Table 3

| | KD (μM) | | |
|---|---|---|---|
| | WT | H0L0 | DNS |
| IgG1 | 1.42 | 1.07 | 1.36 |
| M58 | 1.03 | 0.91 | 1.03 |

As shown in Table 3, it was demonstrated that as a result of conversion of the constant region from the IgG1 type to M58, as with anti-IL-6 receptor antibody WT, the bindings of both the anti-IL-31 receptor antibody H0L0 and anti-RANKL antibody DNS to human FcRn were improved. This suggests the possibility that regardless of the type of antigen or sequence of antibody variable region, the pharmacokinetics in human is improved by converting the constant region from the IgG1 type to M58.

[Example 10] Effect of cysteine in the CH1 domain on heterogeneity and stability

As described in Example 2, cysteines in the hinge region and CH1 domain of IgG2 were substituted to decrease the heterogeneity of natural IgG2. Assessment of various altered antibodies revealed that heterogeneity could be reduced without decreasing stability by using SKSC (SEQ ID NO: ~~15~~438). SKSC (SEQ ID NO: 38) is an altered constant region obtained by substituting serine for cysteine at position 131 and lysine for arginine at position 133, EU numbering, in the H-chain CH1 domain, and serine for cysteine at position 219, EU numbering, in the H-chain upper hinge of the wild type IgG2 constant region sequence.

Meanwhile, another possible method for decreasing heterogeneity is a single substitution of serine for cysteine at position 219, or serine for cysteine at position 220, EU numbering, in the H-chain upper hinge. The altered IgG2 constant region SC (SEQ ID NO: 39) was prepared by substituting serine for cysteine at position 219 and CS (SEQ ID NO: 40) was prepared by substituting serine for cysteine at position 220, EU numbering, in IgG2. WT-SC (SEQ ID NO: 41) and WT-CS (SEQ ID NO: 42) were prepared to have SC and CS, respectively, and compared with WT-IgG1, WT-IgG2, WT-SKSC, and WT-M58 in terms of heterogeneity and thermal stability. Furthermore, F2H/L39-IgG1, F2H/L39-IgG2, F2H/L39-SC, F2H/L39-CS, F2H/L39-SKSC, and F2H/L39-M14, which have the constant region of IgG1 (SEQ ID NO: 1), IgG2 (SEQ ID NO: 2), SC (SEQ ID NO: 39), CS (SEQ ID NO: 40), SKSC (SEQ ID NO: 38), or M14 (SEQ ID NO: 5), respectively, were prepared from F2H/L39 (the amino acid sequences of F2H/L39_VH and F2H/L39_VL as set forth in SEQ ID NOs: 29 and 30, respectively), which is an anti IL-6 receptor antibody different from WT. The antibodies were compared with regard to heterogeneity.

WT-IgG1, WT-IgG2, WT-SC, WT-CS, WT-SKSC, WT-M58, F2H/L39-IgG1,