Humanized Mice

NMG mice with human-derived CD34+ hematopoietic stem cells can be used for reconstruction of multi-lineage human immune cells, and represent effective model animals for studies on immuno-oncology and infectious diseases.

General information

$CD34^+$ humanized mice are model animals constructed by transportation of human umbilical cord blood and fetal liver hematopoietic stem cells (HSCs) into irradiated myeloablative NMG mice. HSCs can colonize in the bone marrow of mice after transplantation and continuously produce various types of hematopoietic or immune cells, such as T cells, B cells, NK cells, and myeloid cells. Since the immune cells are developed in mice and are tolerant to the host, no GvHD will be observed, human-derived immune cells will exist stably, and the types of reconstructed immune cells will be richer than those of PBMC humanized mice. However, the T cell function of this model type is relatively weak due to lack of human thymus required for human T cell development. In addition, the myeloid cells of this model are underdeveloped, and the content of NK cells is relatively low, because the species differences between humans and mice are demonstrated by certain cytokines that regulate the development of these two types of cells.

IL-15 is essential for the development of NK cells, natural killer T cells, and memory $CD8^+$ T cells. The supplementation of human IL-15 by Shanghai Model Organisms Center on the basis of conventional $CD34^+$ humanized mice is able to significantly increase the proportion of NK cells to be suitable for the efficacy evaluation of drug targets on NK cells.

Preparation process

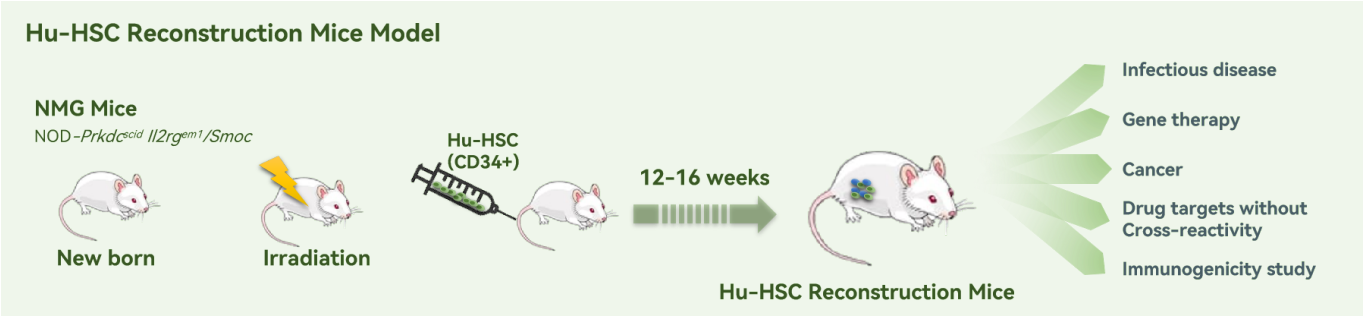

Figure 1. Preparation process of NMG mice transplanted with human hematopoietic stem cells (HSCs).

