NOD/ShiLtJGpt-Rag1/Il2rg-KO

Strain Name: NOD/ShiLtJGpt-Rag1^{em28Cd94}Il2rg^{em26Cd22}/Gpt
Strain Type: Knock-out
Strain ID: T002289
Background: NOD/ShiLtJGpt

Description

Rag1 (Recombination-activating gene 1) is a component of the enzyme complex that catalyzes VDJ recombination, a multiprotein complex that mediates the DNA cleavage phase during V(D)J recombination. V(D)J recombination occurs by rearranging different V (variable), and in some cases D (diversity) and J (ligand) gene fragments, in A variety of immunoglobulin and T cell receptor genes are assembled in developing B and T lymphocytes[1]. The VDJ recombination in Rag1 knockout pure mice does not proceed properly and T and B cells do not develop and mature normally. As a result, there are no mature $CD3^+$ $TCR\alpha\beta^+$ T cells in Rag1 knockout mice, the amount of cells in the thymus is 15-130-fold lower than in wild-type or heterozygous mice, the thymocytes are $CD8^-CD4^-$ and mostly $IL2R^+$, and no IgM or IgD can be detected in the spleen or bone marrow, indicating a complete absence of mature B cells[2] . Compared to the Prkdc-deficient Scid model, the Rag1 knockout model has a more complete deletion of mature lymphocytes and no "leak"[3].

Il2rg (IL-2 receptor subunit gamma) is a common subunit of several interleukin cytokine receptors, including IL-2, IL-4, IL-7, IL-9, IL-15 and IL-21, and is therefore also known as the common gamma chain (gamma c) of receptors[4]. In humans, mutations in gamma c can lead to X-linked severe combined immunodeficiency (X-SCID), which in turn results in the loss of six different cytokine signalling pathways[5], manifested by the loss of T cells and NK cells, and a normal number of B cells but defective function.

Gempharmatech use gene editing technology, Diaphora has inactivated the Rag1 gene and the Il2rg gene in the NOD/ShiLtJGpt background mice by deleting the coding regions of both genes. It was verified that NOD mice with deletion of the Rag1 and Il2rg genes have defective T, B and NK cell development. The completed NOD-Rag1/Il2rg KO mice will be ideal animal models for long-term transplantation and drug evaluation.

Strategy

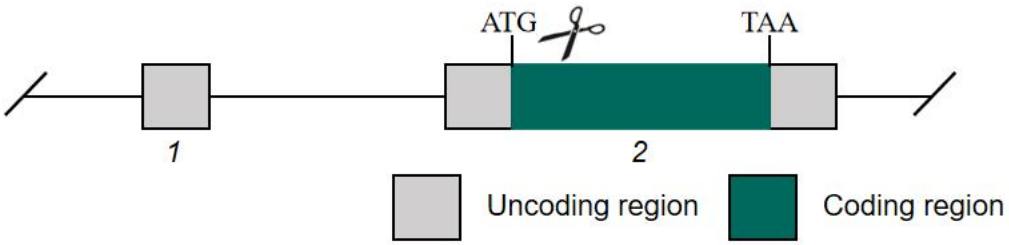

Figure 1 Schematic representation of the Rag1 knockout strategy in NOD-Rag1/Il2rg KO mice

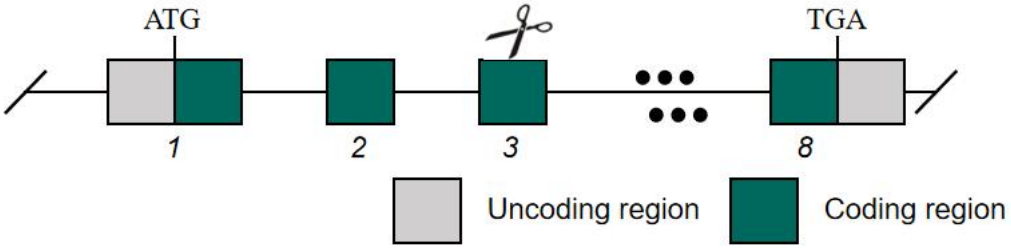

Figure 2 Schematic representation of the Il2rg knockout strategy in NOD-Rag1/Il2rg KO mice

Application

1. Human-derived immune reconstitution mouse models such as BLT humanised mice, PBMC humanised mice and $CD34^+$ humanised mice.
2. Human-derived tumour cells, tumour tissue transplantation (CDX, PDX).
3. Pharmacodynamic evaluation (small molecules, large molecules, combination drugs).
4. Human cancer models.

