RenMab

An Innovative Platform of Biocytogen

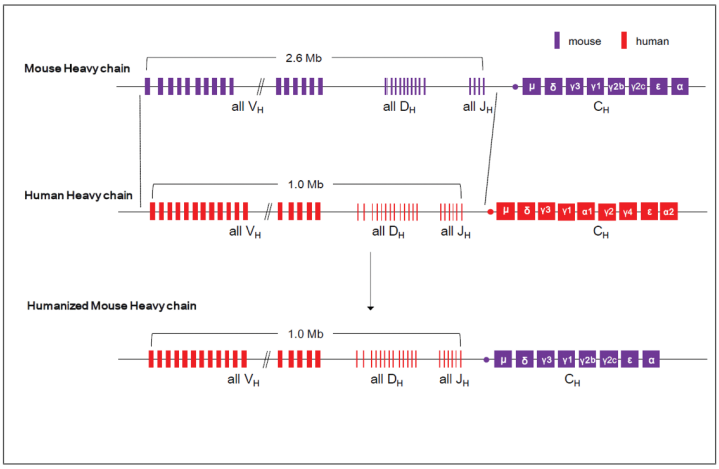
Key Features:

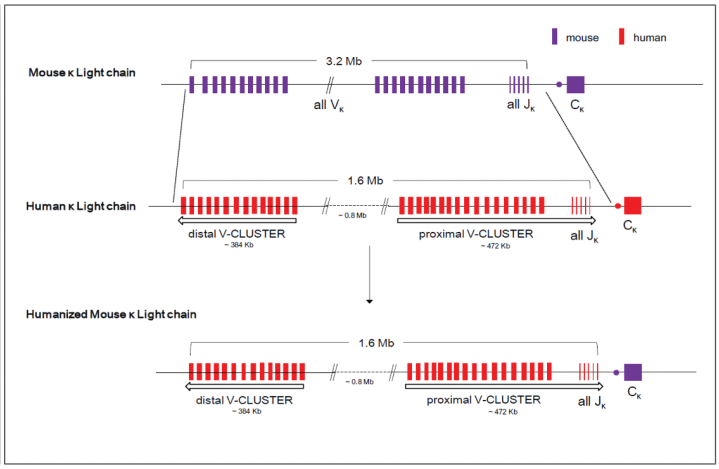
- Developed using Biocytogen's unique Mb-scale chromosome engineering technology
- Variable regions of mouse heavy chain are and k light chain genes are replaced by human counterparts *in situ*
- Constant region is retained to ensure proper B cell development
- Normal immune organs development and good immune response to immunization like WT mouse
- RenMab antibodies exhibit human-like repertoire and high affinity to antigens in subnanomolar range

Generation of RenMab™ Mouse

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 through Mb-scale chromosome engineering technology. 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*



