precision antibody™

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60日で完全ヒトモノクロ抗体の作製

戦略的提携

Precision Antibody, a service division of A&G Pharmaceutical Inc is pleased to announce business alliance with **Trans Chromosomics**

A&G Pharmaceutical Inc/Precision Antibody

- Theranostic antibody development against breast & lung cancer
- Global leader in antibody development

CEO, Ginette Serrero Ph.D.
Established: 1, June 2000
www.agpharma.com

Trans Chromosomics (TC)

- *Global Leader Of Artificial Chromosome Engineering Technology*
- *Innovative Platforms For Biopharmaceuticals, Cell/Gene Therapy, And Xenotransplantation*

President CEO, Mitsuo Oshimura Ph.D.
Established : 17 December 2014
www.trans-chromo.com

President, Jun Hayashi Ph.D.
Established: 1, June 2000
www.precisionantibody.com

概要

- 完全ヒト抗体産生マウス（TC-mAb™マウス）は、免疫抑制がなく、 Precision Antibody社（PA）の技術で短期間に、力価の高い抗原特異的抗体を作製可能
- PAは、TC-mAb™マウスから、約60日で完全ヒトモノクローナル抗体（mAb）を作製可能
- TC-mAb™マウスは100%ヒト抗体を発現
- 作製された完全ヒトmAbは、抗体遺伝子のヒト化といった改変が不要
- 作製された完全ヒトmAbは、正常なヒトIgGレパトアを保持
- 抗原特異的完全ヒトmAb産生ハイブリドーマ細胞を高効率で作製可能
- 多数のクローン・多様なエピトープを保持する抗体を作製可能

事例紹介

事例 1
免疫: ~90KDa protein with ~75% homology with mouse ortholog

期間: 60 days from immunization to expansion of antigen-specific clones.

抗血清の力価（融合前）:

Serum Dilutions	1:1K	1:3K	1:10K	1:30K	1:100K	control
A_{620}	3.40	2.90	1.66	0.64	0.10	0.04

ELISAによる抗原特異的抗体産生細胞数の評価:

antigen: 30 ng/well　　1°Ab: 100 ng/well

OD # of Ag-positive clones (out of 1727 clones)

0.5-1.0	335
1.0-2.0	423
2.0->3.0	387
>3.0	183
Total Positive	**1,228**

~77% of clones were positive against the immunogen.

事例2
免疫: ~50KDa protein no homology to mouse proteins

期間: 60 days from immunization to expansion of antigen-specific clones.

抗血清の力価（融合前）:

Serum Dilutions	1:1K	1:3K	1:10K	1:30K	1:100K	control
A_{620}	3.02	2.94	2.60	1.80	0.95	0.04

ELISAによる抗原特異的抗体産生細胞数の評価:

antigen: 50 ng/well　　1°Ab: 100 ng/well

OD # of Ag-positive clones (out of 1920 clones)

0.5-1.0	358
1.0-2.0	205
2.0-3.0	276
>3.0	118
Total Positive	**957**

~50% of clones were positive against the immunogen.

