

thereof. In one aspect, the present disclosure refers to an IgM antibody ~~or IgM-like antibody~~ with enhanced serum half-life comprising five bivalent antibody binding units ~~or variants or fragments thereof~~ and a variant J-chain ~~or functional fragment thereof~~, wherein each binding unit comprises two IgM heavy chain constant regions ~~or multimerizing fragments or variants thereof~~, each associated with an antigen-binding domain or a heavy chain variable region (VH) subunit thereof, wherein the variant J-chain ~~or functional fragment thereof~~ comprises one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~ relative to a reference J-chain identical to the variant J-chain except for the one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~, and wherein the variant J-chain can affect serum half-life of the IgM antibody ~~or IgM-like antibody~~; ~~and~~ wherein the IgM antibody ~~or IgM-like antibody~~ exhibits an increased serum half-life upon administration to a subject animal relative to a reference IgM antibody ~~or IgM-like antibody~~ that is identical except for the one, two, three, or four ~~or more~~ single amino acid substitutions, ~~deletions, or insertions~~ in the variant J-chain, and is to be administered in the same way to the same animal species; and wherein the variant J-chain comprises an alanine (A), arginine (R), or serine (S) substitution at a position corresponding to amino acid Y102 of SEQ ID NO: 2, an alanine (A) substitution at a position corresponding to amino acid N49 of SEQ ID NO: 2, or an alanine (A), arginine (R), or serine (S) substitution at a position corresponding to amino acid Y102 of SEQ ID NO: 2 and an alanine (A) substitution at a position corresponding to amino acid N49 of SEQ ID NO: 2, wherein the variant J-chain can affect serum half-life of the IgM antibody.

[0008a] In another aspect, the present disclosure refers to an IgM antibody ~~or IgM-like antibody~~ with enhanced serum half-life comprising five or six bivalent antibody binding units ~~or variants or fragments thereof~~, wherein each binding unit comprises two variant IgM heavy chain constant regions ~~or multimerizing fragments thereof~~, each associated with an antigen-binding domain or a heavy variable region (VH) subunit thereof, wherein the variant IgM heavy chain constant regions ~~or multimerizing fragments thereof~~ each comprise one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~ relative to a reference IgM heavy chain constant region identical to the variant IgM heavy chain constant regions except for the one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~, and wherein the variant IgM heavy chain constant regions can affect serum half-life of the IgM antibody ~~or IgM-like antibody~~; wherein the variant IgM heavy chain constant regions comprise an alanine (A) substitution at a position

corresponding to amino acid R344 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid S345 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid S401 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid E402 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid E403 of SEQ ID NO: 12, or alanine (A) substitutions at positions corresponding to amino acids S401 and E402 of SEQ ID NO: 12, and wherein the IgM antibody ~~or IgM-like antibody~~ exhibits an increased serum half-life upon administration to a subject animal relative to a reference IgM antibody ~~or IgM-like antibody~~ that is identical except for the one or more single amino acid substitutions, ~~deletions, or insertions~~ in the IgM heavy chain constant regions, and is to be administered in the same way to the same animal species.

[0008b] In another aspect, the present disclosure refers to a composition comprising the IgM antibody ~~or IgM-like antibody~~ as described herein, and a pharmaceutically acceptable carrier. In yet another aspect, the present disclosure refers to a variant J-chain comprising the amino acid sequence SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, ~~SEQ ID NO: 6,~~ SEQ ID NO: 7, ~~SEQ ID NO: 8,~~ SEQ ID NO: 10, ~~SEQ ID NO: 23,~~ or SEQ ID NO: 24, wherein the variant J-chain can affect the serum half-life of an IgM antibody ~~or IgM-like antibody~~ comprising the variant J-chain. In yet another aspect, the present disclosure refers to an isolated polynucleotide comprising a nucleic acid encoding a subunit polypeptide of the IgM ~~or IgM-like antibody~~ as described herein wherein the subunit polypeptide comprises (a) an IgM ~~or IgM-like~~ heavy chain constant region ~~or multimerizing fragment thereof,~~ (b) an antibody light chain, ~~or~~ (c) a J-chain, or a modified J-chain, ~~or functional fragment or variant thereof,~~ or (d) any combination thereof. In yet another aspect, the present disclosure refers to an expression vector comprising the polynucleotide as described herein. In yet another aspect, the present disclosure refers to a host cell comprising the polynucleotide as described herein or the expression vector as described herein.