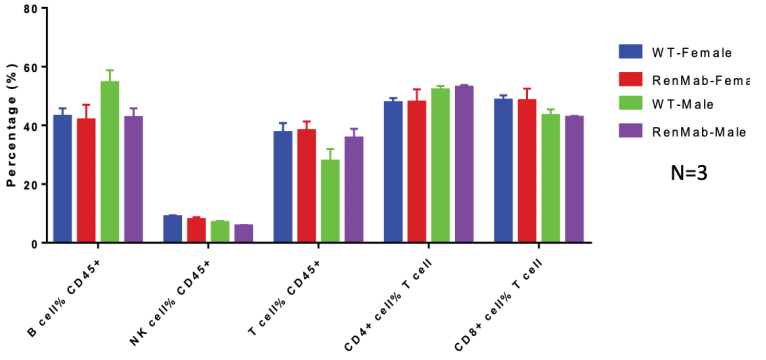


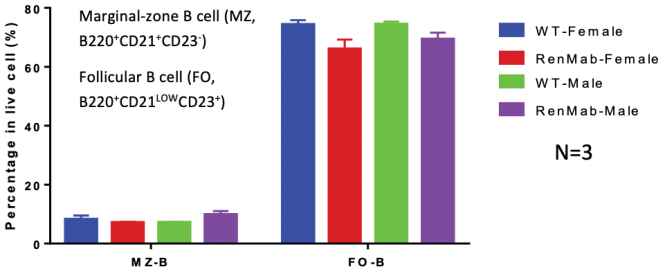
RenMab™ Mouse

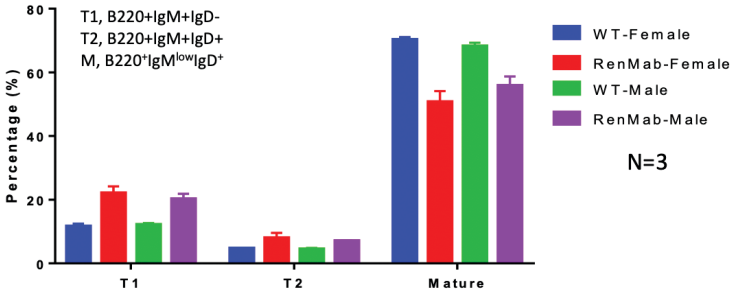
Validation Data

RenMab™ Mouse demonstrates a similar immune system to that of WT mouse

RenMab Mice immune cells profiling suggest a comparable immune system with wild type mice





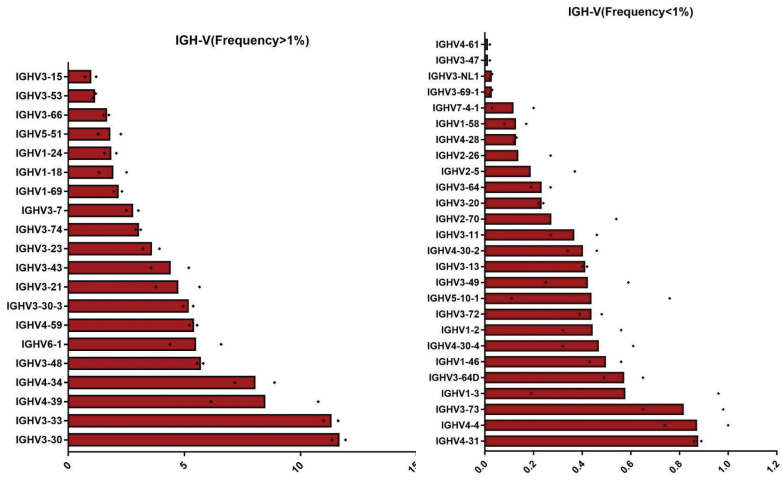


- Bone marrow, PBMC, spleen and lymph node immune cells profiling and B cell development were evaluated (only spleen data were shown on the left; full data sets are available upon request). The same was observed before and after immunization
- In RenMab mice, slight development delay from immature to mature B cells was observed. This observation is in line with other humanized mice like Trianni.

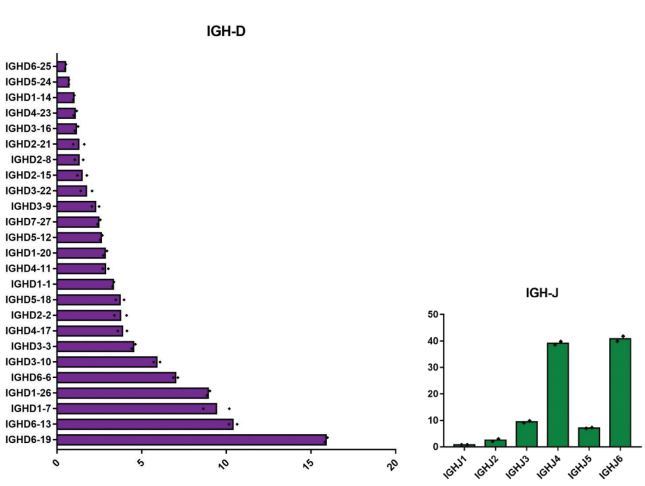
Full human VDJ expression in the variable domains of heavy chain and kappa light chain genes

The RenMab™ mouse shows WT-like expression of antibody levels and full usage of human heavy chain V, D, and J domain segments. Similarly, mouse kappa chain segments were replaced with human V and J segments and also show WT-like expression of antibody levels.

