(2) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 55; SEQ ID NO: 59; SEQ ID NO: 60 and SEQ ID NO: 61; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:64, SEQ ID NO:68 and SEQ ID NO: 69;

(3) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 84; SEQ ID NO: 88; SEQ ID NO: 89; SEQ ID NO: 90; SEQ ID NO: 121; SEQ ID NO: 122; and SEQ ID NO: 123; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:91, SEQ ID NO:95 and SEQ ID NO:96;

(4) the variable heavy chain amino acid sequence set forth in SEQ ID NO:112 and the variable light chain amino acid sequence set forth in SEQ ID NO:103;

(5) the variable heavy chain amino acid sequence set forth in SEQ ID NO:113 and the variable light chain amino acid sequence set forth in SEQ ID NO:104;

(6) the variable heavy chain amino acid sequence set forth in SEQ ID NO:114 and the variable light chain amino acid sequence set forth in SEQ ID NO:105;

(7) the variable heavy chain amino acid sequence set forth in SEQ ID NO:116 and the variable light chain amino acid sequence set forth in SEQ ID NO:107;

(8) the variable heavy chain amino acid sequence set forth in SEQ ID NO:117 and the variable light chain amino acid sequence set forth in SEQ ID NO:108;

(9) the variable heavy chain amino acid sequence set forth in SEQ ID NO:118 and the variable light chain amino acid sequence set forth in SEQ ID NO:109;

(10) the variable heavy chain amino acid sequence set forth in SEQ ID NO:119 and the variable light chain amino acid sequence set forth in SEQ ID NO:110; and

(11) the variable heavy chain amino acid sequence set forth in SEQ ID NO:120 and the variable light chain amino acid sequence set forth in SEQ ID NO:111.

In another aspect, the invention pertains to a binding protein capable of binding prolactin receptor (PRLR), wherein said binding protein comprises an antibody having (i) a heavy chain variable domain CDR set comprising SEQ ID NOs: 40, 41, and 42; and (ii) a light chain variable domain CDR set comprising SEQ ID NOs: 49, 50, and 51.

In another aspect, the invention pertains binding protein capable of binding PRLR that competes with an antibody comprising a heavy chain variable domain and a light chain variable domain selected from the group consisting of:

(1) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 39; SEQ ID NO: 43; SEQ ID NO: 44 and SEQ ID NO: 45; and a

variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO: 53 and SEQ ID NO:54;

(2) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 55; SEQ ID NO: 59; SEQ ID NO: 60 and SEQ ID NO: 61; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:64, SEQ ID NO:68 and SEQ ID NO: 69;

(3) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 84; SEQ ID NO: 88; SEQ ID NO: 89; SEQ ID NO: 90; SEQ ID NO: 121; SEQ ID NO: 122; and SEQ ID NO: 123; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:91, SEQ ID NO:95 and SEQ ID NO:96;

(4) the variable heavy chain amino acid sequence set forth in SEQ ID NO:112 and the variable light chain amino acid sequence set forth in SEQ ID NO:103;

(5) the variable heavy chain amino acid sequence set forth in SEQ ID NO:113 and the variable light chain amino acid sequence set forth in SEQ ID NO:104;

(6) the variable heavy chain amino acid sequence set forth in SEQ ID NO:114 and the variable light chain amino acid sequence set forth in SEQ ID NO:105;

(7) the variable heavy chain amino acid sequence set forth in SEQ ID NO:116 and the variable light chain amino acid sequence set forth in SEQ ID NO:107;

(8) the variable heavy chain amino acid sequence set forth in SEQ ID NO:117 and the variable light chain amino acid sequence set forth in SEQ ID NO:108;

(9) the variable heavy chain amino acid sequence set forth in SEQ ID NO:118 and the variable light chain amino acid sequence set forth in SEQ ID NO:109;

(10) the variable heavy chain amino acid sequence set forth in SEQ ID NO:119 and the variable light chain amino acid sequence set forth in SEQ ID NO:110; and

(11) the variable heavy chain amino acid sequence set forth in SEQ ID NO:120 and the variable light chain amino acid sequence set forth in SEQ ID NO:111;

wherein the binding protein is a monoclonal antibody.

