# Fc RECEPTOR BINDING PROTEINS

## RELATED APPLICATIONS

This application claims priority under 35 U.S.C. §119 to United States Provisional Application No. 61/492,617, filed June 2, 2011, and Provisional Application No. 61/498,266, filed June 17, 2011. ~~The entire contents of both provisional applications are herein incorporated by reference in their entirety~~.

## FIELD OF THE INVENTION

The field of invention relates to proteins that bind the Fc receptor.

## BACKGROUND OF THE INVENTION

The most abundant antibody isotype in the serum is IgG and it has a critical role in mediating protection against pathogens as well as in mediating allergic and inflammatory responses that hasten recruitment of immune system components to the tissues, mucosae, and dermal surfaces (Junghans, Immunologic Research 16(1):29 (1997)). Moreover, it is also a key component of a variety of autoimmune diseases. Under normal conditions, the halflife of IgG in the serum is in the range of 5-7 days in mice and 22-23 days in humans, which is a prolonged period, relative to the serum half life of other plasma proteins. In part, this occurs because the neonatal FcRn receptor (FcRn) rescues pinocytosed IgG from degradative lysosomes and recycles it back to the extracellular compartment (Junghans and Anderson, Proc. Natl. Acad. Sci. USA 93:5512 (1996), Roopenian et al. J. Immunology 170:3528 (2003)).

FcRn binds to the the Fc portion of IgG. The interaction between the IgG Fc region and FcRn is pH-dependent. Upon entry into cells by fluid phase endocytosis, IgG is sequestered into endosomes and binds to FcRn with high affinity at acidic pH (6~6.5); when the IgG-FcRn complex cycles to the plasma membrane, IgG dissociates rapidly from FcRn in the bloodstream at slightly basic pH (~7.4). By this receptor-mediated recycling mechanism, FcRn effectively rescues the IgG from degradation in lysosomes, thereby prolonging the half-life of circulating IgG.

FcRn is a non-covalent heterodimer that typically resides in the endosomes of endothelial and epithelial cells. It is a membrane bound receptor with a single-pass transmembrane having three heavy chain alpha domains ($\alpha$1, $\alpha$2, and $\alpha$3) and a single soluble

Calculations of "homology" or "sequence identity" between two sequences (the terms are used interchangeably herein) are performed as follows. The sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). The optimal alignment is determined as the best score using the GAP program in the GCG software package with a Blosum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences.

In one embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, 80%, 90%, 92%, 95%, 97%, 98%, or 100% of the length of the reference sequence. For example, the reference sequence may be the length of the immunoglobulin variable domain sequence.

A "humanized" immunoglobulin variable region is an immunoglobulin variable region that is modified to include a sufficient number of human framework amino acid positions such that the immunoglobulin variable region does not elicit an immunogenic response in a normal human. Descriptions of "humanized" immunoglobulins include, for example, US 6,407,213 and US 5,693,762.

As used herein, the term "hybridizes under low stringency, medium stringency, high stringency, or very high stringency conditions" describes conditions for hybridization and washing. Guidance for performing hybridization reactions can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6, ~~which is incorporated by reference~~. Aqueous and non-aqueous methods are described in that reference and either can be used. Specific hybridization conditions referred to herein are as follows: (1) low stringency hybridization conditions in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by two washes in 0.2X SSC, 0.1% SDS at least at 50°C (the temperature of the washes can be increased to 55°C for low stringency conditions); (2) medium stringency

The nucleic acid sequece of an exemplary human FcRn (extra-cellular domain) plus GPI DNA sequences (lowercase bold) is set forth below.