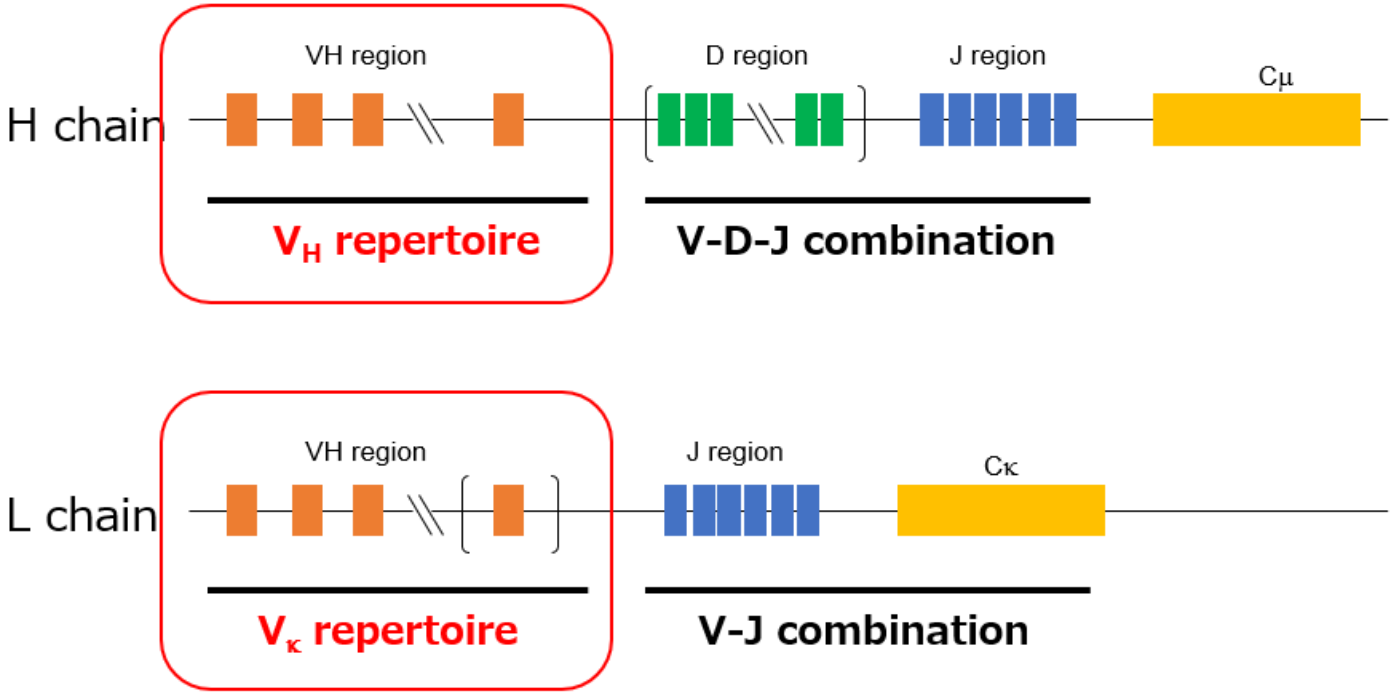
TC-mAb™マウスの治療用抗体開発に対する優位性

	Wild-type	Fully human IgG
Animals	Balb/c, ICR, etc.	TC-mAb mice
Immune response	Mouse IgG	Human IgG
Antibody titer	Exellent	Exellent
IgG subclass	mIgG1,2a, 2b, and 2c	hIgG1, 2, 3, 4
Humanization	The entire region	Not necessary
Ag-specific mAb generation	Normal	High ratio
Size of spleen	Enlarged	Normal
B cell development	Normal	Expanded
Antigen-specific B cells	Normal	Expanded
Ig-gene Repertoire	Normal mouse	Normal human
Somatic hypermutation	Yes	Yes
Length of CDR3H	Mouse (short)	Human (long)

