BIOCYTOGEN

RenMab

Fully Human Antibody Mouse Revolutionizes Antibody Drug Discovery

Key Features of RenMab™ Mouse:

1. An intact immune system compared to wild-type mouse
2. Full human VDJ expression in the variable domains of heavy chain and kappa light chain genes
3. Fully human antibody repertoire as shown by CDR3 analysis
4. Highly similar immune responses compared to wild-type mouse

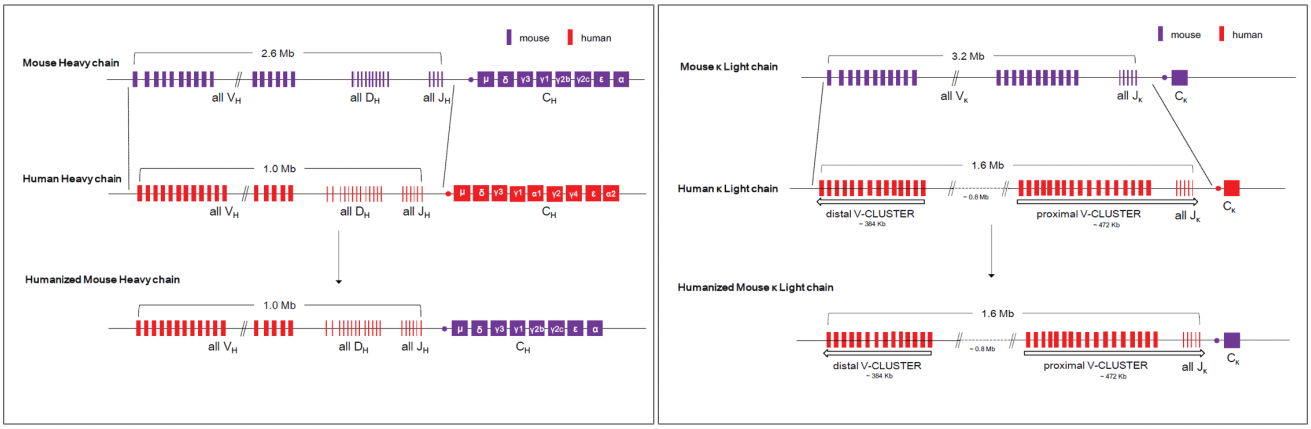
RenMab™ Mouse

Generation of RenMab™ Mouse

RenMab

Biocytogen has developed a fully human antibody mouse (RenMab™ Mouse), whose genes that encode entire antibody variable regions are replaced *in situ* by human Ig heavy chain and κ light chain using Mb-scale chromosome. Constant region of mouse gene has been maintained to ensure proper B cell development. RenMab™ Mouse provides an efficient platform for fully human antibody generation, characterization, therapeutic antibody discovery, and rapid *in vivo* efficacy screening.

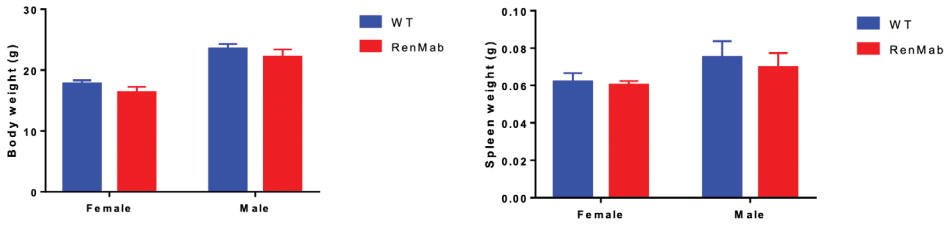
Mouse variable regions of the heavy and k light chains are replaced by the human counterparts *in situ*