[0008c] In a further aspect, the present disclosure refers to a method of identifying variant J-chains that can increase the serum half-life of pentameric IgM antibodies or pentameric IgM-like antibodies comprising the variant J-chains, the method comprising: 1(a) testing pentameric IgM antibodies or pentameric IgM-like antibodies comprising variant J-chains ~~or fragments thereof~~ for increased serum half-life in a subject animal relative to a reference pentameric IgM antibody or pentameric IgM-like antibody, wherein

the variant J-chains ~~or fragments thereof~~ comprise defined amino acid ~~insertions, deletions, or~~ substitutions, and wherein the reference pentameric IgM antibody or pentameric IgM-like antibody comprises a J-chain ~~or fragment thereof~~ identical to the variant J-chains except for the defined amino acid ~~insertions, deletions or~~ substitutions; and (b) recovering those variant J-chains ~~or fragments thereof~~ that confer increased serum half-life upon the pentameric IgM antibodies or pentameric IgM-like antibodies relative to reference pentameric IgM antibody or pentameric IgM-like antibody; or 2)(a) testing pentameric IgM antibodies or pentameric IgM-like antibodies comprising variant J-chains ~~or fragments thereof~~ for their level of binding to the Fc alpha-mu receptor (FcαμR), the polymeric Ig receptor (pIgR), or both the FcαμR and the pIgR, wherein the variant J-chains ~~or fragments thereof~~ comprise defined amino acid ~~insertions, deletions, or~~ substitutions; and (b) recovering those variant J-chains ~~or fragments thereof~~ that confer reduced FcαμR binding ability, reduced pIgR binding ability, or reduced FcαμR and pIgR binding ability upon the pentameric IgM antibodies or pentameric IgM-like antibodies relative to a reference pentameric IgM antibody or pentameric IgM-like antibody comprising a J-chain ~~or fragment thereof~~ identical to the variant J-chains except for the defined amino acid ~~insertions, deletions or~~ substitutions.

[0008d] In a further aspect, the present disclosure refers to a method of identifying variant IgM heavy chain constant regions that can increase the serum half-life of an IgM antibody ~~or IgM-like antibody~~ comprising the variant IgM heavy chain constant regions, comprising: (1)(a) testing IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions for increased serum half-life in a subject animal relative to a reference pentameric IgM antibody or pentameric IgM-like antibody, wherein the variant IgM heavy chain constant regions comprise defined amino acid ~~insertions, deletions, or~~ substitutions, and wherein the reference IgM antibody ~~or IgM-like antibody~~ comprises IgM heavy chain constant regions identical to the variant IgM heavy chain constant regions except for the defined amino acid ~~insertions, deletions or~~ substitutions; and (b)

recovering those IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions that confer increased serum half-life upon the IgM antibodies or IgM-like antibodies comprising the variant IgM heavy chain constant regions relative to the reference IgM antibody ~~or IgM-like antibody~~; or (2)(a) testing IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions for their level of binding to the Fc alpha-mu receptor (FcαμR), Fc mu receptor (FcμR), the polymeric Ig

receptor (pIgR), any combination of two of the receptors, or all three of the receptors, wherein the variant IgM heavy chain constant regions comprise defined amino acid ~~insertions, deletions, or~~ substitutions; and (b) recovering those IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions that confer reduced FcαμR binding ability, reduced FcμR binding ability, reduced pIgR binding ability, reduced ability to bind to any two of the receptors, or reduced ability to bind to all three of the receptors, upon the IgM antibodies or IgM-like antibodies comprising the variant IgM heavy chain constant regions relative to a reference IgM antibody ~~or IgM-like antibody~~ comprising IgM heavy chain constant regions identical to the variant IgM heavy chain constant regions except for the defined amino acid ~~insertions, deletions, or~~ substitutions.