Phenotypic analysis

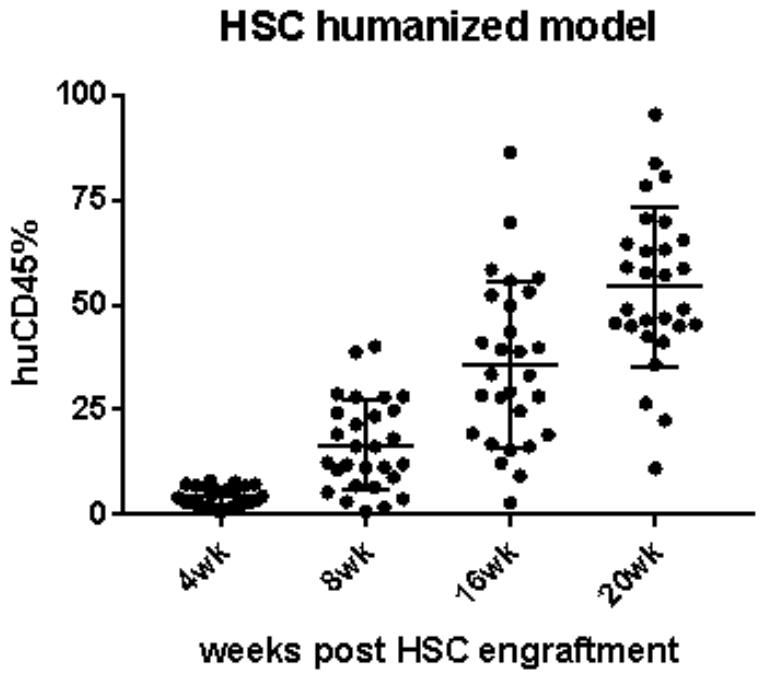

Figure 2. Reconstructed hematopoietic system of NMG mice transplanted with human hematopoietic stem cells (HSCs), indicating continuously increased level of human-derived CD45+ immune cells in peripheral blood.

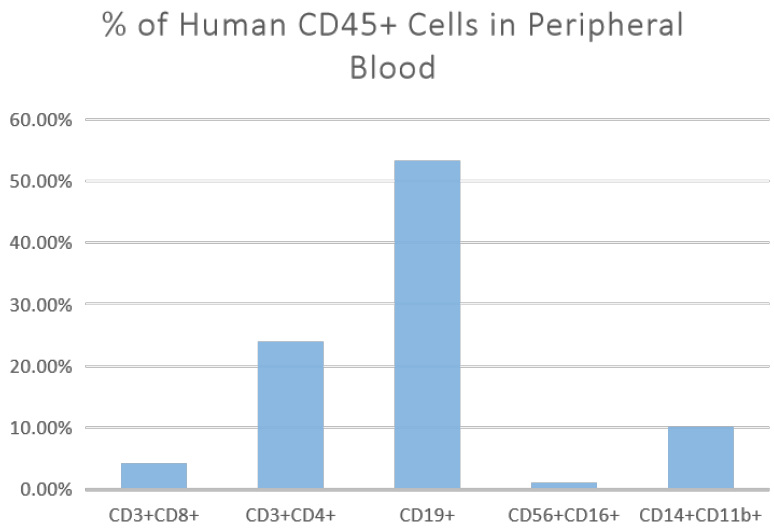

Figure 3. Proportions of various types of hematopoietic/immune cells at 20 weeks after the mice are transplanted with human hematopoietic stem cells (HSCs), including human-derived T (CD3+CD4+ and CD3+CD8+ cells), B (CD19+ cells), NK lymphocytes (CD56+CD16+ cells), and monocytes (CD14+CD11b+ cells).

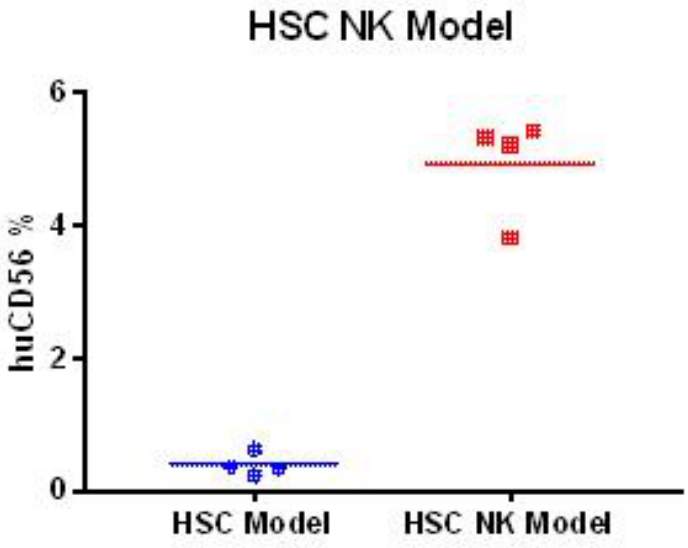

Figure 4. Reconstructed hematopoietic system of NMG mice transplanted with human hematopoietic stem cells (HSCs), with supplementation of human-derived IL-15, which can significantly increase the proportion of NK cells and is suitable for the efficacy evaluation of drug targets on NK cells.