RenMab™ Technical Advantages

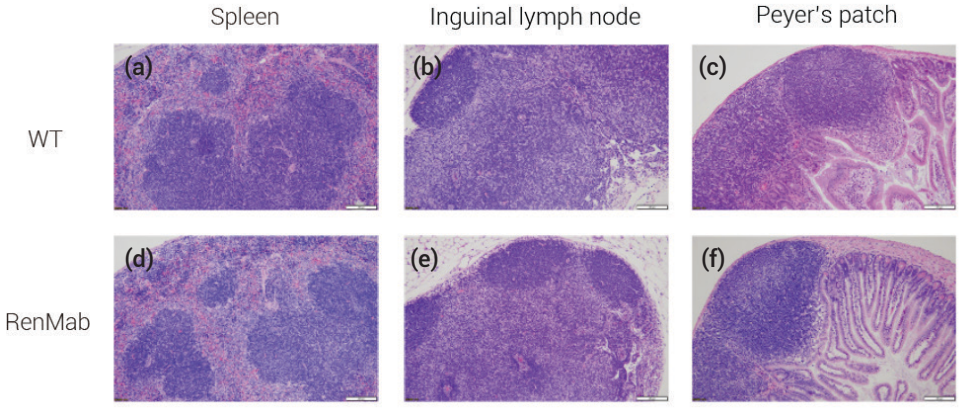
I: RenMab™ Mouse demonstrates an intact immune system compared to wild-type mouse

Body Weight and Spleen Wight Measurement



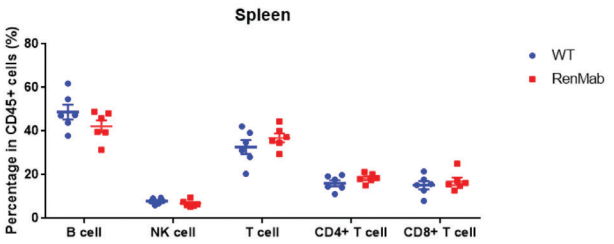
RenMab™ mouse exhibits healthy growth, which is essentially identical to that of wild-type mouse.

Lymphoid Organ Histology



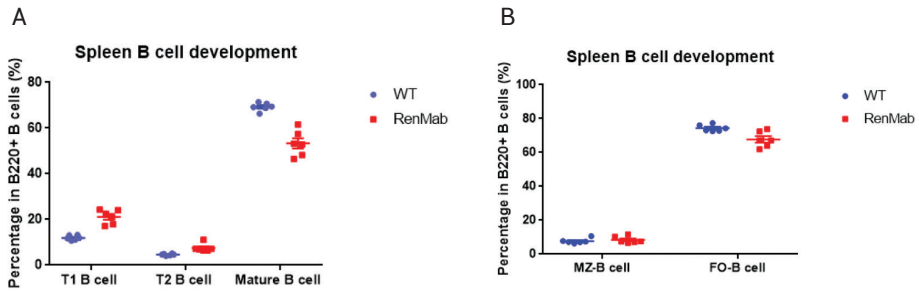
Representative sections of spleen (a and d), inguinal lymph node (b and e), and Peyer's patch (c and f) from WT (a-c) or RenMab™ (d-f) mice were H&E stained. Both WT (C57BL/6) and RenMab™ mice demonstrate normal anatomical structures with well-defined follicles and show no significant difference in histological morphology.

Immune Cell Profiling



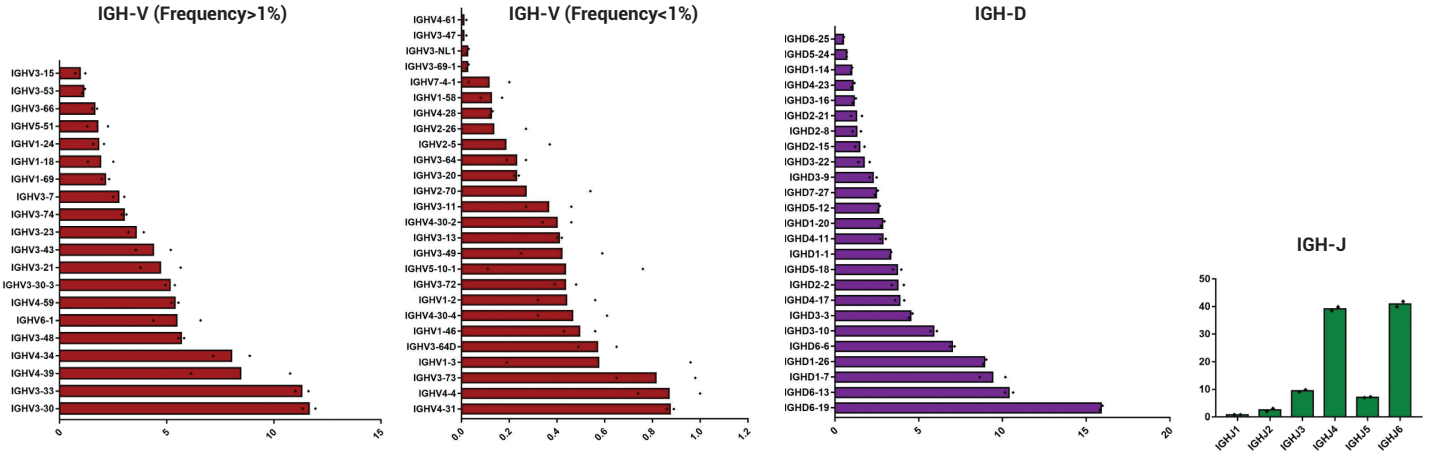
The percentages of immune cells in spleen were analyzed by flow cytometry. In RenMab™ Mouse, the percentage of B cells,T cells, NK cells, CD4+ T cells and CD8+ T cells in spleen were identical to those of wild type mice.