[0008e] In certain examples the variant J-chain or functional fragment thereof includes one or more single amino acid substitutions, deletions, or insertions relative to a reference J-chain identical to the variant J-chain except for the one or more single amino acid substitutions, deletions, or insertions. The provided variant J-chain can affect serum half-life of the provided IgM antibody or IgM-like antibody. For example, in certain examples the IgM antibody or IgM-like antibody exhibits an increased serum half-life upon administration to a subject animal relative to a reference IgM antibody or IgM-like antibody that is identical except for the one or more single amino acid substitutions,

WHAT IS CLAIMED IS:

1. An IgM antibody ~~or IgM-like antibody~~ with enhanced serum half-life comprising five bivalent antibody binding units ~~or variants or fragments thereof~~ and a variant J-chain ~~or functional fragment thereof~~,

wherein each binding unit comprises two IgM heavy chain constant regions ~~or multimerizing fragments or variants thereof~~, each associated with an antigen-binding domain or a heavy chain variable region (VH) subunit thereof,

wherein the variant J-chain ~~or functional fragment thereof~~ comprises one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~ relative to a reference J-chain identical to the variant J-chain except for the one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~, and wherein the variant J-chain can affect serum half-life of the IgM antibody ~~or IgM-like antibody~~; and

wherein the IgM antibody ~~or IgM-like antibody~~ exhibits an increased serum half-life upon administration to a subject animal relative to a reference IgM antibody ~~or IgM-like antibody~~ that is identical except for the one, two, three, or four ~~or more~~ single amino acid substitutions, ~~deletions, or insertions~~ in the variant J-chain, and is to be administered in the same way to the same animal species; and wherein the variant J-chain comprises an alanine (A), arginine (R), or serine (S) substitution at a position corresponding to amino acid Y102 of SEQ ID NO: 2, an alanine (A) substitution at a position corresponding to amino acid N49 of SEQ ID NO: 2, or an alanine (A), arginine (R), or serine (S) substitution at a position corresponding to amino acid Y102 of SEQ ID NO: 2 and an alanine (A) substitution at a position corresponding to amino acid N49 of SEQ ID NO: 2, wherein the variant J-chain can affect serum half-life of the IgM antibody.

2. ~~The IgM antibody or IgM-like antibody of claim 1, wherein the variant J chain or functional fragment thereof comprises an amino acid substitution at the amino acid position corresponding to amino acid Y102 of the wild-type human J-chain (SEQ ID NO: 2).~~

3. ~~The IgM antibody or IgM-like antibody of claim 2, wherein the amino acid corresponding to Y102 of SEQ ID NO: 2 is substituted with alanine (A), serine (S) or arginine (R).~~

4. ~~The IgM antibody or IgM-like antibody of claim 3, wherein the amino acid corresponding to Y102 of SEQ ID NO: 2 is substituted with alanine (A).~~

2. The IgM antibody or IgM-like antibody of claim 1, wherein the J-chain is a variant human J-chain and comprises the amino acid sequence SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 10, or SEQ ID NO: 24.

5.3. The IgM antibody or IgM-like antibody of claim 1, wherein the J-chain is a variant human J-chain and comprises the amino acid sequence SEQ ID NO: 3.

~~6.~~ The IgM antibody or IgM-like antibody of claim 1, wherein the variant J-chain or functional fragment thereof comprises an amino acid substitution at the amino acid position corresponding to amino acid T103, N49, or S51 of the wild-type human J-chain (SEQ ID NO: 2).