Data Support

1. Comparison of mice organs

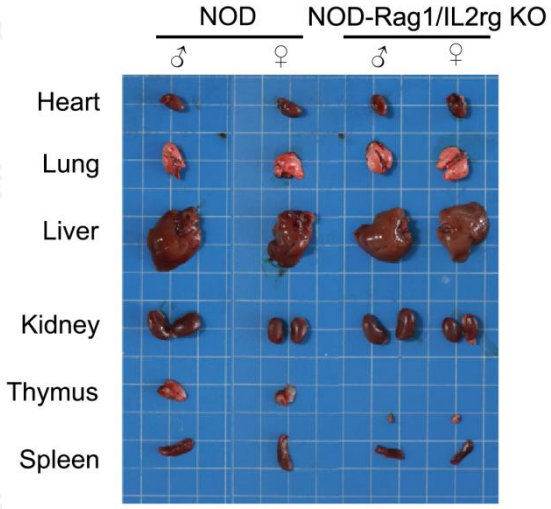

Figure 1 Comparison of major organs in mice

The main organs of NOD mice and NOD-Rag1/IL2rg KO mice were collected and photographed, and the results are shown in Figure 1. Both the thymus and spleen of NOD-Rag1/Il2rg KO mice were smaller compared to NOD mice.

2. Detection of T/B/NK cell ratio in spleen

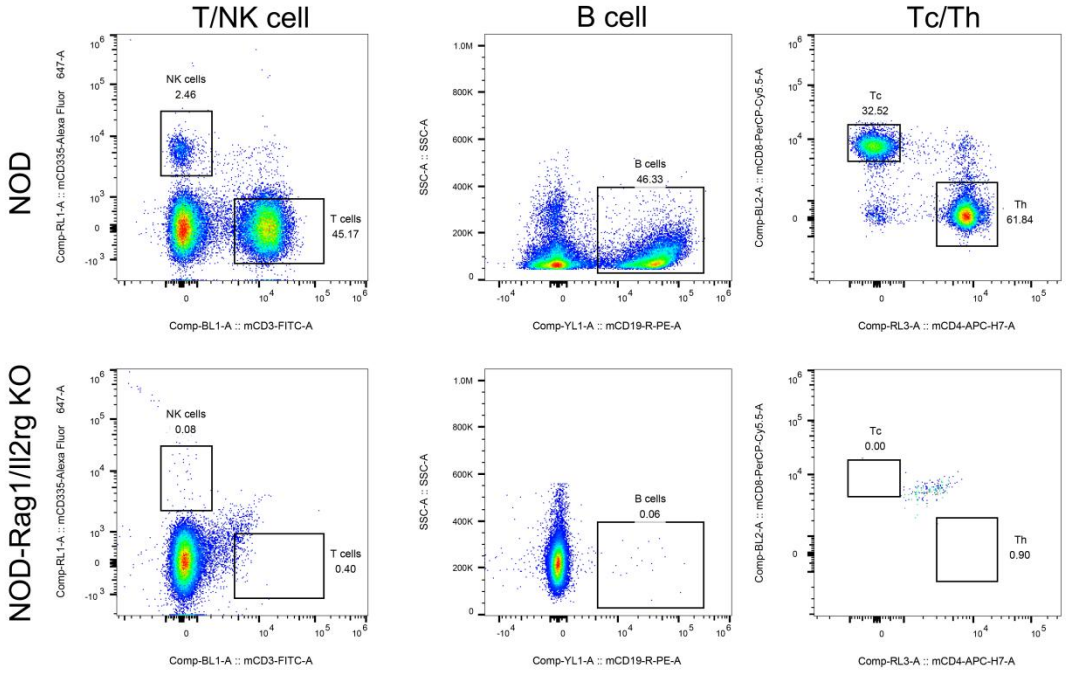

Figure 2 T/B/NK cell expression in the spleen

The expression of T, B and NK cells in the spleen of NOD mice and NOD-Rag1/Il2rg KO mice was detected by flow cytometry, and the results are shown in Figure 2. Compared with NOD mice, T, B and NK cells in the spleen of NOD-Rag1/Il2rg KO mice were undetectable.