ATGGGGGTCCCGCGGCCTCAGCCCTGGGCGCTGGGGCTCCTGCTCTTTCTCCTTCCTGGGAGCCTGGGCG
CAGAAAGCCACCTCTCCCTCCTGTACCACCTTACCGCGGTGTCCTCGCCTGCCCCGGGGACTCCTGCCTT
CTGGGTGTCCGGCTGGCTGGGCCCGCAGCAGTACCTGAGCTACAATAGCCTGCGGGGCGAGGCGGAGCCC
TGTGGAGCTTGGGTCTGGGAAAACCAGGTGTCCTGGTATTGGGAGAAAGAGACCACAGATCTGAGGATCAA
GGAGAAGCTCTTTCTGGAAGCTTTCAAAGCTTTGGGGGGAAAAGGTCCCTACACTCTGCAGGGCCTGCTGG
GCTGTGAACTGGGCCCTGACAACACCTCGGTGCCCACCGCCAAGTTCGCCCTGAACGGCGAGGAGTTCATG
AATTTCGACCTCAAGCAGGGCACCTGGGGTGGGGACTGGCCCGAGGCCCTGGCTATCAGTCAGCGGTGGCA
GCAGCAGGACAAGGCGGCCAACAAGGAGCTCACCTTCCTGCTATTCTCCTGCCCGCACCGCCTGCGGGAGC
ACCTGGAGAGGGGCCGCGGAAACCTGGAGTGGAAGGAGCCCCCCTCCATGCGCCTGAAGGCCCGACCCAGC
AGCCCTGGCTTTTCCGTGCTTACCTGCAGCGCCTTCTCCTTCTACCCTCCGGAGCTGCAACTTCGGTTCCT
GCGGAATGGGCTGGCCGCTGGCACCGGCCAGGGTGACTTCGGCCCCAACAGTGACGGATCCTTCCACGCCT
CGTCGTCACTAACAGTCAAAAGTGGCGATGAGCACCACTACTGCTGCATTGTGCAGCACGCGGGGCTGGCG
CAGCCCCTCAGGGTGGAGCTGGAATCTCCAGCCAAGTCCTCC**cggccgctcgacgggctacgagcatcagt**
**aacactactaggcgcaggcctactactatcactactaccagcactactacgatttgggccataa** (SEQ ID NO:6)

An exemplary nucleic acid sequence encoding a Beta-2-microglobulin (β2M) can include the following sequences:

Beta-2-microglobulin (B2M) nucleotide (*Homo sapiens*):

AATATAAGTGGAGGCGTCGCGCTGGCGGGCATTCCTGAAGCTGACAGCATTCGGGCCGAGATGTCTCGCT
CCGTGGCCTTAGCTGTGCTCGCGCTACTCTCTCTTTCTGGCCTGGAGGCTATCCAGCGTACTCCAAAGAT
TCAGGTTTACTCACGTCATCCAGCAGAGAATGGAAAGTCAAATTTCCTGAATTGCTATGTGTCTGGGTTT
CATCCATCCGACATTGAAGTTGACTTACTGAAGAATGGAGAGAGAATTGAAAAAGTGGAGCATTCAGACT
TGTCTTTCAGCAAGGACTGGTCTTTCTATCTCTTGTACTACACTGAATTCACCCCCACTGAAAAAGATGA
GTATGCCTGCCGTGTGAACCATGTGACTTTGTCACAGCCCAAGATAGTTAAGTGGGATCGAGACATGTAA
GCAGCATCATGGAGGTTTGAAGATGCCGCATTTGGATTGGATGAATTCCAAATTCTGCTTGCTTGCTTTT
TAATATTGATATGCTTATACACTTACACTTTATGCACAAAATGTAGGGTTATAATAATGTTAACATGGAC
ATGATCTTCTTTATAATTCTACTTTGAGTGCTGTCTCCATGTTTGATGTATCTGAGCAGGTTGCTCCACA
GGTAGCTCTAGGAGGGCTGGCAACTTAGAGGTGGGGAGCAGAGAATTCTCTTATCCAACATCAACATCTT
GGTCAGATTTGAACTCTTCAATCTCTTGCACTCAAAGCTTGTTAAGATAGTTAAGCGTGCATAAGTTAAC
TTCCAATTTACATACTCTGCTTAGAATTTGGGGGAAAATTTAGAAATATAATTGACAGGATTATTGGAAA
TTTGTTATAATGAATGAAACATTTTGTCATATAAGATTCATATTTACTTCTTATACATTTGATAAAGTAA
GGCATGGTTGTGGTTAATCTGGTTTATTTTTGTTCCACAAGTTAAATAAATCATAAAACTTGATGTGTTA
TCTCTTA (SEQ ID NO:7)