Summary

- 正常なヒトIgGレパトアを保持
- 完全なヒト抗体かつ、親和性が成熟しているため、その後の改変が不要

TC-mAb™マウスにおけるヒト抗体遺伝子のレパトア解析 I

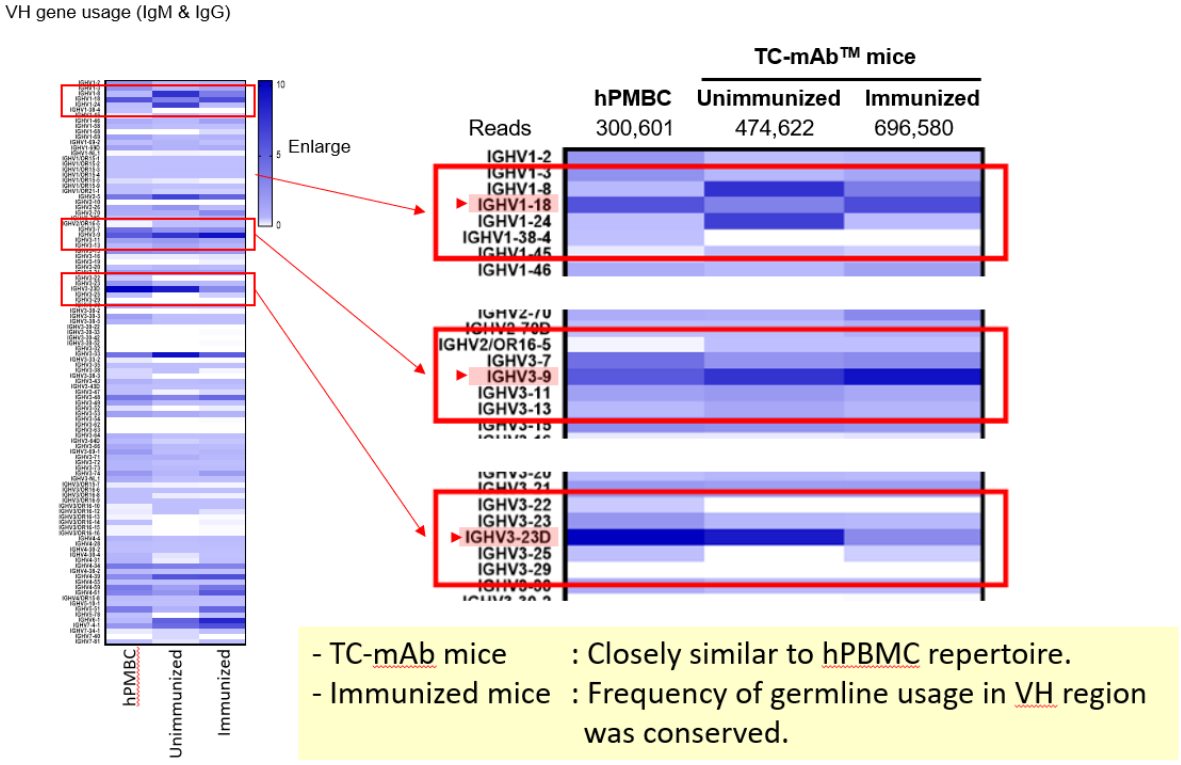


Pooled samples were analyzed by NGS.

Heat map representation of VH and Vκ -gene usage

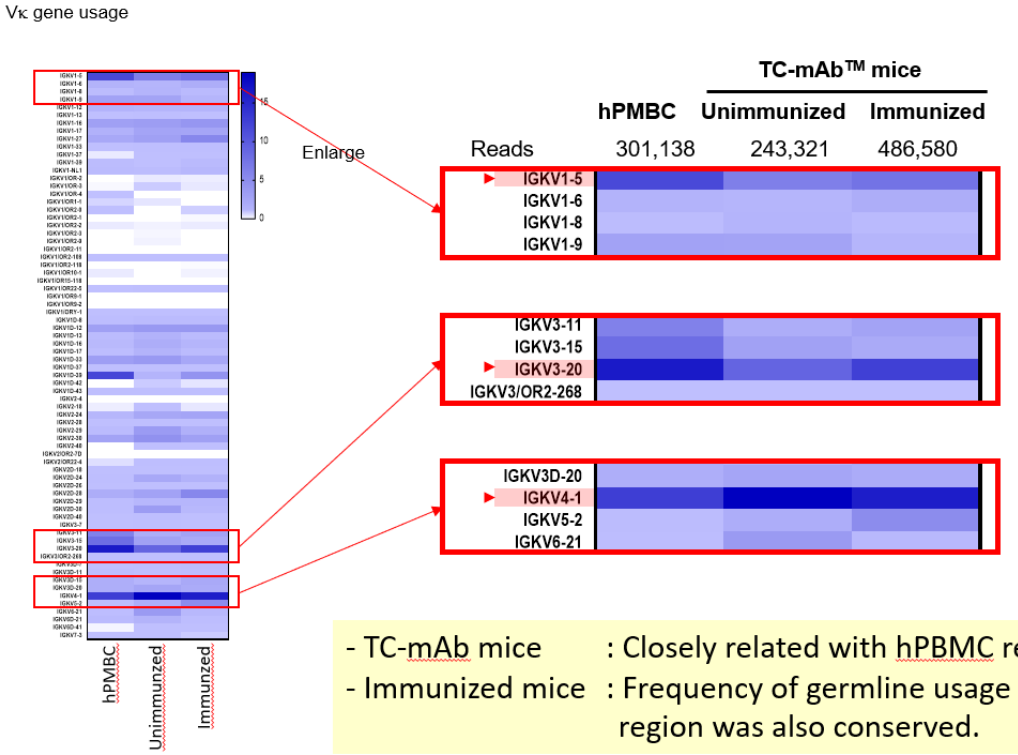
TC-mAb™マウスにおけるヒト抗体遺伝子のレパトア解析Ⅱ

VH gene usage (IgM&IgG)



- TC-mAb mice : Closely similar to hPBMC repertoire.
- Immunized mice : Frequency of germline usage in VH region was conserved.

