Claims

1. A method for improving pharmacokinetics of an antigen-binding molecule by increasing its human FcRn-binding activity of the antigen-binding molecule in the neutral pH range and reducing its antigen-binding activity in the acidic pH range to less than that in the neutral pH range, wherein the antigen-binding molecule comprises an antigen-binding domain and a human FcRn-binding domain, and has a human FcRn-binding activity in the acidic pH range, wherein the acidic pH range is pH 5.8 and the neutral pH range is pH 7.4, and wherein the antigen-binding domain is any one of the following (a), (b), and (c):

(a) an antigen-binding domain comprising substitution of histidine for at least one amino acid or insertion of at least one histidine;

(b) an antigen-binding domain comprising substitution of histidine for at least one amino acid or insertion of at least one histidine in the CDR(s) of the antigen-binding molecule; and

(c) an antigen-binding domain comprising substitution of histidine for at least one amino acid or insertion of at least one histidine at the amino acid position(s) selected from the following:

Heavy chain: H27, H31, H32, H33, H35, H50, H58, H59, H61, H62, H63, H64, H65, H99, H100b, and H102 (Kabat numbering);

Light chain: L24, L27, L28, L32, L53, L54, L56, L90, L92, and L94 (Kabat numbering).

2. The method of claim 1, wherein the increase in the human FcRn-binding activity in the neutral pH range is an increase by substituting a different amino acid for at least one amino acid in the parent IgG Fc domain of the human FcRn-binding domain.

3. The method of claim 1 or 2, wherein the increase in the human FcRn-binding activity in the neutral pH range is an increase by substituting a different amino acid for at least one amino acid selected from those at positions 237, 238, 239, 248, 250, 252, 254, 255, 256, 257, 258, 265, 270, 286, 289, 297, 298, 303, 305, 307, 308, 309, 311, 312, 314, 315, 317, 325, 332, 334, 360, 376, 380, 382, 384, 385, 386, 387, 389, 424, 428, 433, 434, and 436 according to EU numbering in the parent IgG Fc domain of the human FcRn-binding domain.

4. The method of any one of claims 1 to 3, wherein the antigen-binding domain is obtained from antigen-binding domain library.

5. The method of any one of claims 1 to 4, wherein the decrease in the antigen-binding activity is represented by an increase in the value of KD (pH 5.8) /KD (pH 7.4), which is a ratio of antigen-binding activity in the acidic pH range and neutral pH range,

relative to before histidine substitution or insertion.

6. The method of any one of claims 1 to 5, wherein the decrease in the antigen-binding activity is represented by the value of KD (pH 5.8) /KD (pH 7.4), which is a ratio of KD (dissociation constant) against an antigen in the acidic pH range and neutral pH range, of 2 or greater.

7. The method of any one of claims 1 to 5, wherein the decrease in the antigen-binding activity is represented by the value of k_d (pH 5.8) / k_d (pH 7.4), which is a ratio of k_d (dissociation rate constant) against an antigen in the acidic pH range and neutral pH range, of 2 or greater.

8. The method of any one of claims 1 to 7, wherein the antigen-binding molecule is an antibody.