RenMab™ Naive Mouse Heavy Chain IGHV Germline Usage

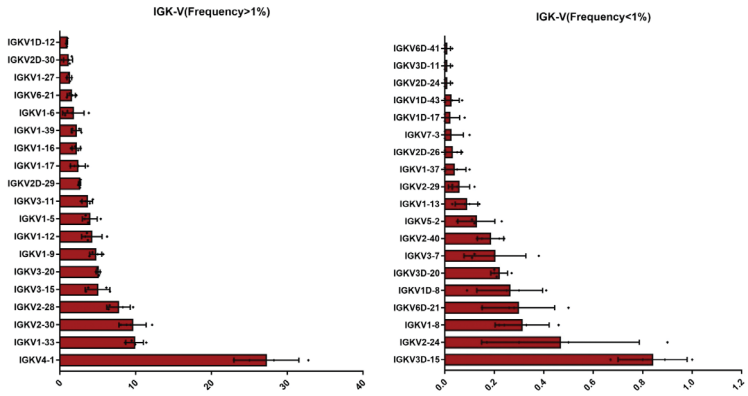


RenMab™ Naive Mouse Heavy Chain IGHD & IGHJ Germline

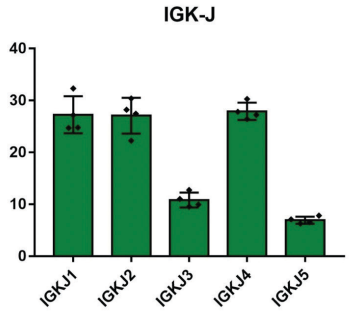


RenMab™ Mouse

RenMab™ Naive Mouse Kappa Chain IGKV Germline Usage

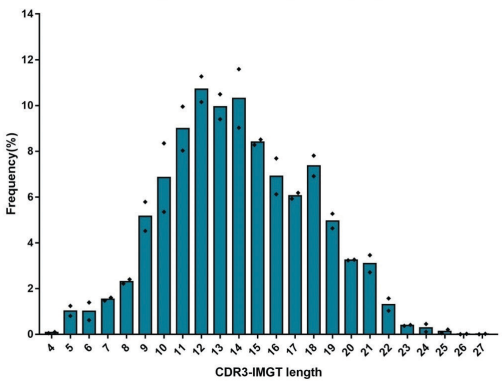


RenMab™ Naive Mouse Kappa Light Chain IGKJ Germline Usage



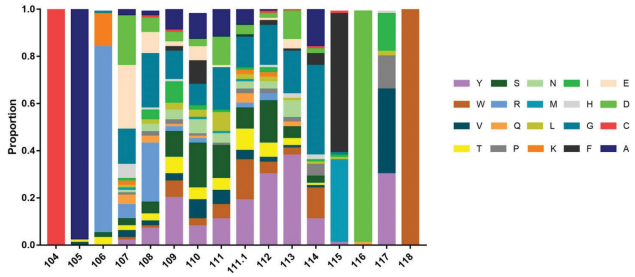
RenMab™ Mouse produces human-like antibody repertoire as shown by CDR3 analysis

CDRH3 length (amino acids) IgM-Native RenMab™ spleen cell (n=2)



