B6-IL10 KO

Strain Name：B6/JGpt-Il10^{em1Cd4885}/Gpt

Strain type：Knock Out

Strain number：T005959

Background：C57BL/6JGpt

Description

Interleukin-10 (IL10) belongs to the interferon family of cytokines and plays a critical role in the shaping of immune responses. Almost all innate and adaptive immune cells can secrete IL10, such as macrophage, monocyte, dendritic cells, epithelial cells, mast cells, T lymphocytes, B lymphocytes, NK cells[1,2]. But principally by activated macrophage and Th2 T cells, IL-10 generally promotes the development of humoral, Th2 cytokine-driven immune responses. IL-10 can down-regulates the expression of Th1 cytokines, MHC class II Ags, and costimulatory molecules on macrophages. It also enhances B cell survival, proliferation, and antibody production[3]. At the same time, after IL10 binding to its receptor, it activates signaling pathways that can inhibit tumor necrosis factor alpha (TNF- α), IL-1, IL-6, IL-8, granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF) synthesis, thereby playing an anti-inflammatory role[4]. IL-10 can inhibit tumor-related inflammation by regulating the balance between Treg cells and TH17 cells[5].

IL-10 deficient mice spontaneously develop enterocolitis when housed in conventional environments, but when housed in SPF conditions IL-10-deficient mice develop inflammation limited to the colon, and introduction of enteric flora play can promote the development of spontaneous colitis in these mice[6-7]. B6-IL10 KO mice develop colitis at 6 month age. B6-IL10 KO mice can used for the study of colitis, tumor, immunity, inflammation.

Strategy

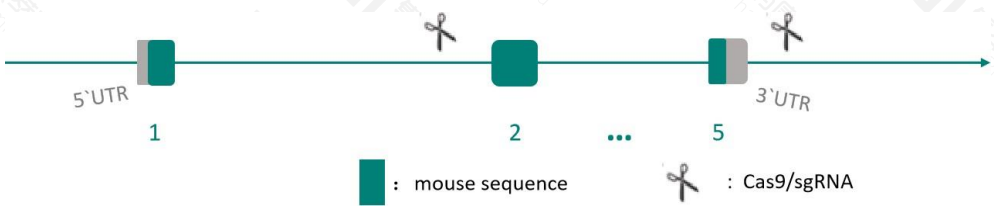


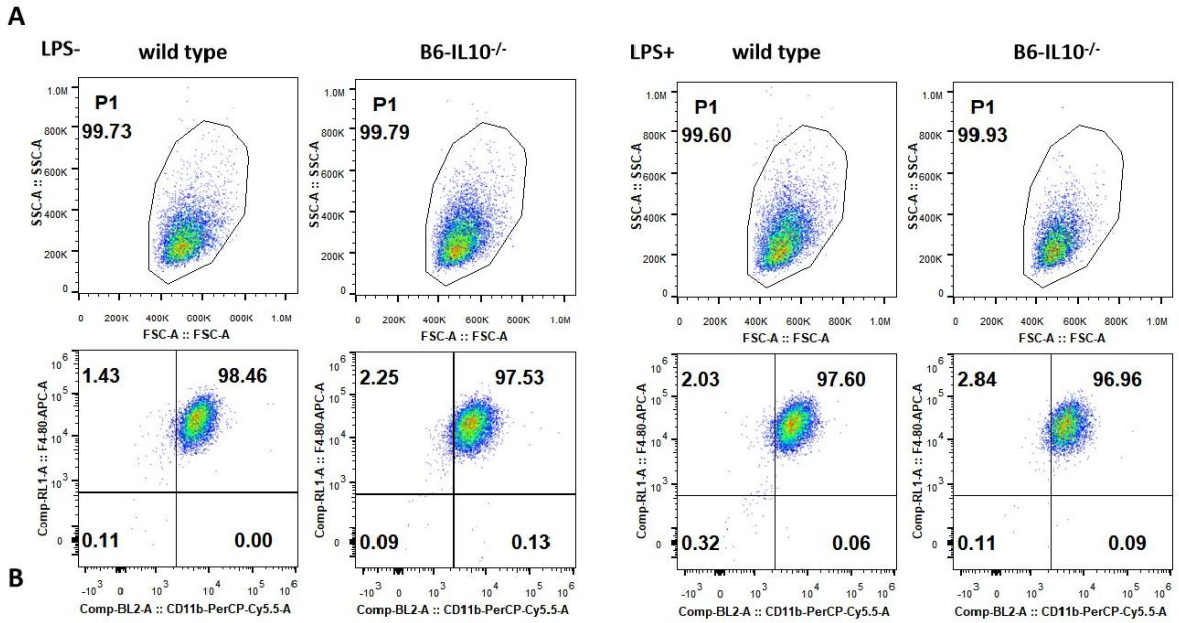
Fig.1 Schematic diagram of B6-IL10 KO mice strategy.

