The present inventors have conducted diligent studies and consequently developed a polypeptide comprising an antigen binding domain and a carrying moiety having an inhibiting domain that inhibits the binding activity of the antigen binding domain, and having a longer half-life than the half-life of the antigen binding domain which exists alone. It is considered that use of the polypeptide can allow the antigen binding domain to restore its antigen binding activity in a disease tissue and exert the antigen binding activity in the disease tissue. Furthermore, the systemic distribution of an activated form of the antigen binding domain can be suppressed owing to the difference in half-life between the polypeptide comprising the antigen binding domain whose antigen binding activity is inhibited and a polypeptide comprising the antigen binding domain whose antigen binding activity is restored. Moreover, the present inventors have found that the polypeptide or a pharmaceutical composition comprising the polypeptide is useful in disease treatment and also found that: the polypeptide or the pharmaceutical composition is useful in disease treatment which involves administering the polypeptide; and the polypeptide is useful in the production of a drug for disease treatment. The present inventors have further developed methods for screening for and producing the polypeptide, methods for producing and screening for a single-domain antibody whose antigen binding activity can be inhibited by associating with particular VL, VH or VHH, and a library including a single-domain antibody whose antigen binding activity can be inhibited by associating with particular VL, VH or VHH, completing the present disclosure.

[0013a] In one aspect, the invention refers to a polypeptide comprising an antigen binding domain and a carrying moiety, the carrying moiety having an inhibiting domain that inhibits the antigen binding activity of the antigen binding domain, and the antigen binding domain having a shorter half-life in blood than that of the carrying moiety, wherein the antigen binding domain comprises a single-domain antibody or is a single-domain antibody, and the inhibiting domain of the carrying moiety is VHH, antibody VH, or antibody VL, wherein the inhibiting domain of the carrying moiety associates with the antigen binding domain and thereby inhibits the antigen binding activity of the antigen binding domain, wherein the polypeptide comprises a cleavage site, wherein the cleavage site is cleaved so that the association of the inhibiting domain of the carrying moiety with the antigen binding domain is canceled, wherein the molecular weight of the antigen binding domain is smaller than that of the carrying moiety, wherein the molecular weight of the antigen binding domain is 60 kDa or smaller, wherein the carrying moiety has FcRn binding activity, and the antigen binding domain has no FcRn binding activity or has weaker FcRn binding activity than that of the carrying moiety.

[0013b] In another aspect, the invention refers to a pharmaceutical composition comprising the polypeptide as described herein.

[0013c] In another aspect, the invention refers to a host cell comprising a polynucleotide encoding the polypeptide as described herein, or a vector comprising the polynucleotide as described herein.

[0013d] In another aspect, the invention refers to a method for producing the polypeptide as described herein.

[0014]

The present disclosure is based on these findings and specifically encompasses exemplary examples described below.

(1) A polypeptide comprising an antigen binding domain and a carrying moiety, the carrying moiety having an inhibiting domain that inhibits the antigen binding activity of the antigen binding domain, and the antigen binding domain having a shorter half-life in blood than that of the carrying moiety.

(2) The polypeptide according to (1), wherein the molecular weight of the antigen binding domain is smaller than that of the carrying moiety.

(3) The polypeptide according to (1) or (2), wherein the molecular weight of the antigen binding domain is 60 kDa or smaller.

(4) The polypeptide according to any of (1) to (3), wherein the carrying moiety has FcRn binding activity, and the antigen binding domain has no FcRn binding activity or has weaker FcRn binding activity than that of the carrying moiety.

(5) The polypeptide according to any of (1) to (4), wherein the antigen binding domain is capable of being released from the polypeptide, and the antigen binding domain released from the polypeptide has higher antigen binding activity than that before the release

CLAIMS

1. A polypeptide comprising an antigen binding domain and a carrying moiety, the carrying moiety having an inhibiting domain that inhibits the antigen binding activity of the antigen binding domain, and the antigen binding domain having a shorter half-life in blood than that of the carrying moiety,
wherein the antigen binding domain comprises a single-domain antibody or is a single-domain antibody, and the inhibiting domain of the carrying moiety is VHH, antibody VH, or antibody VL,
wherein the inhibiting domain of the carrying moiety associates with the antigen binding domain and thereby inhibits the antigen binding activity of the antigen binding domain,
wherein the polypeptide comprises a cleavage site, wherein the cleavage site is cleaved so that the association of the inhibiting domain of the carrying moiety with the antigen binding domain is canceled~~.~~

~~2. The polypeptide according to claim 1~~, wherein the molecular weight of the antigen binding domain is smaller than that of the carrying moiety~~.~~

~~3. The polypeptide according to claim 1 or 2~~, wherein the molecular weight of the antigen binding domain is 60 kDa or smaller~~.~~

~~4. The polypeptide according to any one of claims 1 to 3~~, wherein the carrying moiety has FcRn binding activity, and the antigen binding domain has no FcRn binding activity or has weaker FcRn binding activity than that of the carrying moiety.

~~5~~2. The polypeptide according to ~~any one of claims 1 to 4~~claim 1, wherein the antigen binding domain is capable of being released from the polypeptide, and the antigen binding domain released from the polypeptide has higher antigen binding activity than that before the release.

~~6~~3. The polypeptide according to claim ~~5~~2, wherein the polypeptide comprises a cleavage site, wherein the cleavage site is cleaved so that the antigen binding domain becomes capable of being released from the polypeptide.

~~7~~4. The polypeptide according to any one of claims 1 to ~~6~~3, wherein the cleavage

site comprises a protease cleavage sequence.

~~8~~5. The polypeptide according to claim ~~7~~4, wherein the protease is a target tissue specific protease.

~~9~~6. The polypeptide according to any of claims 1 to ~~8~~5, wherein the carrying moiety comprises an antibody constant region.

~~10~~7. The polypeptide according to claim ~~9~~6, wherein the polypeptide has a protease cleavage sequence, wherein the protease cleavage sequence is located near the boundary between the antigen binding domain and the antibody constant region.

8. The polypeptide of claim 7, wherein the antigen binding domain is a single-domain antibody prepared from VH, or VHH, and the protease cleavage sequence is located at any position between amino acid position 109 (Kabat numbering) of the single-domain antibody of the antigen binding domain and amino acid position 122 (EU numbering) of the antibody heavy chain constant region.

9. The polypeptide of claim 7, wherein the antigen binding domain is a single-domain antibody prepared from VL, and the protease cleavage sequence is located at any position between amino acid position 109 (Kabat numbering) of the single-domain antibody of the antigen binding domain and amino acid position 113 (EU numbering) (Kabat numbering position 113) of the antibody light chain constant region.

~~11~~10. A pharmaceutical composition comprising the polypeptide of any of claims 1 to ~~10~~9.

~~12~~11. A host cell comprising a polynucleotide encoding the polypeptide according to any one of claims 1 to ~~10~~9, or a vector comprising the polynucleotide aforementioned.

~~13~~12. A method for producing the polypeptide of any one of claims 1 to ~~10~~9.