Heavy chain CDR3 length distribution: median length 14.2 amino acids

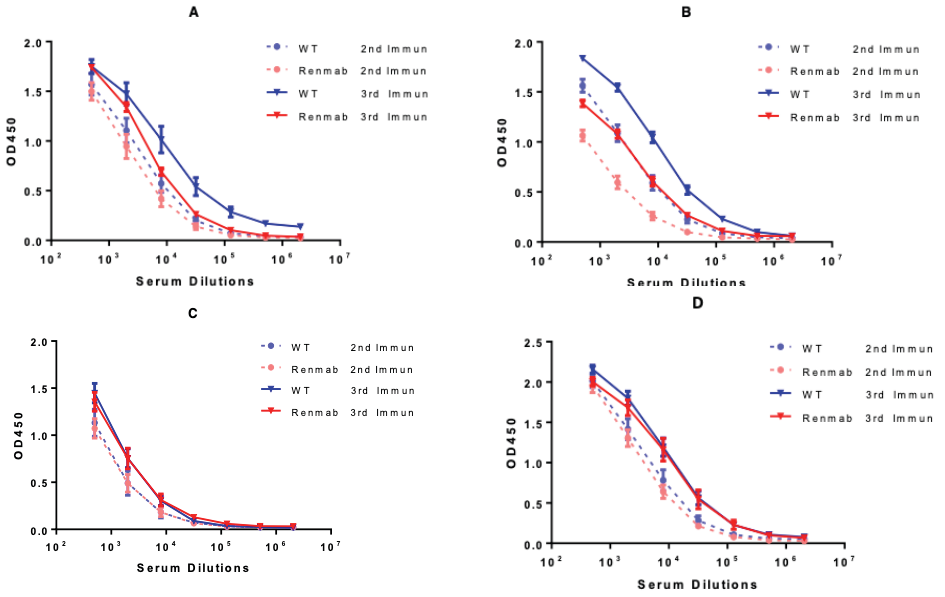
RenMab™ Heavy Chain CDR3 Amino Acid Usage Frequency



Human-like heavy chain V-D-J recombination pattern: (1) length-dependent usage of tyrosine; (2) preferred usage of D, E and G at IMGT position 107; (3) IMGT position 115 and 117 are conserved due to human JH4 and JH6 usage; (4) Usage of cysteine residue in CDR3, indicative of human DH2 gene family usage in V-D-J recombination

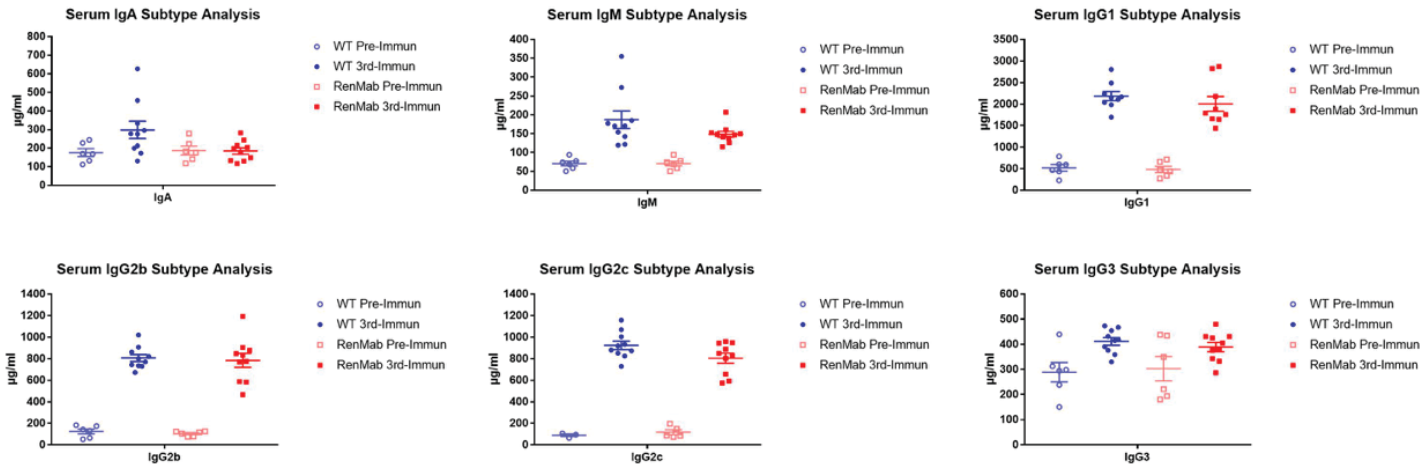
RenMab™ Mouse demonstrates highly similar immune responses compared to WT mouse