7.4. The IgM antibody ~~or IgM-like antibody~~ of any one of claims 1 to 36, wherein the IgM heavy chain constant regions ~~or multimerizing fragments thereof~~ are variant IgM heavy chain constant regions comprising one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~ relative to a reference IgM heavy chain constant region identical to the variant IgM heavy chain constant regions except for the one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~, wherein the variant IgM heavy chain constant regions can affect serum half-life of the IgM antibody ~~or IgM-like antibody~~, and wherein the IgM antibody ~~or IgM-like antibody~~ exhibits a further increased serum half-life upon administration to a subject animal relative to a reference IgM antibody ~~or IgM-like antibody~~ that is identical except for the one or more single amino acid substitutions, ~~deletions, or insertions~~ in the IgM heavy chain constant regions, and is to be administered in the same way to the same animal species, wherein the variant IgM heavy chain constant regions comprise an alanine (A) substitution at a position corresponding to amino acid R344 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid S345 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid S401 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid E402 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid E403 of SEQ ID NO: 12, or alanine (A) substitutions at positions corresponding to amino acids S401 and E402 of SEQ ID NO: 12.

8.5. An IgM antibody ~~or IgM-like antibody~~ with enhanced serum half-life comprising five or six bivalent antibody binding units ~~or variants or fragments thereof~~,

wherein each binding unit comprises two variant IgM heavy chain constant regions ~~or multimerizing fragments thereof~~, each associated with an antigen-binding domain or a heavy chain variable region (VH) subunit thereof,

wherein the variant IgM heavy chain constant regions ~~or multimerizing fragments thereof~~ each comprise one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~ relative to a reference IgM heavy chain constant region identical to the variant IgM heavy chain constant regions except for the one, two, three, or four single amino acid substitutions, ~~deletions, or insertions~~, and wherein the variant IgM heavy chain constant regions can affect serum half-life of the IgM antibody ~~or IgM-like antibody~~; wherein the variant IgM heavy chain constant regions comprise an alanine (A) substitution at a position corresponding to amino acid R344 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid S345 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid S401 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid E402 of SEQ ID NO: 12, an alanine (A) substitution at a position corresponding to amino acid E403 of SEQ ID NO: 12, or alanine (A) substitutions at positions corresponding to amino acids S401 and E402 of SEQ ID NO: 12, and

wherein the IgM antibody ~~or IgM-like antibody~~ exhibits an increased serum half-life upon administration to a subject animal relative to a reference IgM antibody ~~or IgM-like antibody~~ that is identical except for the one or more single amino acid substitutions, ~~deletions, or insertions~~ in the IgM heavy chain constant regions, and is to be administered in the same way to the same animal species.

~~9. The IgM antibody or IgM-like antibody of claim 7 or claim 8, wherein the variant IgM heavy chain constant regions comprise an amino acid substitution at the amino acid position corresponding to amino acid R344, E345, S401, E402, or E403 of the wild-type human IgM constant region SEQ ID NO: 12.~~

~~10. The IgM antibody or IgM-like antibody of claim 9, wherein the amino acid corresponding to R344, E345, S401, E402, or E403 of SEQ ID NO: 12 is substituted with alanine (A).~~

~~6. The IgM antibody or IgM-like antibody of claim 510, wherein the variant IgM heavy chain constant regions are variant human IgM heavy chain constant region and comprise the amino acid sequence SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID NO: 34.~~

~~11.7. The IgM antibody of claim 5 or claim 6, further comprising a J-chain.~~

~~12.8. The IgM antibody or IgM-like antibody of any one of claims 1 to 711, wherein the increased serum half-life comprises an increased alpha half-life ($t_{1/2\alpha}$), an increased beta half-life ($t_{1/2\beta}$), or an increased $t_{1/2\alpha}$ and an increased $t_{1/2\beta}$ and/or wherein the IgM antibody ~~or IgM-like~~~~

~~antibody~~ further exhibits an increased peak plasma concentration (C_{max}), an increased area under the curve (AUC), a modified clearance time, or any combination thereof relative to the reference antibody.

~~13.9.~~ The IgM antibody ~~or IgM-like antibody~~ of any one of claims 1 to ~~128~~, wherein the IgM heavy chain constant regions ~~or multimerizing fragments or variants thereof~~ each comprise a C_μ4 domain and an IgM tailpiece (tp) domain.