FcRn binding antibodies

DX2504 is an FcRn binding antibody that is described in WO2009/131702 and US-2009-0324614-A1. ~~Both WO2009/131702 and US-2009-0324614-A1 are incorporated by reference into this application in their entirety.~~ DX2504 was generated by a combination of monoclonal antibody technology and phage display experiments using FcRn polypeptides or cells expressing FcRn as the target. In addition, the sequence of DX2504 was germlined to lower immunogenicity. The sequences of DX2504 light chain and heavy chain are shown below:

Humanized antibodies can be generated by replacing sequences of the Fv variable region that are not directly involved in antigen binding with equivalent sequences from human Fv variable regions. General methods for generating humanized antibodies are provided by Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi et al., 1986, *BioTechniques* 4:214, and by Queen et al. US Patent Nos. 5,585,089, US 5,693,761 and US 5,693,762. Those methods include isolating, manipulating, and expressing the nucleic acid sequences that encode all or part of immunoglobulin Fv variable regions from at least one of a heavy or light chain. Sources of such nucleic acid are well known to those skilled in the art and, for example, may be obtained from a hybridoma producing an antibody against a predetermined target, as described above. The recombinant DNA encoding the humanized antibody, or fragment thereof, can then be cloned into an appropriate expression vector.

An FcRn-binding antibody may also be modified by specific deletion of human T cell epitopes or "deimmunization" by the methods disclosed in WO 98/52976 and WO 00/34317~~, the contents of which are specifically incorporated by reference herein~~. Briefly, the heavy and light chain variable regions of an antibody can be analyzed for peptides that bind to MHC Class II; these peptides represent potential T-cell epitopes (as defined in WO 98/52976 and WO 00/34317). For detection of potential T-cell epitopes, a computer modeling approach termed "peptide threading" can be applied, and in addition a database of human MHC class II binding peptides can be searched for motifs present in the $V_H$ and $V_L$ sequences, as described in WO 98/52976 and WO 00/34317. These motifs bind to any of the 18 major MHC class II DR allotypes, and thus constitute potential T cell epitopes. Potential T-cell epitopes detected can be eliminated by substituting small numbers of amino acid residues in the variable regions or by single amino acid substitutions. As far as possible conservative substitutions are made, often but not exclusively, an amino acid common at this position in human germline antibody sequences may be used. Human germline sequences are disclosed in Tomlinson, I.A. et al., 1992, *J. Mol. Biol.* 227:776-798; Cook, G. P. et al., 1995, *Immunol. Today* Vol. 16 (5): 237-242; Chothia, D. et al., 1992, *J. Mol. Bio.* 227:799-817. The V BASE directory provides a comprehensive directory of human immunoglobulin variable region sequences (compiled by Tomlinson, I.A. et al. MRC Centre for Protein Engineering, Cambridge, UK). After the deimmunizing changes are identified, nucleic acids encoding $V_H$ and $V_L$ can be constructed by mutagenesis or other synthetic methods (e.g., de novo

be in the form of particles, e.g., less than 10 mm to about 10 nM in diameter). Particles can have ferromagnetic, antiferromagnetic, or superparamagnetic properties. Particles can include, e.g., magnetite ($Fe_3O_4$), $\gamma$-$Fe_2O_3$, ferrites, and other magnetic mineral compounds of transition elements. Magnetic particles may include: one or more magnetic crystals with and without nonmagnetic material. The nonmagnetic material can include synthetic or natural polymers (such as sepharose, dextran, dextrin, starch and the like.