3. Detection of the proportion of myeloid cells in the spleen

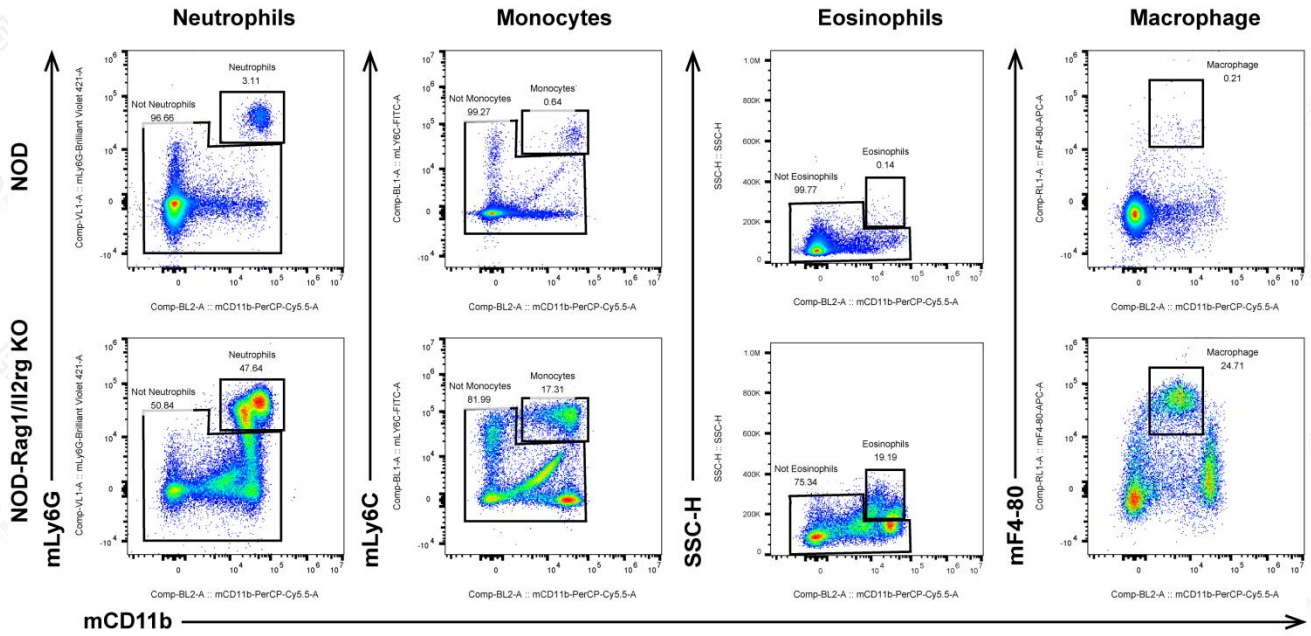

Figure 3 Expression of myeloid cells in the spleen

The expression of neutrophils, monocytes, eosinophils and macrophages in the spleen of NOD mice and NOD-Rag1/Il2rg KO mice were detected by flow cytometry, and the results are shown in Figure 3, the spleen of NOD-Rag1/Il2rg KO mice showed a significant increase in neutrophils, monocytes, eosinophils and macrophages compared to NOD mice.

References

1. Zhao Y, Su H, Shen X, et al . The immunological function of CD52 and its targeting in organ transplantation. Inflamm Res. 2017 Jul;66(7):571-578.
2. Adegoke AO, Lin J, Anderson CC. Loss of thymic function promotes EAE relapse in anti-CD52-treated mice. Curr Res Immunol. 2022 Mar 8;3:37-41.
3. Kasarello K, Mirowska-Guzel D. Anti-CD52 Therapy for Multiple Sclerosis: An Update in the COVID Era. Immunotargets Ther. 2021 Jul 7;10:237-246.
4. Bhamidipati K, Silberstein JL, Chaichian Y, et al. CD52 Is Elevated on B cells of SLE Patients and Regulates B Cell Function. Front Immunol. 2021 Feb 4;11:626820.
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