~~14.10.~~ The IgM antibody ~~or IgM-like antibody~~ of claim ~~139~~, wherein the IgM heavy chain constant regions ~~or multimerizing fragments or variants thereof~~ each further comprise a C_μ3 domain, a C_μ2 domain, a C_μ1 domain, or any combination thereof.

~~15.~~ ~~The IgM antibody or IgM-like antibody of any one of claims 1 to 14, wherein the antigen-binding domain subunit comprises a heavy chain variable region (VH).~~

~~11.~~ The IgM antibody ~~or IgM-like antibody~~ of any one of claims 1 to ~~1015~~, wherein each binding unit further comprises two light chain constant regions ~~or fragments or variants thereof~~ each associated with an antigen-binding domain or a light chain variable region (VL) ~~subunit~~ thereof.

~~16.~~

~~17.12.~~ The IgM antibody ~~or IgM-like antibody~~ of any one of claims 1 to ~~164~~ or ~~6~~ to ~~11~~, wherein the J-chain ~~or functional fragment~~ or variant ~~thereof~~ J chain further comprises one or more heterologous polypeptides directly or indirectly fused to the J-chain ~~or functional fragment~~ or variant ~~thereof~~ J-chain.

~~18.13.~~ The IgM antibody ~~or IgM-like antibody~~ of claim ~~1217~~, wherein the one or more heterologous polypeptides is/are fused to the J-chain ~~or fragment thereof~~ or variant J-chain via a peptide linker comprising at least 5 amino acids, but no more than 25 amino acids.

~~19.14.~~ The IgM antibody ~~or IgM-like antibody~~ of claim ~~171212~~ or claim ~~1813~~, wherein the one or more heterologous polypeptides is/are fused to the N-terminus of the J-chain ~~or fragment~~ or variant J-chain ~~thereof~~, the C-terminus of the J-chain ~~or fragment~~ or variant ~~thereof~~ J-chain, or wherein heterologous polypeptides are fused to both the N-terminus and C-terminus of the J-chain ~~or fragment~~ or variant ~~thereof~~ J-chain, wherein the heterologous polypeptides can be the same or different.

~~20.15.~~ The IgM antibody ~~or IgM-like antibody~~ of claims ~~1712~~ to ~~1914~~, wherein at least one heterologous polypeptide comprises a binding domain comprising an antibody or ~~antigen-binding fragment thereof~~ an scFv.

~~21. The IgM antibody or IgM-like antibody of claim 20, wherein the antigen-binding fragment is a scFv fragment.~~

~~22.16.~~ The IgM antibody ~~or IgM-like antibody~~ of claim ~~2015 or 21~~, wherein at least one heterologous polypeptide can specifically bind to CD3ε.

~~23.17.~~ A composition comprising the IgM antibody ~~or IgM-like antibody~~ of any one of claims 1 to 16, and a pharmaceutically acceptable carrier.

~~24.18.~~ A variant J-chain comprising the amino acid sequence SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, ~~SEQ ID NO: 6~~, SEQ ID NO: 7, ~~SEQ ID NO: 8~~, SEQ ID NO: 10, ~~SEQ ID NO: 23~~, or SEQ ID NO: 24, wherein the variant J-chain can affect the serum half-life of an IgM antibody ~~or IgM-like antibody~~ comprising the variant J-chain.

~~25.19.~~ An isolated polynucleotide comprising a nucleic acid encoding a subunit polypeptide of the IgM ~~or IgM-like antibody~~ of any one of claims 1 to ~~1622~~, wherein the subunit polypeptide comprises (a) an IgM ~~or IgM-like~~ heavy chain constant region ~~or multimerizing fragment thereof~~, (b) an antibody light chain, ~~or~~ (c) a J-chain, ~~or~~ a modified J-chain, ~~or functional fragment or variant thereof~~, or (d) any combination thereof.