The FcRn-binding antibody can also be labeled with an indicating group containing of the NMR active $^{19}F$ atom, or a plurality of such atoms inasmuch as (i) substantially all of naturally abundant fluorine atoms are the $^{19}F$ isotope and, thus, substantially all fluorine containing compounds are NMR active; (ii) many chemically active polyfluorinated compounds such as trifluoracetic anhydride are commercially available at relatively low cost; and (iii) many fluorinated compounds have been found medically acceptable for use in humans such as the perfluorinated polyethers utilized to carry oxygen as hemoglobin replacements. After permitting such time for incubation, a whole body MRI is carried out using an apparatus such as one of those described by Pykett, 1982, *Sci. Am.* 246:78 88 to locate and image tissues expressing FcRn.

The disclosure also features kits comprising an antibody that binds to FcRn and instructions for diagnostic use, e.g., the use of the FcRn-binding antibody or antigen-binding fragment thereof, to detect FcRn, in vitro, e.g., in a sample, e.g., a biopsy or cells from a patient having an autoimmune disorder, or in vivo, e.g., by imaging a subject. The kit can further contain a least one additional reagent, such as a label or additional diagnostic agent. For *in vivo* use the antibody can be formulated as a pharmaceutical composition.

The present invention is further illustrated by the following Examples, which in no way should be construed as further limiting. ~~The entire contents of all of the references (including literature references, issued patents, published patent applications, and co-pending patent applications) cited throughout this application are hereby expressly incorporated by reference, in particular for the teaching that is referenced hereinabove.~~

EXAMPLE 1: DX2504 and Cysteine Mutants Thereof

The light chain of the DX-2504 anti-FcRn antibody has an unpaired cysteine in the first position of CDR3. This cysteine is adjacent to the cysteine in the FR3 that pairs with the

The toxicokinetic parameters for both DX-2504 and DX-2507 were substantially consistent on days 0 and 7. The overall exposure of DX-2507 was greater than that observed for DX-2504. The mean maximum concentration ($C_{max}$) and plasma/serum concentration-time curve ($AUC_{last}$) values for DX-2507 on either Day 0 or Day 7 were between 2 to 3-fold greater than the corresponding values calculated for DX-2504. In addition, the corresponding mean apparent clearance (CL/F) and distribution volume (Vz/F) values for DX-2504 were between 2 to 12-fold greater than DX-2507.

~~Equivalents~~

~~The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by examples provided, since the examples are intended as a single illustration of one aspect of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention.~~

~~The contents of all references, patents and published patent applications cited throughout this application are incorporated herein by reference in their entirety, particularly for the use or subject matter referenced herein.~~

What is claimed is:

1. An isolated antibody that binds human FcRn, the isolated antibody comprising a light chain variable region ($V_L$) that comprises a $V_L$ CDR1, a $V_L$ CDR2, and a $V_L$ CDR3,

wherein the $V_L$ CDR3 has at least 85% homology with the following sequence: SSYAGSGIYV (SEQ ID NO:12) or ASYAGSGIYV (SEQ ID NO:13), and

wherein the isolated antibody does not have a cysteine at the first position of at least one CDR3 region.

2. The isolated antibody of claim 1, wherein the $V_L$ CDR1 and $V_L$ CDR2 of the isolated antibody have at least 85% homology with TGTGSDVGSYNLVS (SEQ ID NO:14) and GDSQRPS (SEQ ID NO:15), respectively.

3. The isolated antibody of claim 1 or claim 2, wherein:

the $V_L$ CDR1 has at least 90% homology with TGTGSDVGSYNLVS (SEQ ID NO:14),

the $V_L$ CDR2 has at least 90% homology with GDSQRPS (SEQ ID NO:15), and/or

the $V_L$ CDR3 has at least 90% homology with SSYAGSGIYV (SEQ ID NO:12) or ASYAGSGIYV (SEQ ID NO:13).

4. The isolated antibody of any of claims 1-3, wherein:

(a) the $V_L$ CDR1 is TGTGSDVGSYNLVS (SEQ ID NO:14),

(b) the $V_L$ CDR2 is GDSQRPS (SEQ ID NO:15), and/or

(c) the $V_L$ CDR3 is SSYAGSGIYV (SEQ ID NO:12) or ASYAGSGIYV (SEQ ID NO:13).

