Claims:

1. Antibody Mat3 or antigen-binding fragments thereof which antagonize prolactin receptor-mediated signaling, whereby the antibody comprises a variable heavy region with an amino acid sequence according to SEQ ID NO: 1, and a variable light region an amino acid sequence according to SEQ ID NO: 2.

2. Antibody or antigen-binding fragments thereof according to claim 1 to 2, whereby the antibody consists of an antigen-binding region that binds specifically to one or more regions of the extracellular domain of PRLR from human, monkey and mouse, and whereby the amino acid sequences of the human PRLR are depicted by the amino acid sequences from position 1 to 210 of SEQ ID NO: 12 and human polymorphic variants of SEQ ID NO: 12, by the amino acid sequences from position 1 to 210 of the monkey PRLR according to SEQ ID NO: 11 and of the mouse PRLR according to SEQ ID NO: 13.

3. Antibody or antigen-binding fragments thereof according to claim 2, whereby the affinity to the extracellular domain of PRLR from human, monkey and mouse is from 100 nM to 0.1 nM.

4. Antibody or antigen-binding fragments thereof according to claim 3, whereby the affinity is 0.1 nM.

5. Antibody or antigen-binding fragments thereof according to claim 1 to 2, whereby the antibody consists of an antigen-binding region that binds specifically to one or more regions of the extracellular domain of human PRLR and whereby the affinity is from 10 nM to 0.1nM.

6. Antibody or antigen-binding fragments thereof according to any of claims 1 to 5 wherein the heavy chain constant domains is a modified or unmodified IgG1, IgG2, IgG3 or IgG4.

7. An isolated nucleic acid sequence encoding an antibody or antigen-binding fragment according to any of the claims 1 to 6.

8. An isolated nucleic acid sequence according to claim 7, whereby the isolated nucleic acid sequences are according to SEQ ID NO: 3 and 4.

9. Expression vector comprising a nucleic acid sequence of claim 7 or 8.

10. Host cell comprising the vector of claim 9 or a nucleic acid molecule of claim 7 or 8, whereby the host cell is a higher eukaryotic host cell, a lower eukaryotic host cell, or a prokaryotic cell.

11. Host cell of claim 10, whereby the higher eukaryotic host cell is a mammalian cell.

12. Host cell of claim 10, whereby the lower eukaryotic host cell is a yeast cell.

13. Host cell of claim 10, whereby the prokaryotic cell is a bacterial cell.

14. A method of using the host cell of any of claims 10 to 13 to produce an antibody or antigen-binding fragment, comprising culturing the host cell of claim 10 under suitable conditions and recovering said antibody.

15. An antibody or antigen-binding fragment produced by the method of claim 14.

16. An antibody or antigen-binding fragment of any of claims 1 to 6 that is purified to at least 95% homogeneity by weight.

17. An antibody or antigen-binding fragment according to claims 1 to 6 as a medicament.

18. A pharmaceutical composition comprising the antibody or antigen-binding fragment according to any of claims 1 to 6 and a pharmaceutically acceptable carrier comprising excipients and auxiliaries.

19. Kits comprising an antibody of claim 1 to 6 comprising a therapeutically effective amount of antibody Mat3, packaged in a container, said kit optionally containing a second therapeutic agent, and further comprising a label attached to or packaged with the container, the label describing the contents of the container and providing indications and/or instructions regarding the use of the contents of the container to treat endometriosis, adenomyosis, benign breast disease and mastalgia, lactation inhibition, hyper- and normoprolactinemic hair loss, benign prostate hyperplasia, fibroids or for use in non-hormonal female contraception or to treat women under combined hormone therapy (i.e. estrogen plus progestin therapy) to inhibit mammary epithelial cell proliferation or for treatment and prevention of antiestrogen-resistant breast cancer.

20. Antibody or antigen-binding fragment according to any of claims 1 to 6 for use in a method of treatment and/or prevention of endometriosis and adenomyosis (endometriosis interna).

21. Antibody or antigen-binding fragment according to any of claims 1 to 6 for use in a method of treatment of benign breast disease and mastalgia.

22. Antibody or antigen-binding fragment according to any of claims 1 to 6 for use in a method of treatment or prevention of antiestrogen-resistant breast cancer.

23. Pharmaceutical composition according to claim 18 comprising PRLR antibodies or antigen-binding fragment according to any of claims 1 to 6, in combination with at least one other agent.

Claims:

1. Antibody Mat3 or antigen-binding fragments thereof which antagonize prolactin receptor-mediated signaling, whereby the antibody comprises a variable heavy region with an amino acid sequence according to SEQ ID NO: 1, and a variable light region an amino acid sequence according to SEQ ID NO: 2.