Robust immune response in RenMab™ elicited by a panel of antigens



- Robust immune responses against strong/weak antigens were observed
- Accelerated immunization strategies are being evaluated
- Several immunization strategies for difficult targets are being optimized for better outcome
- RenMab-based KO antibody discovery is ongoing

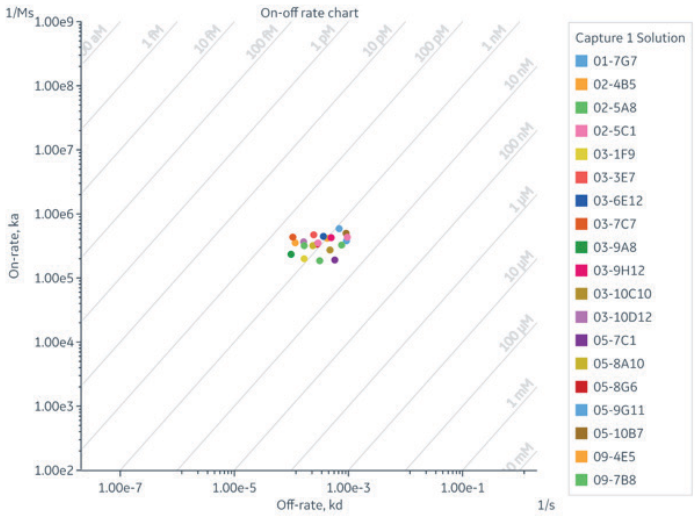
Consistent Ig isotype ratios in naive and immunized RenMab™ mice suggested successful class switch of antibodies



No significant differences in serum total IgG1, IgG2b, IgG2c, IgG3 and IgM levels were observed between RenMab and C57BL/6

RenMab™ antibodies exhibit high affinity against antigens at subnanomolar range

Clone ID	ka (1/Ms)	kd (1/s)	KD (M)	Rmax (RU)
03-7C7	4.35E+05	1.06E-04	2.43E-10	60.1
03-10D12	3.56E+05	1.07E-04	3.00E-10	75.8
09-4E5	3.54E+05	1.17E-04	3.30E-10	98.3
03-9A8	2.35E+05	9.86E-05	4.20E-10	68.0
03-3E7	4.72E+05	2.46E-04	5.22E-10	61.8
02-5A8	3.20E+05	1.68E-04	5.24E-10	56.5
05-8A10	3.19E+05	2.38E-04	7.44E-10	68.7
03-6E12	4.47E+05	3.63E-04	8.14E-10	58.5
05-8G6	3.37E+05	2.81E-04	8.32E-10	85.9
03-1F9	2.00E+05	1.67E-04	8.35E-10	90.9
02-5C1	3.67E+05	3.63E-04	9.90E-10	34.6
02-4B5	4.16E+05	4.25E-04	1.02E-09	37.6
03-9H12	4.26E+05	4.98E-04	1.17E-09	54.5
05-9G11	5.89E+05	6.87E-04	1.17E-09	62.5
09-7B8	1.86E+05	3.13E-04	1.68E-09	24.7
03-10C10	2.74E+05	4.74E-04	1.73E-09	4.9
05-10B7	4.99E+05	9.09E-04	1.82E-09	38.6
02-5C1	4.34E+05	9.54E-04	2.20E-09	31.9
02-5A8	3.27E+05	7.59E-04	2.32E-09	30.3
01-7G7	3.80E+05	9.23E-04	2.43E-09	68.3
05-7C1	1.91E+05	5.75E-04	3.01E-09	55.6



RenMab Commercial Benefits

Licensing Options
License directly with Biocytogen
Option to use through other CROs or in-house

Co-development Opportunities
Exclusive partnership and co-development opportunities for Project Intergrum

Flexibility
Flexible terms tailored to accommodate different antibody programs

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