Application

1. Studying colitis and immunoregulatory pathways
2. Inflammatory bowel disease
3. Endocrine deficiency research

Data support

1. IL10 expression analysis



SampleNo.	2-ΔΔCT
B6	1
wt-1(LPS⁻)	35.3
wt-1(LPS⁺)	166.96
wt-2#(LPS⁻)	30.7
wt-2#(LPS⁺)	185.89
wt-3(LPS⁻)	25.6
wt-3(LPS⁺)	164.47
IL10 KO-45#(LPS⁻)	#DIV/0!
IL10 KO-45#(LPS⁺)	#DIV/0!
IL10 KO-50#(LPS⁻)	#DIV/0!
IL10 KO-50#(LPS⁺)	#DIV/0!

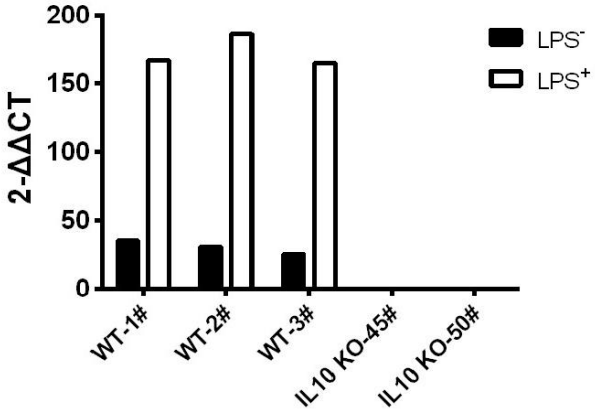


Figure.2 Detection of IL10 expression in B6-IL10 KOm mice. Bone marrow cells were isolated and cultured with M-CSF-containing culture medium for 7 days. After stimulation with LPS for 1 h at D7, macrophage was detected, and IL-10 expression in macrophage was detected by RT-QPR. The results showed that after 7 days inducted and stimulated, $CD11b^{+}$ $F4/80^{+}$ cells could be detected in wild type and B6-IL10 KO mice regardless of whether they were stimulated with LPS, and the ratio was similar (Figure A) . The expression of IL10 mRNA can be detected in wild type mouse and increased after LPS stimulation. In B6-IL10 KO mice, IL-10 expression was not detected with or without LPS stimulation. indicating successful IL10 gene knockout (Figure B). **The results showed that** the IL10 gene was successfully knocked out in B6-IL10 KO mice.