In another embodiment, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, competes with an antibody comprising a heavy chain variable domain and a light chain variable domain selected from the group consisting of:

(1) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 39; SEQ ID NO: 43; SEQ ID NO: 44 and SEQ ID NO: 45; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO: 53 and SEQ ID NO:54;

(2) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 55; SEQ ID NO: 59; SEQ ID NO: 60 and SEQ ID NO: 61; and a

CLAIMS

We claim:

1. A binding protein capable of binding prolactin receptor (PRLR), wherein said binding protein comprises an antibody having (i) a heavy chain variable domain CDR set comprising SEQ ID NOs: 40, 41, and 42; and (ii) a light chain variable domain CDR set comprising SEQ ID NOs: 49, 50, and 51.

2. The binding protein of claim 1, wherein the antibody comprises a heavy chain variable domain comprising SEQ ID NO: 44 and a light chain variable domain comprising SEQ ID NO: 52.

3. The binding protein according to claim 1, further comprising a human acceptor framework.

4. The binding protein according to claim 3, wherein said human acceptor framework comprises at least one Framework Region amino acid substitution, wherein the amino acid sequence of the framework is at least 65% identical to the sequence of said human acceptor framework and comprises at least 70 amino acid residues identical to said human acceptor framework.

5. The binding protein according to claim 4, wherein said human acceptor framework comprises at least one Framework Region amino acid substitution at a key residue, said key residue selected from the group consisting of:
a residue adjacent to a CDR;
a glycosylation site residue;
a residue capable of interacting with human PRLR;
a residue capable of interacting with a CDR;
a contact residue between heavy chain variable region and light chain variable region;
a residue within a Vernier zone; and
a residue in a region that overlaps between a Chothia-defined variable heavy chain CDR1 and a Kabat-defined first heavy chain framework.

6. The binding protein according to claim 5, wherein said key residue is selected from the group consisting of 2L, 43L, 48L, 58L, 64L, 87L, 27H, 48H, 60H, 63H, 64H, 65H, 67H, 69H, 71H, 73H, 75H, 93H.

7. The binding protein according to claim 6, wherein the binding protein is a consensus human variable domain.

8. The binding protein according to any one of the preceding claims, wherein the binding protein binds the ligand binding D1 domain of PRLR.

9. The binding protein according to any one of the preceding claims, wherein the binding protein inhibits binding of prolactin to PRLR.

10. The binding protein according to any one of the preceding claims, wherein the binding protein is capable of neutralizing PRLR.

11. The binding protein according to any one of the preceding claims, wherein said binding protein has an on rate constant (K_{on}) to PRLR selected from the group consisting of: at least about $10^2M^{-1}s^{-1}$; at least about $10^3M^{-1}s^{-1}$; at least about $10^4M^{-1}s^{-1}$; at least about $10^5M^{-1}s^{-1}$; and at least about $10^6M^{-1}s^{-1}$; as measured by surface plasmon resonance.

12. The binding protein according to any one of the preceding claims, wherein said binding protein has an off rate constant (K_{off}) to PRLR selected from the group consisting of: at most about $10^{-3}s^{-1}$; at most about $10^{-4}s^{-1}$; at most about $10^{-5}s^{-1}$; and at most about $10^{-6}s^{-1}$, as measured by surface plasmon resonance.

13. The binding protein according to any one of the preceding claims, wherein said binding protein has a dissociation constant (K_D) to PRLR selected from the group consisting of: at most about 10^{-7} M; at most about 10^{-8} M; at most about 10^{-9} M; at most about 10^{-10} M; at most about 10^{-11} M; at most about 10^{-12} M; and at most 10^{-13} M.

14. A binding protein capable of binding PRLR and competing with an antibody comprising a heavy chain having the amino acid sequence of SEQ ID NO: 129; and a light chain having the amino acid sequence of SEQ ID NO: 126.