Proper B cell development of RenMab compared to WT mice



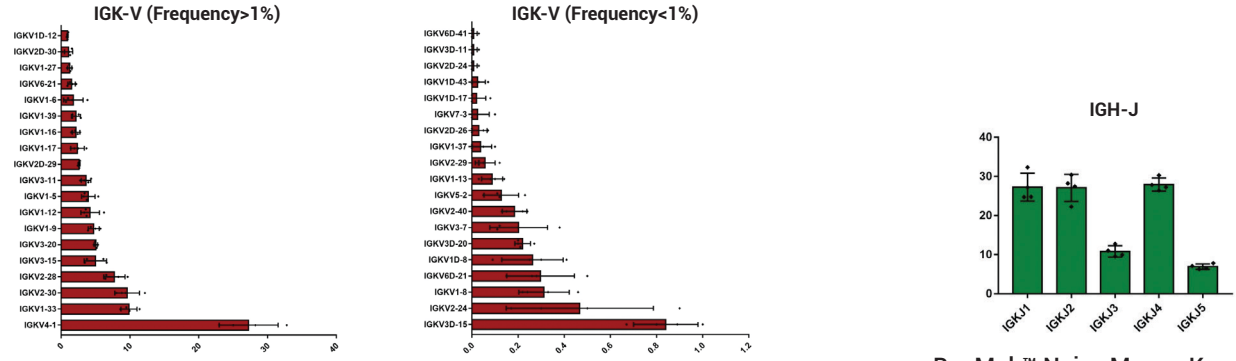
(A) IgM and IgD expression on B220$^+$ splenocytes were analyzed by flow cytometry. Transitional type 1 (T1, B220$^+$IgM$^+$IgD$^-$), Transitional type 2 (T2, B220$^+$IgM$^+$IgD$^+$), Mature (M, B220$^+$IgM^{low}IgD$^-$) cell population. (B) CD21 and CD23 expression on the surface of B220$^+$ splenocytes were analyzed by flow cytometry. Marginal-zone (MZ, B220$^+$CD21$^+$CD23$^-$) and Follicular (FO, B220$^+$CD21^{LOW}CD23$^+$) B cells were quantitatively analyzed. No significant difference was observed between RenMab™ mouse and wild type mouse.

