
 - Cryostat / microtome
- LightCycler® 480 System for real time PCR

Diagnostic Support

Analysed Parameters:

- Pharmacokinetics of compounds – composition of cell populations – organ repair
- Inflammatory markers
- Cytotoxicity
- Hematopoiesis
- Immune reaction markers

Standard Methods:

- Histology / immune histology
- ELISA
- Elispot
- Three part differential hematology analyzer
- FACS
- Proliferation assays
- Molecular diagnostics (real-time PCR)

Reference Project

- Using humanized mice a xenogeneic GvHD model was established.
- Using humanized mice stem cell protocols were established and new stem cell sources were tested for their effect on hematopoietic stem cell transplantations.

Publications

- Fricke et al., PLoS One (2009) Jul 7;4(7):e6157.
- Fricke et al. Cell Mol Life Sci. (2010) Dec;67(23):4095-106.
- Fricke et al. Methods Mol Biol. (2011);690:315-32.
- Fricke et al. FlowCytometryPart A (2012); in press
- Fricke et al. Cytometry A. 2012 Apr 20.
doi: 10.1002/cyto.a.22061.
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Application Example: Survival rate with / without anti-human CD4 antibody treatment