Efficacy evaluation

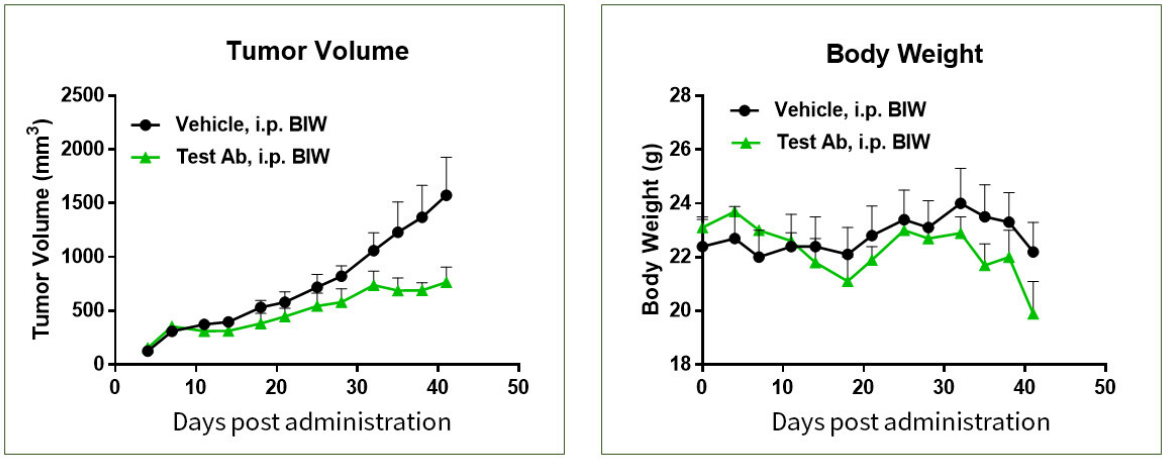

Figure 5. Example 1 of anti-tumor efficacy validation in Hu-HSC tumor-bearing mouse model

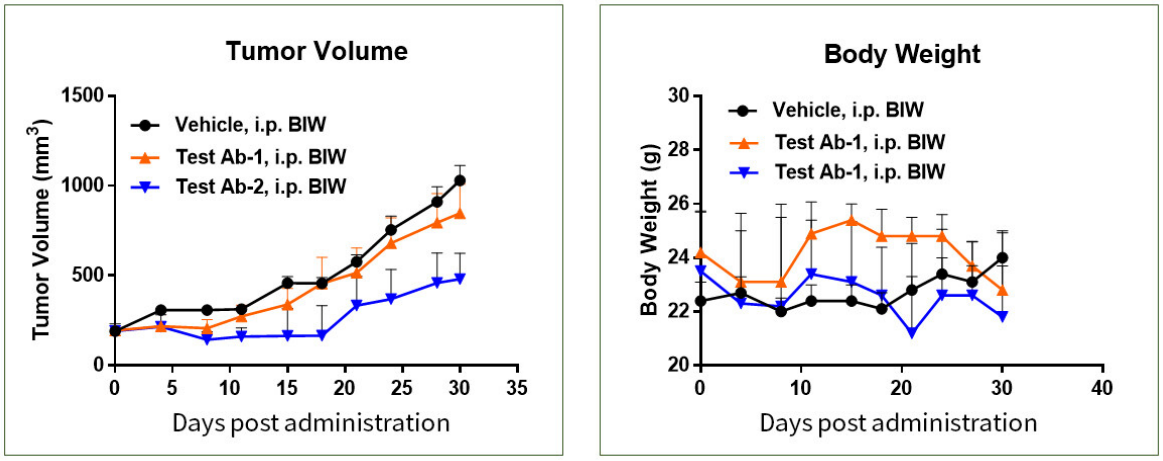

Figure 6. Example 2 of anti-tumor efficacy validation in Hu-HSC tumor-bearing mouse model

Application field

- Immuno-oncology study
- Hematological disease study
- Infectious disease study
- Gene therapy
- Study on drug targets without cross reactions
- Immunogenicity assay

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