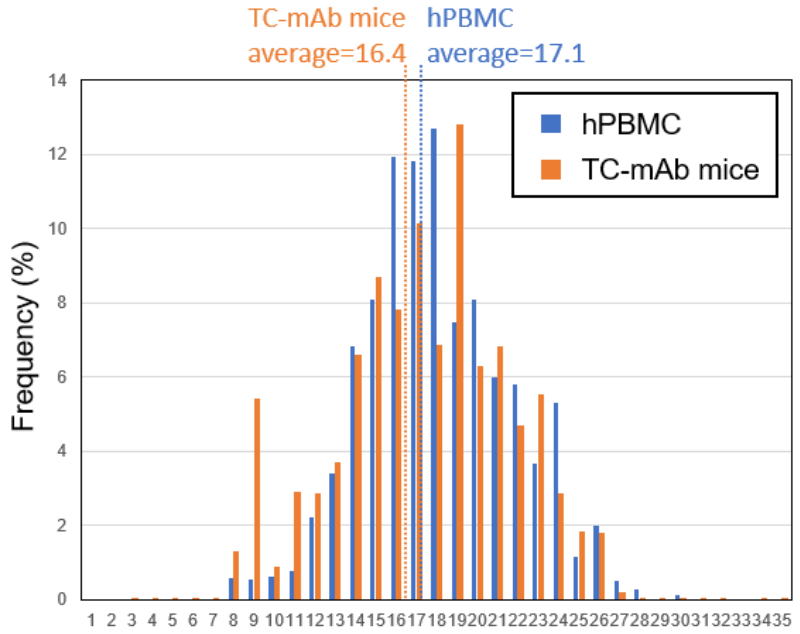
Vκ gene usage



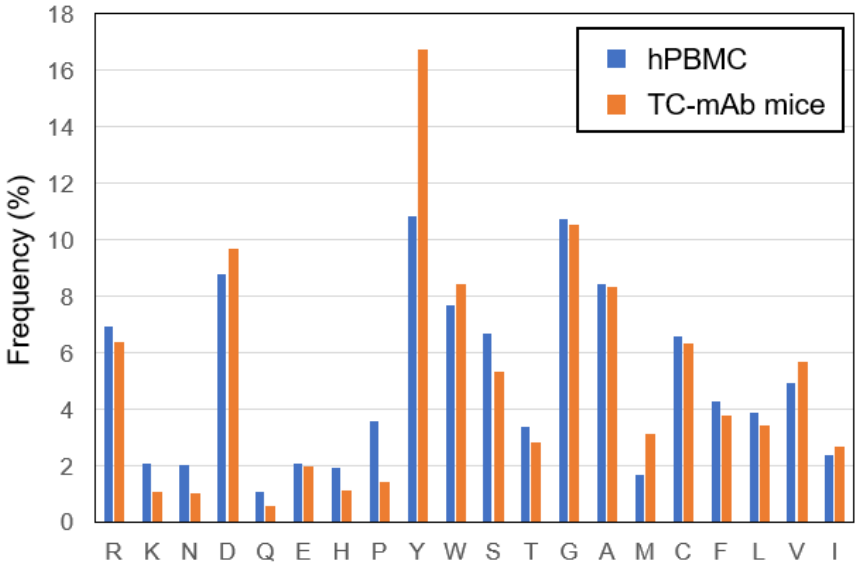
- TC-mAb mice : Closely related with hPBMC repertoire.
- Immunized mice : Frequency of germline usage in Vκ region was also conserved.

TC-mAb™マウスにおけるヒト抗体遺伝子のレパトア解析Ⅲ

CDR3H Length



CDR3H Amino acids usage



Both amino acid length and composition in CDR3 region of the antibody heavy chain variable region (VH) were almost the same with human PBMC.
It was speculated that antibodies similar to human individuals can be produced from TC-mAb mice.