5. The isolated antibody claim 4, wherein:

the $V_L$ CDR1 is TGTGSDVGSYNLVS (SEQ ID NO:14),

the $V_L$ CDR2 is GDSQRPS (SEQ ID NO:15), and

the $V_L$ CDR3 is SSYAGSGIYV (SEQ ID NO:12) or ASYAGSGIYV (SEQ ID NO:13).

6. The isolated antibody of any of claims 1-5, wherein the $V_L$ of the isolated antibody comprises an amino acid sequence having at least 85% homology with SEQ ID NO:10 or SEQ ID NO:11.

7. The isolated antibody of claim 6, wherein the $V_L$ of the isolated antibody comprises the amino acid sequence of SEQ ID NO:10 or SEQ ID NO:11.

8. An isolated antibody that binds human FcRn, the antibody comprising a light chain variable region ($V_L$) that comprises a $V_L$ CDR1, a $V_L$ CDR2, and a $V_L$ CDR3 region,

wherein the $V_L$ CDR3 region has up to 3 amino acid substitutions as compared to the following sequence: SSYAGSGIYV (SEQ ID NO:12) or ASYAGSGIYV (SEQ ID NO:13), and

wherein the isolated antibody does not have a cysteine at the first position of at least one CDR3 region.

9. The isolated antibody of claim 8, wherein the $V_L$ CDR1, $V_L$ CDR2 and $V_L$ CDR3 collectively have up to 10 amino acid substitutions as compared to the following sequences

(a) CDR1: TGTGSDVGSYNLVS (SEQ ID NO:14)

(b) CDR2: GDSQRPS (SEQ ID NO:15)

(c) CDR3: SSYAGSGIYV (SEQ ID NO:12), or ASYAGSGIYV (SEQ ID NO:13).

10. The isolated antibody of any of claims 1-9, further comprising a heavy chain variable region ($V_H$) that comprises a $V_H$ CDR1, a $V_H$ CDR2, and a $V_H$ CDR3, wherein the $V_H$ CDR3 has at least 85% homology with LAIGDSY (SEQ ID NO:24).

11. The isolated antibody of claim 10, wherein the $V_H$ CDR1 and $V_H$ CDR2 of the isolated antibody have at least 85% homology with EYAMG (SEQ ID NO:22) and SIGSSGGQTKYADSVKG (SEQ ID NO:23), respectively.

12. The isolated antibody of claim 10, wherein:

(a) the $V_H$ CDR1 has at least 90% homology with EYAMG (SEQ ID NO:22),

(b) the $V_H$ CDR2 has at least 90% homology with SIGSSGGQTKYADSVKG (SEQ ID NO:23), and/or

(c) the $V_H$ CDR3 has at least 90% homology with LAIGDSY (SEQ ID NO:24).

13. The isolated antibody of claim 12, wherein:

(a) the $V_H$ CDR1 is EYAMG (SEQ ID NO:22),

(b) the $V_H$ CDR2 is SIGSSGGQTKYADSVKG (SEQ ID NO:23), and/or

(c) the $V_H$ CDR3 is LAIGDSY (SEQ ID NO:24).

14. The isolated antibody of claim 10, wherein the $V_H$ of the isolated antibody comprises an amino acid sequence at least 85% identical to SEQ ID NO:9.

15. The isolated antibody of claim 14, wherein the $V_H$ of the isolated antibody comprises the amino acid sequence of SEQ ID NO:9.

16. An isolated antibody comprising a heavy chain that comprises a heavy chain variable region ($V_H$) and a heavy chain constant region, wherein the $V_H$ comprises a CDR3 region having at least 85% homology with LAIGDSY (SEQ ID NO:24) and the constant region has a deletion at the position corresponding to the C-terminal lysine residue of SEQ ID NO:17.

17. The isolated antibody of claim 16, wherein the $V_H$ further comprises a $V_H$ CDR1 and a $V_H$ CDR2, which have at least 85% homology with EYAMG (SEQ ID NO:22), and SIGSSGGQTKYADSVKG (SEQ ID NO:23), respectively.