2. B6-IL 10 KO mice kept in SPF conditions developed colitis

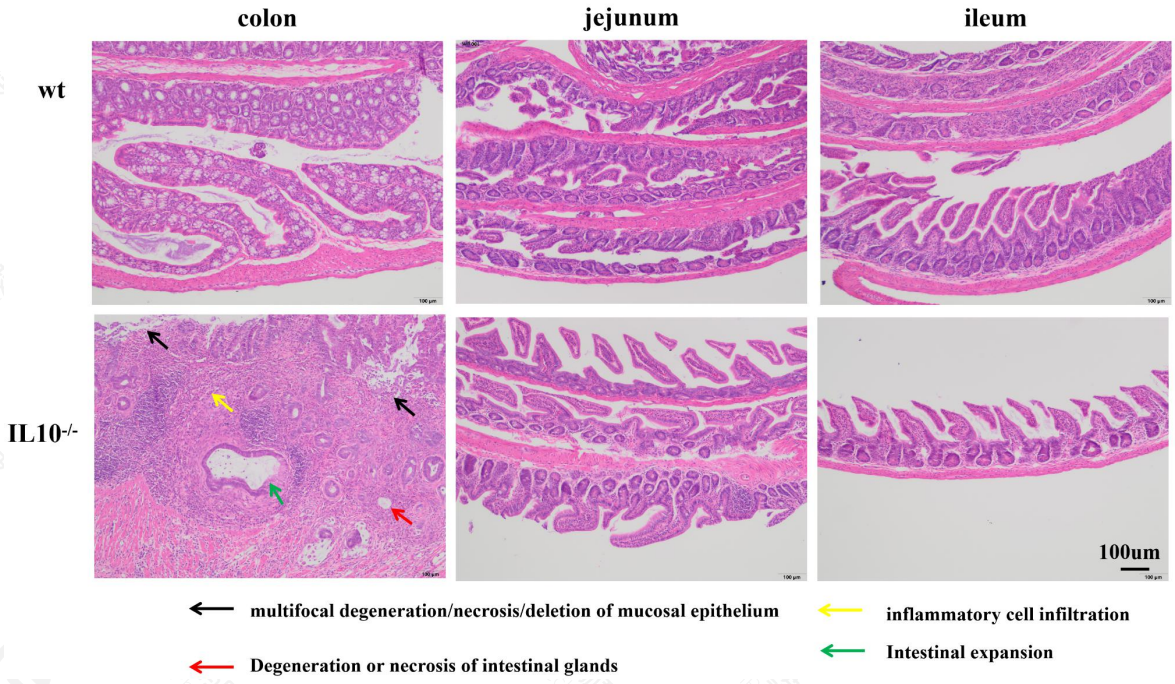


Figure.3 Histopathology of colonic changes in IL-10 KO mice. Under SPF conditions, B6-IL10 KO mice were fed to 6 months of age, and pathological changes of the colon, jejunum, and ileum were analyzed. The results showed that compared with WT mice, the colon of B6-IL10 KO mice showed multifocal degeneration/necrosis/deletion of mucosal epithelium and intestinal gland. Only a few mucosal epithelium and intestinal gland were observed, some intestinal glands were compensatory dilated, necrotic and exfoliated glandular epithelial cells were found in the lumen. Lamina propria and submucosa infiltrated inflammatory cells and accompanied by fibrous hyperplasia, a small amount of inflammatory cell infiltration can be seen in the muscle layer, and the inflammatory cells are mainly neutrophils.

Compared with WT mice, jejunum and ileum showed no lesions. These results indicate that b6-IL10 KO mice developed colitis under SPF conditions **(**Note: Colitis in this model is highly microbiome-dependent; disease severity and age of onset will be affected by different facility microbiomes).

References

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2. Asadullah, K., W. Sterry, and H. D. Volk. "Interleukin-10 therapy—review of a new approach." *Pharmacological reviews* 55.2 (2003): 241-269.

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4. de Waal Malefyt, Rene, et al. "Interleukin 10 (IL-10) inhibits cytokine synthesis by human monocytes: an autoregulatory role of IL-10 produced by monocytes." *The Journal of experimental medicine* 174.5 (1991): 1209-1220.

5. Rubtsov, Yuri P., et al. "Regulatory T cell-derived interleukin-10 limits inflammation at environmental interfaces." *Immunity* 28.4 (2008): 546-558.