

## B6-hIGHA1

**Strain Name:** C57BL/6JGpt-IGHA1<sup>em1Cin(hIGHA1)</sup>/Gpt

**Strain Type:** Knock-in

**Strain ID:** T056195

**Background:** C57BL/6JGpt

### Description

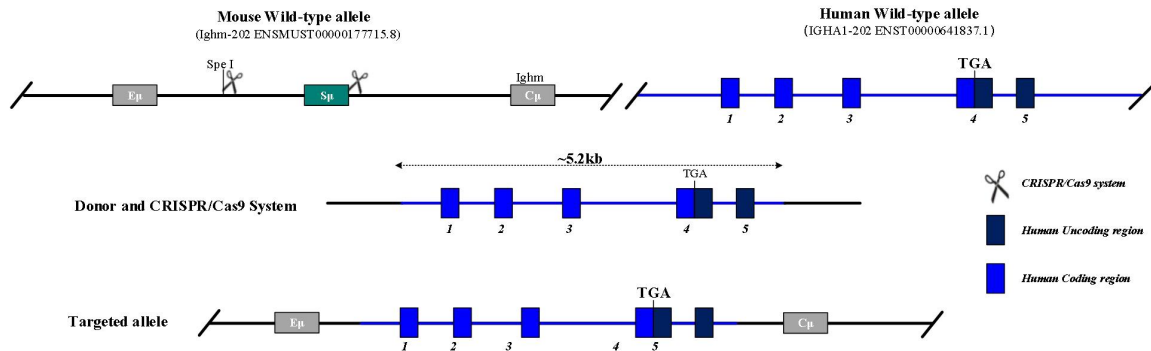
B cells can produce many types of antibodies, including IgM, IgA, IgG, IgE, IgD. Differentiation of classes or isotypes of antibodies is based on the constant region of the heavy chain. IGHA1 is the immunoglobulin heavy chain constant region  $\alpha$  1, or IgA1 isotype heavy chain constant region. There are two isotypes of IgA in humans, IgA1 and IgA2. Mice have only one type of IgA, which is similar to human IgA2.

Human IgA exists in two forms, monomeric and dimeric, with monomeric IgA comprising 5-15% of serum immunoglobulins, and dimeric IgA in mucosal surfaces such as saliva, gastrointestinal secretions, bronchial fluid, and milk. Mucosal IgA plays an important role in host defense by neutralizing infectious agents at mucosal surfaces. IgA deficiency is the most common immunodeficiency in which serum and mucosal IgA production is insufficient<sup>[1]</sup>.

IGHA1, involved in antibacterial humoral response, glomerular filtration, and positive regulation of respiratory burst. IgA nephropathy is due to the deposition of immune complexes composed of galactose-deficient IgA1 in the patient's glomerulus, thereby activating mesangial cells and inducing renal injury through cell proliferation and excessive production of extracellular matrix components, cytokines, and chemokines<sup>[2]</sup>. In addition, in patients with autoimmune diseases such as rheumatoid arthritis and ankylosing spondylitis, there are excessively high IgA1 autoreactive antibodies.

GemPharmatech developed the C57BL/6-hIGHA1 humanized mouse by inserting the gene encoding the secreted and membrane forms of human  $\alpha$ 1 HC into the E $\mu$  (IgM enhancer) and C $\mu$  (IgM constant region) to replace S $\mu$ <sup>[3]</sup>. This strain is an ideal model for studying B cell development, IgA abnormal related disease, e.g. IgA nephropathy, and drugs efficacy and safety evaluation targeting IGHA1.

## Strategy



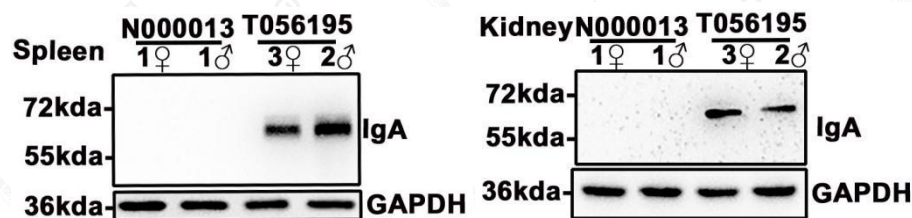
**Fig.1 Schematic diagram of IGHA1 humanization strategy in C57BL/6-hIGHA1 mice.**

## Application

1. Research on effects of IgA-like receptors throughout B-cell differentiation
2. Research on IgA nephropathy
3. Research on autoimmune diseases related to IgA1 autoreactive antibodies
4. Efficacy and safety evaluation for Anti-IGHA1 drugs

## Data support

### 1. hIGHA1 protein expression analysis



**Fig.2 Detection of IGHA1 expression in C57BL/6-hIGHA1 mice.**

The expression of human IGHA1 protein can be detected in spleen and kidney of B6-hIGHA1 but not B6 wild type mice through western blot.

## References

1. Suzuki H, Kaneko H, Fukao T, et al. Various expression patterns of alpha1 and alpha2 genes in IgA deficiency. *Allergol Int.* 2009;58(1):111-117.
2. Knoppova B, Reily C, Maillard N, et al. The Origin and Activities of IgA1-Containing Immune Complexes in IgA Nephropathy. *Front Immunol.* 2016;7:117.
3. Duchez S, Amin R, Cogné N, et al. Premature replacement of mu with alpha immunoglobulin chains impairs lymphopoiesis and mucosal homing but promotes plasma cell maturation. *Proc Natl Acad Sci U S A.* 2010;107(7):3064-3069.