[Patent Document 1] International Publication WO2009/125825
[Patent Document 2] International Publication WO2011/122011
[Non-patent Documents]
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[Non-patent Document 2] Pavlou AK, Belsey MJ., The therapeutic antibodies market to 2008., Eur. J. Pharm. Biopharm. (2005) 59 (3), 389-396
[Non-patent Document 3] Kim SJ, Park Y, Hong HJ., Antibody engineering for the development of therapeutic antibodies, Mol. Cells. (2005) 20 (1), 17-29
[Non-patent Document 4] Hinton PR, Xiong JM, Johlfs MG, Tang MT, Keller S, Tsurushita N, J. Immunol. (2006) 176 (1), 346-356
[Non-patent Document 5] Ghetie V, Popov S, Borvak J, Radu C, Matesoi D, Medesan C, Ober RJ, Ward ES., Nat. Biotechnol. (1997) 15 (7), 637-640
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Summary of the ~~Invention~~Present Disclosure

[Problems to be Solved by the ~~Invention~~Present Disclosure]

The present ~~invention~~ disclosure was achieved in view of the above circumstances. An objective of the present ~~invention~~ disclosure is to provide uses of antigen-binding molecules for eliminating antigens from plasma; methods for eliminating antigens from plasma, which comprise administering antigen-binding molecules; pharmaceutical compositions comprising antigen-binding molecules that are capable of eliminating antigens from plasma; methods of screening for antigen-binding molecules for eliminating antigens from plasma; and methods for producing antigen-binding molecules for eliminating antigens from plasma.

[Means for Solving the Problems]

The present inventors conducted dedicated studies to achieve the above-described objectives. As a result, the present inventors produced antigen-binding molecules comprising (i) an Fc region and (ii) two or more antigen-binding domains where at least one of the domains is an antigen-binding domain whose antigen binding activity varies depending on the ion concentration condition, which are antigen-binding molecules that can form an immune complex comprising (a) two or more of the antigen-binding molecules and (b) two or more antigen

molecules comprising two or more antigenic binding units. Furthermore, the present inventors discovered that the antigen-binding molecules can be used to eliminate antigens from plasma. Furthermore, the present inventors discovered that the antigen-binding molecules are useful as pharmaceutical compositions, and they produced methods for eliminating antigens from plasma, which comprise administering the antigen-binding molecules. Furthermore, the present inventors discovered methods of screening for antigen-binding molecules having the aforementioned properties, and created methods for producing the molecules, thereby completing the present ~~invention~~disclosure.

More specifically, the present ~~invention~~ disclosure provides the following:

[1] use of an antigen-binding molecule comprising
(i) an Fc region and
(ii) two or more antigen-binding domains,
wherein at least one of the domains is an antigen-binding domain of which antigen-binding activity varies depending on an ion concentration condition, and
wherein the antigen-binding molecule can form an immune complex which comprises
(a) two or more of the antigen-binding molecules and
(b) two or more antigens, wherein the antigens comprise two or more antigenic binding units,
in the manufacture of a medicament for eliminating the antigens from plasma;

[2] the use of [1], wherein the ion concentration condition is a calcium ion concentration condition;

[3] the use of [2], wherein the antigen-binding domain has an antigen-binding activity under a low calcium-ion concentration condition that is lower than the antigen-binding activity under a high calcium-ion concentration condition;

[4] the use of any one of [1] to [3], wherein the ion concentration condition is a pH condition;

[5] the use of [4], wherein the antigen-binding domain has an antigen binding activity in an acidic pH range that is lower than the antigen-binding activity in a neutral pH range condition;

[6] the use of any one of [1] to [5], wherein the antigens comprising two or more antigenic binding units are multimers;

[7] the use of [6], wherein the antigen is any one of GDF, GDF-1, GDF-3 (Vgr-2), GDF-5 (BMP-14, CDMP-1), GDF-6 (BMP-13, CDMP-2), GDF-7 (BMP-12, CDMP-3), GDF-8 (myostatin), GDF-9, GDF-15 (MIC-1), TNF, TNF-alpha, TNF-alphabeta, TNF-beta2, TNFSF10 (TRAIL Apo-2 ligand, TL2), TNFSF11 (TRANCE/RANK ligand ODF, OPG ligand), TNFSF12 (TWEAK Apo-3 ligand, DR3 ligand), TNFSF13 (APRIL TALL2), TNFSF13B (BAFF BLYS, TALL1, THANK, TNFSF20), TNFSF14 (LIGHT HVEM ligand, LTg), TNFSF15 (TL1A/VEGI), TNFSF18 (GITR ligand AITR ligand, TL6), TNFSF1A (TNF-a Conectin, DIF, TNFSF2), TNFSF1B (TNF-b LTa, TNFSF1), TNFSF3 (LTb TNFC, p33), TNFSF4 (OX40 ligand gp34,

CLAIMS

1. Use of an antigen-binding molecule comprising
(i) an Fc region and
(ii) two or more antigen-binding domains,
wherein at least one of the domains is an antigen-binding domain of which antigen-binding activity varies depending on an ion concentration condition, and
wherein the antigen-binding molecule can form an immune complex which comprises
(a) two or more of the antigen-binding molecules and
(b) two or more antigens, wherein the antigens comprise two or more antigenic binding units,
in the manufacture of a medicament for eliminating the antigens from plasma.

2. The use of claim 1, wherein the ion concentration condition is a calcium ion concentration condition.

3. The use of claim 2, wherein the antigen-binding domain has an antigen-binding activity under a low calcium-ion concentration condition that is lower than the antigen-binding activity under a high calcium-ion concentration condition.

4. The use of any one of claims 1 to 3, wherein the ion concentration condition is a pH condition.

5. The use of claim 4, wherein the antigen-binding domain has an antigen binding activity in an acidic pH range that is lower than the antigen-binding activity in a neutral pH range condition.

6. The use of any one of claims 1 to 5, wherein the antigens comprising two or more antigenic binding units are multimers.

7. The use of claim 6, wherein the antigen is any one of GDF, GDF-1, GDF-3 (Vgr-2), GDF-5 (BMP-14, CDMP-1), GDF-6 (BMP-13, CDMP-2), GDF-7 (BMP-12, CDMP-3), GDF-8 (myostatin), GDF-9, GDF-15 (MIC-1), TNF, TNF-alpha, TNF-alphabeta, TNF-beta2, TNFSF10 (TRAIL Apo-2 ligand, TL2), TNFSF11 (TRANCE/RANK ligand ODF, OPG ligand), TNFSF12 (TWEAK Apo-3 ligand, DR3 ligand), TNFSF13 (APRIL TALL2), TNFSF13B (BAFF BLYS, TALL1, THANK, TNFSF20), TNFSF14 (LIGHT HVEM ligand, LTg), TNFSF15 (TL1A/VEGI), TNFSF18 (GITR ligand AITR ligand, TL6), TNFSF1A (TNF-a Conectin, DIF, TNFSF2), TNFSF1B (TNF-b LTa, TNFSF1), TNFSF3 (LTb TNFC, p33), TNFSF4 (OX40 ligand gp34,