II. Full human VDJ expression in the variable domains of heavy chain and kappa light chain genes



RenMab™ Naive Mouse Heavy Chain IGHV Germline Usage

RenMab™ Naive Mouse Heavy Chain IGHD & IGHJ Germline

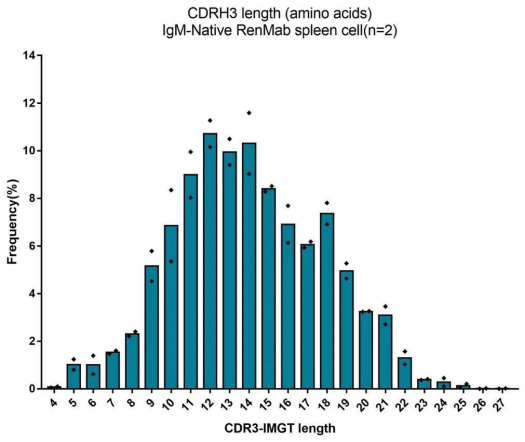


RenMab™ Naive Mouse Kappa Light Chain IGKV Germline Usage

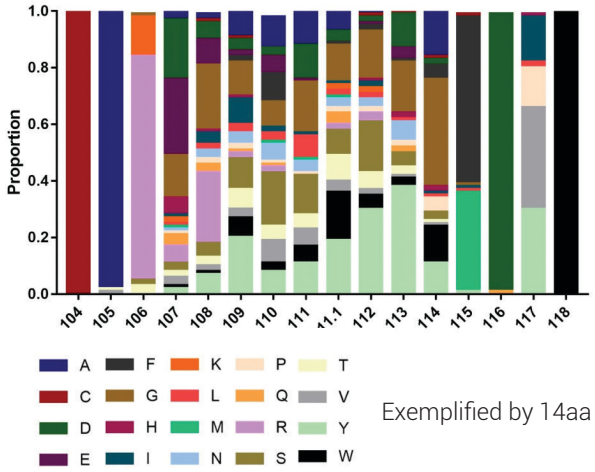
RenMab™ Naive Mouse Kappa Light Chain IGKJ Germline Usage

III. RenMab™ Mouse produces fully human antibody repertoire as shown by CDR3 analysis

RenMab™ Heavy Chain CDR3 Length Distribution from analysis



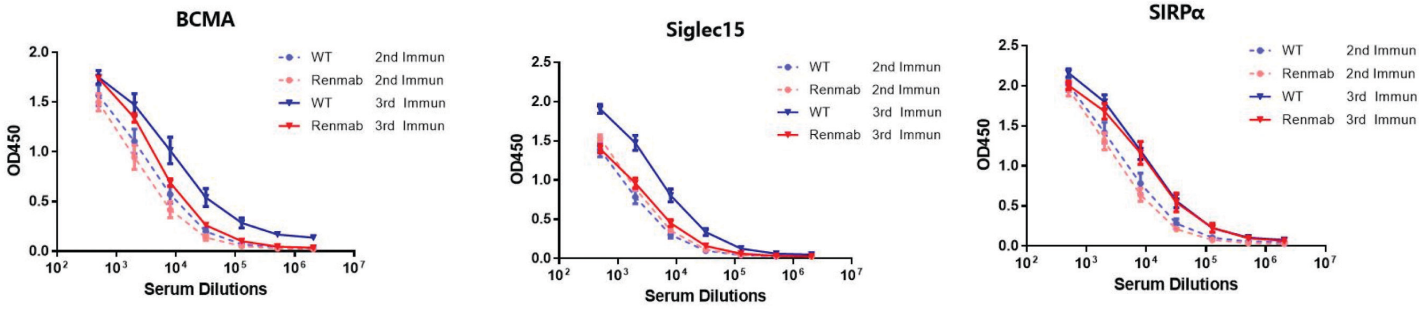
RenMab™ Heavy Chain CDR3 Amino Acid Usage Frequency



Exemplified by 14aa length

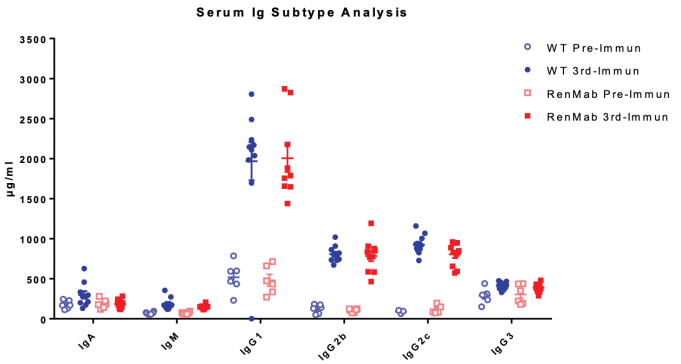
IV. RenMab™ Mouse demonstrates highly similar immune responses compared to WT mouse

Antibody Titer Post 2nd and 3rd Immunization



After 2nd and 3rd immunization with BCMA, Siglec15, and SIRPα antigens, antigen-specific antibody titer of blood taken from WT (C57BL/6) and RenMab™ mice were analyzed by ELISA.The results showed that the immune effects of RenMab™ and WT mice were consistent.

Serum Ig Subtype Levels of RenMab™ Mouse vs. WT mouse



Different Ig subtypes in the serum of RenMab™ and WT mice were quantitatively measured by ELISA (n=6). No significant differences (n=6) in IgA, IgG1, IgG2b, IgG2c, IgG3 and IgM levels were observed.

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