~~26.20.~~ An expression vector comprising the polynucleotide of claim ~~1925~~.

~~27.21.~~ A host cell comprising the polynucleotide of claim ~~1925~~ or the expression vector of claim ~~2026~~.

~~28.22.~~ A method of identifying variant J-chains that can increase the serum half-life of pentameric IgM antibodies or pentameric IgM-like antibodies comprising the variant J-chains, the method comprising:

1(a) testing pentameric IgM antibodies or pentameric IgM-like antibodies comprising variant J-chains ~~or fragments thereof~~ for increased serum half-life in a subject animal relative to a reference pentameric IgM antibody or pentameric IgM-like antibody, wherein the variant J-chains ~~or fragments thereof~~ comprise defined amino acid ~~insertions, deletions, or~~ substitutions, and wherein the reference pentameric IgM antibody or pentameric IgM-like antibody comprises a J-chain ~~or fragment thereof~~ identical to the variant J-chains except for the defined amino acid ~~insertions, deletions or~~ substitutions; and

(b) recovering those variant J-chains~~-or fragments thereof~~ that confer increased serum half-life upon the pentameric IgM antibodies or pentameric IgM-like antibodies relative to reference pentameric IgM antibody or pentameric IgM-like antibody; or

(2)(a) testing pentameric IgM antibodies or pentameric IgM-like antibodies comprising variant J-chains~~-or fragments thereof~~ for their level of binding to the Fc alpha-mu receptor (FcαμR), the polymeric Ig receptor (pIgR), or both the FcαμR and the pIgR, wherein the variant J-chains~~-or fragments thereof~~ comprise defined amino acid ~~insertions, deletions, or~~ substitutions; and

(b) recovering those variant J-chains~~-or fragments thereof~~ that confer reduced FcαμR binding ability, reduced pIgR binding ability, or reduced FcαμR and pIgR binding ability upon the pentameric IgM antibodies or pentameric IgM-like antibodies relative to a reference pentameric IgM antibody or pentameric IgM-like antibody comprising a J-chain~~-or fragment thereof~~ identical to the variant J-chains except for the defined amino acid ~~insertions, deletions or~~ substitutions.

29.23. A method of identifying variant IgM heavy chain constant regions that can increase the serum half-life of an IgM antibody~~-or IgM-like antibody~~ comprising the variant IgM heavy chain constant regions, comprising:

(1)(a) testing IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions for increased serum half-life in a subject animal relative to a reference pentameric IgM antibody or pentameric IgM-like antibody, wherein the variant IgM heavy chain constant regions comprise defined amino acid ~~insertions, deletions, or~~ substitutions, and wherein the reference IgM antibody~~-or IgM-like antibody~~ comprises IgM heavy chain constant regions identical to the variant IgM heavy chain constant regions except for the defined amino acid ~~insertions, deletions or~~ substitutions; and

(b) recovering those IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions that confer increased serum half-life upon the IgM antibodies or IgM-like antibodies comprising the variant IgM heavy chain constant regions relative to the reference IgM antibody~~-or IgM-like antibody~~; or

(2)(a) testing IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions for their level of binding to the Fc alpha-mu receptor (FcαμR), Fc mu receptor (FcμR), the polymeric Ig receptor (pIgR), any combination of two of the receptors, or all three of the receptors, wherein the variant IgM heavy chain constant regions comprise defined amino acid ~~insertions, deletions, or~~ substitutions; and

(b) recovering those IgM antibodies or IgM-like antibodies comprising variant IgM heavy chain constant regions that confer reduced FcαμR binding ability, reduced FcμR binding ability, reduced pIgR binding ability, reduced ability to bind to any two of the receptors, or reduced ability to bind to all three of the receptors, upon the IgM antibodies or IgM-like antibodies comprising the variant IgM heavy chain constant regions relative to a reference IgM antibody ~~or IgM-like antibody~~ comprising IgM heavy chain constant regions identical to the variant IgM heavy chain constant regions except for the defined amino acid ~~insertions, deletions or~~ substitutions.