2. Antibody or antigen-binding fragments thereof according to any of claim 1 to 2, whereby the antibody consists of an antigen-binding region that binds specifically to one or more regions of the extracellular domain of PRLR from human, monkey and mouse, and whereby the amino acid sequences of the human PRLR are depicted by the amino acid sequences from position 1 to 210 of SEQ ID NO: 12 and human polymorphic variants of SEQ ID NO: 12, by the amino acid sequences from position 1 to 210 of the monkey PRLR according to SEQ ID NO: 11 and of the mouse PRLR according to SEQ ID NO: 13.

3. Antibody or antigen-binding fragments thereof according to claim 2, whereby the affinity to the extracellular domain of PRLR from human, monkey and mouse is from 100 nM to 0.1 nM.

4. Antibody or antigen-binding fragments thereof according to claim 3, whereby the affinity is 0.1 nM.

5. Antibody or antigen-binding fragments thereof according to any of claims 1 to 2, whereby the antibody consists of an antigen-binding region that binds specifically to one or more regions of the extracellular domain of human PRLR and whereby the affinity is from 10 nM to 0.1nM.

6. Antibody or antigen-binding fragments thereof according to any of claims 1 to 5 wherein the heavy chain constant domains is a modified or unmodified IgG1, IgG2, IgG3 or IgG4.

7. An isolated nucleic acid sequence encoding an antibody or antigen-binding fragment according to any of the claims 1 to 6.

8. An isolated nucleic acid sequence according to claim 7, whereby the isolated nucleic acid sequences are according to SEQ ID NO: 3 and 4.

9. Expression vector comprising a nucleic acid sequence of claim 7 or 8.

10. Host cell comprising the vector of claim 9 or a nucleic acid molecule of claim 7 or 8, whereby the host cell is a higher eukaryotic host cell, a lower eukaryotic host cell, or a prokaryotic cell.

11. Host cell of claim 10, whereby the higher eukaryotic host cell is a mammalian cell.

12. Host cell of claim 10, whereby the lower eukaryotic host cell is a yeast cell.

13. Host cell of claim 10, whereby the prokaryotic cell is a bacterial cell.

14. A method of using the host cell of any of claims 10 to 13 to produce an antibody or antigen-binding fragment, comprising culturing the host cell of claim 10 under suitable conditions and recovering said antibody.

15. An antibody or antigen-binding fragment of any of claims 1 to 6 that is purified to at least 95% homogeneity by weight.

16. An antibody or antigen-binding fragment according to any of claims 1 to 6 for use as a medicament.

17. A pharmaceutical composition comprising the antibody or antigen-binding fragment according to any of claims 1 to 6 and a pharmaceutically acceptable carrier comprising excipients and auxiliaries.

18. Kits comprising an antibody of any of claims 1 to 6 comprising a therapeutically effective amount of antibody Mat3, packaged in a container, said kit optionally containing a second therapeutic agent, and further comprising a label attached to or packaged with the container, the label describing the contents of the container and providing indications and/or instructions regarding the use of the contents of the container to treat endometriosis, adenomyosis, benign breast disease and mastalgia, lactation inhibition, hyper- and normoprolactinemic hair loss, benign prostate hyperplasia, fibroids or for use in non-hormonal female contraception or to treat women under combined hormone therapy (i.e. estrogen plus progestin therapy) to inhibit mammary epithelial cell proliferation or for treatment and prevention of antiestrogen-resistant breast cancer.

19. Use of an antibody or antigen-binding fragment according to any of claims 1 to 6 in the manufacture of a medicament for treatment and/or prevention of endometriosis and adenomyosis (endometriosis interna).

20. Use of an antibody or antigen-binding fragment according to any of claims 1 to 6 in the manufacture of a medicament for treatment of benign breast disease and mastalgia.

21. Use of an antibody or antigen-binding fragment according to any of claims 1 to 6 in the manufacture of a medicament for treatment or prevention of antiestrogen-resistant breast cancer.

22. Pharmaceutical composition according to claim 18 comprising PRLR antibodies or antigen-binding fragment according to any of claims 1 to 6, in combination with at least one other agent.

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35 40 45

His Glu Cys Pro Asp Tyr Ile Thr Gly Gly Pro Asn Ser Cys His Phe
50 55 60

Gly Lys Gln Tyr Thr Ser Met Trp Arg Thr Tyr Val Met Met Val Asn
65 70 75 80

Ala Thr Asn Gln Met Gly Ser Ser Phe Ser Asp Glu Leu Tyr Val Asp
85 90 95

Val Thr Tyr Ile Val Gln Pro Asp Pro Pro Leu Glu Leu Thr Val Glu
100 105 110

Val Lys Gln Pro Glu Asp Arg Lys Pro Tyr Leu Trp Met Lys Trp Ser
115 120 125

Pro Pro Thr Leu Ile Asp Leu Lys Thr Gly Trp Phe Thr Leu Leu Tyr
130 135 140