18. The isolated antibody of claim 16 or claim 17, wherein the constant region comprises the amino acid sequence of SEQ ID NO:26.

19. The isolated antibody of any of claims 16-18, further comprising a light chain variable region ($V_L$) that comprises a $V_L$ CDR3 at least 85% identical to CSYAGSGIYV (SEQ ID NO:25).

20. The isolated antibody of claim 19, wherein the $V_L$ further comprises a $V_L$ CDR1 and a $V_L$ CDR2, which are at least 85% identical TGTGSDVGSYNLVS (SEQ ID NO:14) and GDSQRPS (SEQ ID NO:15), respectively.

21. The isolated antibody of claim 20, wherein:

(a) the $V_L$ CDR1 is TGTGSDVGSYNLVS (SEQ ID NO:14),

(b) the $V_L$ CDR2 is GDSQRPS (SEQ ID NO:15), and/or

(c) the $V_L$ CDR3 is CSYAGSGIYV (SEQ ID NO:25), SSYAGSGIYV (SEQ ID NO:12), or ASYAGSGIYV (SEQ ID NO:13).

22. The isolated antibody of claim 21, wherein the $V_L$ comprises the amino acid sequence of SEQ ID NO:8, SEQ ID NO:10, or SEQ ID NO:11.

23. The antibody of any one of claims 1-22, wherein the antibody binds human FcRn with a dissociation constant ($K_D$) of less than 10 nM.

24. The antibody of any one of claims 1-23, wherein the antibody is a full-length antibody.

25. The antibody of any one of claims 1-24, wherein the antibody is a human or humanized antibody or is non-immunogenic in a human.

26. The antibody of any one of claims 1-25, wherein the antibody comprises a human antibody framework region.

27. The antibody of any one of claims 1-24, wherein the antibody is a murine antibody.

~~28. The antibody of any one of claims 1-24, wherein the antibody is chimeric.~~

29. The antibody of any one of claims 1-23 and 25-28, wherein the antibody is selected from the group consisting of Fab, F(ab)'2, Fv, and scFv.

30. The antibody of any one of claims 1-29, wherein the antibody is a monoclonal antibody.

31. A pharmaceutical composition comprising the antibody of any one of claims 1-30 and a pharmaceutically acceptable carrier.

32. An isolated nucleic acid comprising a sequence that encodes the antibody of any of claims 1-30.

33. A vector comprising the nucleic acid of claim 32.

34. A host cell comprising the vector of claim 33.

35. A method of detecting an FcRn in a sample, the method comprising:
contacting the sample with the antibody of any one of claims 1-30, and
detecting an interaction between the antibody and the FcRn if present.

36. A method of detecting an FcRn in a subject, the method comprising:
administering to the subject the antibody of any one of claims 1-30, and
detecting an interaction between the antibody and the FcRn if present.

37. A method of modulating an FcRn activity, the method comprising:
contacting an FcRn with the antibody of any one of claims 1-30 thereby modulating the activity of the FcRn.

~~38. The method of claim 37, wherein the contacting step is performed *in vitro*.~~

39. A method of treating an autoimmune disorder in a subject, the method comprising:

administering to the subject the antibody of any one of claims 1-30 in an amount sufficient to treat the autoimmune disorder.

40. A method of modulating the half life/levels of circulating IgG in a subject, the method comprising:

administering to the subject the antibody of any one of claims 1-30 in an amount effective to modulate the half life/levels of circulating IgG in the subject.

41. A pharmaceutical composition for use in treating an autoimmune disorder in a subject, the pharmaceutical composition comprising the antibody of any one of claims 1-30 and a pharmaceutically acceptable carrier.

42. A pharmaceutical composition for use in modulating the half life/levels of circulating IgG in a subject, the pharmaceutical composition comprising the antibody of any one of claims 1-30 and a pharmaceutically acceptable carrier.

43. A pharmaceutical composition for use in modulating an FcRn activity in a subject, the pharmaceutical composition comprising the antibody of any one of claims 1-30 and a pharmaceutically acceptable carrier.

