NCG-BAFF

Strain Name: NOD/ShiLtJGpt-*Prkdc*^{em26Cd52}*Il2rg*^{em26Cd22}*Baff*$^{em1Cin(hBAFF)}$/Gpt

Strain Type: Knock-in

Strain ID: T006835

Background: NOD/ShiLtJGpt

Description

B-cell activating factor (BAFF), encoded by the TNFSF13B gene, is also known as tumor necrosis factor ligand superfamily member 13B, B lymphocyte stimulator (BLyS), or dendritic cell-derived TNF-like molecule (CD257). BAFF is a cytokine that belongs to the tumor necrosis factor (TNF) ligand family, which expressed on various cell types including monocytes, dendritic cells, bone marrow stromal cells and epithelial cells[1].

BAFF is an important regulator of peripheral B-cell survival, maturation, immunoglobulin production and immunoglobulin class-switch recombination (CSR) [1, 2]. BAFF-deficient mice exhibit defects in peripheral B-cell maturation and decreased levels of immunoglobulins[3]. Conversely, overexpression of BAFF leads to B-cell hyperplasia, abnormally high antibody production, which results in systemic lupus erythematosus, rheumatoid arthritis, and many other autoimmune diseases[1, 2].

However, substantial differences exist between human and mouse immune system. Findings in mouse models are hard to be directly translatable to human, particularly in the development and evaluation of drugs. The use of hematopoietic humanized mice has partially solved this problem. Nevertheless, maturation of human B cells and development in T cells remains inefficient in current humanized mice.

Because of the importance of BAFF in B cells maturation and inefficient interaction of the hBAFF receptor with mBAFF, GemPharmatech use gene editing technology to develop the BAFF humanized mice by replacing the mBAFF-encoding gene with full-length hBAFF cDNA in NCG mice background. Although the replacement of hBAFF in BRGS background did not improve the mature and effector human B cells in hu-mice, but it maybe due to the decreased T-cell numbers[4]. Thus, the humanization of BAFF couldn't significantly improved the mature and effector human B cells, but bred with other cytokine

humanized mice maybe make a big difference. Besides, the humanized hBAFF mice are ideal preclinical models testing therapies in autoimmune diseases, such as RA, SLE, etc[5,6].

Strategy

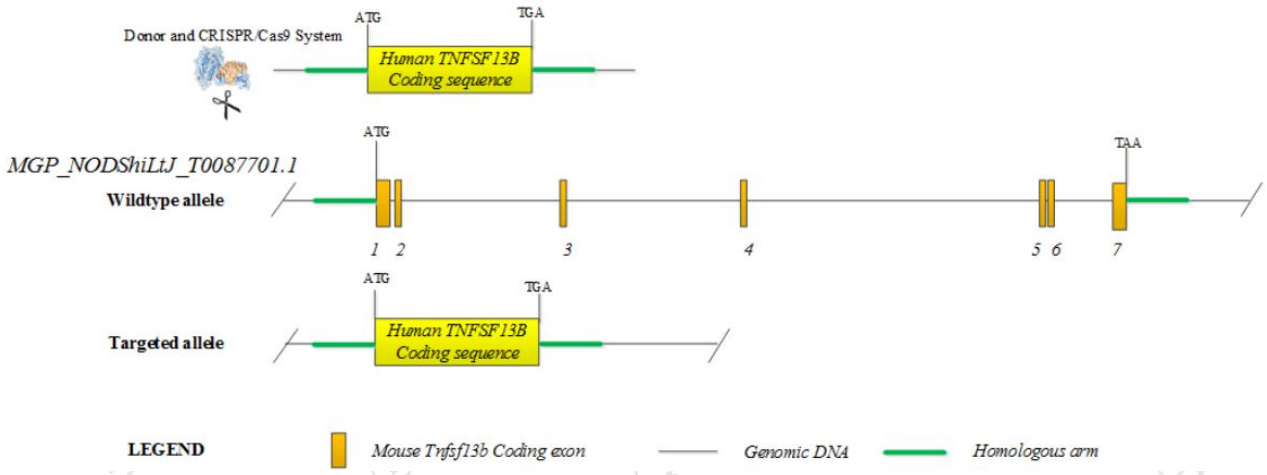

Fig 1. Schematic diagram of humanization strategy in NCG-BAFF mice.

Application

1. Human immune system development
2. Research on humanized mice
3. Research on autoimmune diseases

Data support

1. hBAFF protein expression analysis

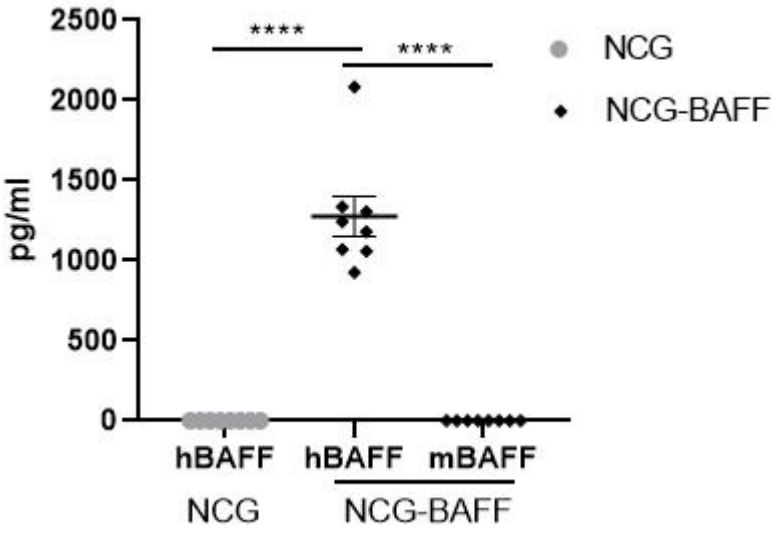

Fig 2. Detection of BAFF in NCG-BAFF mice. Human BAFF and mouse BAFF concentration in the serum of NCG and NCG-BAFF mice was quantified by ELISA (n = 8, bar represents the smallest, error bar represents SEM, *****P <0 .0001). The NCG-BAFF mice expressed hBAFF but not mBAFF, while wild-type NCG mice could not detect human BAFF protein expression.

References

[1] G, A, Lied, A. Berstad. Functional and Clinical Aspects of the B-Cell-Activating Factor (BAFF): A Narrative Review[J]. Scandinavian Journal of Immunology, 2011.

[2] Mackay F, Browning JL. BAFF: a fundamental survival factor for B cells. Immunology 2002;2:465–75.

[3] Schiemann B, Gommerman JL, Vora K, et al. An essential role for BAFF in the normal development of B cells through a BCMA independent pathway. Science. 2001;293(5537):2111–2114.

[4] Lang J , Zhang B , Kelly M , et al. Replacing mouse BAFF with human BAFF does not improve B-cell maturation in hematopoietic humanized mice[J]. Blood Advances, 2017, 1(27):2729.

[5] Gunawan M , Her Z , Liu M , et al. A Novel Human Systemic Lupus Erythematosus Model in Humanised Mice[J]. Scientific Reports, 2017, 7(1):16642.

[6] Schinnerling K , Rosas C , Soto L , et al. Humanized Mouse Models of Rheumatoid Arthritis for Studies on Immunopathogenesis and Preclinical Testing of Cell-Based Therapies[J]. Frontiers in Immunology, 2019, 10.