44. Use of the antibody of any one of claims 1-30 in manufacturing a medicament for use in treating an autoimmune disorder.

What is claimed is:

1. An isolated antibody comprising a light chain variable region (VL) and a heavy chain variable region (VII), wherein the antibody binds to human FcRn; and wherein the VL comprises:

(i) a VL CDR1 comprising the amino acid sequence TGTGSDVGSYNLVS (SEQ ID NO: 14);

(ii) a VL CDR2 comprising the amino acid sequence GDSQRPS (SEQ ID NO: 15), and

(iii) a VL CDR3 comprising the amino acid sequence SSYAGSGIYV (SEQ ID NO: 12) or ASYAGSGIYV (SEQ ID NO: 13); and

the VH comprises;

(i) a VH CDR1 comprising the amino acid sequence EYAMG (SEQ ID NO: 22);

(ii) a VH CDR2 comprising the amino acid sequence SIGSSGGQTKYADSVKG (SEQ ID NO: 23): and

(iii) a VH CDR3 comprising the amino acid sequence LAIGDSY (SEQ ID NO: 24).

2. The isolated antibody of claim 1, wherein the VL of the isolated antibody comprises the amino acid sequence of SEQ ID NO: 10 or SEQ ID NO: 11.

3. The isolated antibody of claim 1, wherein the VH of the isolated antibody comprises the ammo acid sequence of SEQ ID NO: 9.

4. An isolated antibody comprising a light chain variable region (VL), a heavy chain variable region (VH), and a heavy chain constant region (CH), wherein the antibody binds to human FcRn; and wherein the VL comprises:

(i) a VL CDR1 comprising the amino acid sequence TGTGSDVGSYNLVS (SEQ ID NO: 14);

(ii) a VL CDR2 comprising the amino acid sequence GDSQRPS (SEQ ID NO: 15): and

(iv) a VL CDR3 comprising the amino acid sequence CSYAGSGIYV

(SEQ ID NO: 25), SSYAGSGIYV (SEQ ID NO: 12) or ASYAGSGIYV (SEQ ID NO: 13); and

the VH comprises:

(i) a VH CDR1 comprising the amino acid sequence EYAMG (SEQ ID NO: 22);

(ii) a VH CDR2 comprising the amino acid sequence SIGSSGGQTKYADSVKG (SEQ ID NO: 23); and

(iii) a VH CDR3 comprising the amino acid sequence LAIGDSY (SEQ ID NO: 24);

and the CH has a deletion corresponding to the C-terminal lysine residue at the last position of SEQ ID NO: 17.

5. The isolated antibody of claim 4, wherein the VL of the isolated antibody comprises the amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 11.

6. A pharmaceutical composition comprising the antibody of claim 1 or 4 and a pharmaceutically acceptable carrier.

7. An isolated nucleic acid comprising a nucleotide sequence that encodes the antibody of claim 1 or 4.

8. A vector comprising the nucleic acid of claim 7.

9. A host cell comprising the vector of claim 8.

10. An *in vitro* method of detecting an FcRn in a sample, the method comprising:

contacting the sample with the antibody of claim 1 or 4, and

detecting an interaction between the antibody and the FcRn if present.

11. The antibody of claim 1 or 4, for use in detecting an FcRn in a subject.

12. Use of the antibody of claim 1 or 4 in manufacturing a medicament for modulating an FcRn activity.

13. Use of the antibody of claim 1 or 4 in manufacturing a medicament for treating an autoimmune disorder In a subject.

14. Use of the antibody of claim 1 or 4 in manufacturing a medicament for modulating the half life/levels of circulating IgG in a subject.

15. The antibody of claim 1 or 4, wherein the antibody binds human FcRn with a dissociation constant (KD) of less than 10 nM.

16. The antibody of claim 1 or 4, wherein the antibody is a human or humanized antibody or is non-immunogenic in a human.

17. The antibody of claim 1 or 4, wherein the antibody is chimeric.

18. The antibody of claim 1 or 4, wherein the antibody is selected from the group consisting of a Fab, a F(ab)'2, an Fv, and an scFv.