

CLAIMS

1. A panel for non-invasively characterizing endometriosis in a biological sample of a subject, the panel comprising polypeptide markers Apolipoprotein A1 (ApoA1), β 2-microglobulin (B2M), Cancer Antigen 125 (CA125), Transferrin (TRF), Transthyretin (TT)/Prealbumin (PREA), Human Epididymis Protein 4 (HE4), Follicle Stimulating Hormone (FSH), and one of the following polypeptide markers: Chemokine 4 (CCL4, MIP-1 β), Immunoglobulin M (IgM), Luteinizing Hormone (LH), Macrophage Derived Chemokine (MDC, CCL22), and Progesterone (P4) or polynucleotides encoding such polypeptides.
2. A panel for non-invasively characterizing endometriosis in a biological sample of a subject, the panel comprising polypeptide markers β 2-microglobulin (B2M), Cancer Antigen 125 (CA125), Follicle Stimulating Hormone (FSH), Chemokine 4 (CCL4, MIP-1 β), Immunoglobulin M (IgM), Luteinizing Hormone (LH), Macrophage Derived Chemokine (MDC, CCL22), and Progesterone (P4) or polynucleotides encoding such polypeptides.
3. A panel for non-invasively characterizing endometriosis in a biological sample of a subject, the panel comprising polypeptide markers Cancer Antigen 125 (CA125), Apolipoprotein A1 (ApoA1), Transferrin (TRF), β 2-microglobulin (B2M), Follicle Stimulating Hormone (FSH), Human Epididymis Protein 4 (HE4), and Prealbumin (PREA) or polynucleotides encoding such polypeptides.
4. A panel for non-invasively characterizing endometriosis in a biological sample of a subject, the panel comprising polypeptide markers Cancer Antigen 125 (CA125), Macrophage Derived Chemokine (MDC, CCL22), Progesterone (P4), EN-RAGE (S100A12), Immunoglobulin M (IgM), Chemokine 4 (CCL4, MIP-1 β), β 2-microglobulin (B2M), Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), and Cystatin C (CST3) or polynucleotides encoding such polypeptides.
5. A panel for non-invasively characterizing endometriosis in a biological sample of a subject, the panel comprising polypeptide markers Cancer Antigen 125 (CA125), Macrophage Derived Chemokine (MDC, CCL22), Progesterone (P4), and Apolipoprotein A1 (ApoA1) or polynucleotides encoding such polypeptides.

6. A panel for non-invasively characterizing endometriosis in a biological sample of a subject, the panel comprising polypeptide markers Cancer Antigen 125 (CA125), Apolipoprotein A1 (ApoA1), Macrophage Derived Chemokine (MDC, CCL22), Progesterone (P4), EN-RAGE (S100A12), Immunoglobulin M (IgM), Chemokine 4 (CCL4, MIP-1 β , HCC4), β 2-microglobulin (B2M), Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), and or polynucleotides encoding such polypeptides.

7. A panel for non-invasively characterizing endometriosis in a biological sample of a subject, the panel comprising polypeptide markers Apolipoprotein A1 (ApoA1), β 2-microglobulin (B2M), Cancer Antigen 125 (CA125), Transferrin (TRF), Transthyretin (TT)/Prealbumin (PREA), Human Epididymis Protein 4 (HE4), Follicle Stimulating Hormone (FSH) and one or more of the following polypeptide markers: Alpha 1 Microglobulin (A1M), Alpha Fetoprotein (AFP), Angiopoietin 2 (Ang-2), Apolipoprotein B (ApoB), Apolipoprotein E (ApoE), Cystatin C (CST3), CD 40 Antigen (CD40), Chromogranin A (CgA), Chemokine 4 (CCL4, MIP-1 β), Clusterin (CLU, ApoJ), Eotaxin 1 (CCL11), Endostatin, EN-RAGE (S100A12), Fatty Acid Binding Protein (adipocyte)(FABP4), Fatty Acid Binding Protein (heart) (H-FABP, FABP3), Fas Ligand Receptor (Fas, FasR), Ferritin (FTL), Galectin 3 (Gal-3), Growth Hormone (GH, somatotropin, human growth hormone, HGH), Glutathione S Transferase alpha (GST α), Human Chorionic Gonadotropin (hCG), Hepatocyte Growth Factor (HGF), Haptoglobin (Hp), Immunoglobulin E (IgE), Insulin like Growth Factor Binding Protein 4 (IGFBP4), Insulin like Growth Factor I (IGF-I), Immunoglobulin M (IgM), Interleukin 8 (IL-8, CXCL8), Interferon gamma Induced Protein 10 (IP-10, CXCL10), Interferon inducible T cell alpha chemoattractant (I-TAC, CXCL11), Kallikrein 5 (KLK5), Leptin (LEP), Luteinizing Hormone (LH), Monocyte Chemotactic Protein 1 (MCP-1, CCL2), Monocyte Chemotactic Protein 4 (MCP-4, CCL13), Macrophage Derived Chemokine (MDC, CCL22), Monokine Induced by Gamma Interferon (Mig, CXCL9), Macrophage Inflammatory Protein 1 alpha (MIP-1 α , CCL3), Matrix Metalloproteinase 3 (MMP-3), Myoglobin (Mb), N terminal prohormone of brain natriuretic peptide (NT-proBNP), Osteoprotegerin (OPG, TNFRSF11B), Pulmonary and Activation Regulated Chemokine (PARC), Proastasin (PRSS8), Phosphoserine Aminotransferase (PSAT), Stem Cell Factor (SCF), Thymus Expressed Chemokine (TECK), Trefoil Factor 3 (TFF3), Tumor Necrosis Factor alpha (TNF α , TNF), Tumor Necrosis Factor Receptor 1 (TNFR1), Tumor Necrosis Factor Receptor 2 (TNFR2),

Tissue type Plasminogen activator (tPA/PLAT), Urokinase type Plasminogen Activator (uPA), Urokinase type Plasminogen Activator Receptor (uPAR, CD87), Vascular Endothelial Growth Factor (VEGF), von Willebrand Factor (VWF), YKL-40 (CHI3L1), or polynucleotides encoding such polypeptides.

8. The panel of any one of claims 1-7, wherein the markers are bound to a capture molecule.
9. The panel of claim 8, wherein the capture molecule is bound to a substrate.
10. A panel of capture molecules, wherein each capture molecule binds a polypeptide biomarker of any one of claims 1-7.
11. The panel of any one of claims 8-10, wherein the capture molecule is an antibody.
12. The panel of any one of claims 8-10, wherein the capture molecule is a polynucleotide.
13. Use of a gonadotropin-releasing hormone (GnRH) antagonist or a GnRH agonist in the preparation of a medicament for the treatment of endometriosis in a selected subject , wherein the subject is selected by characterizing a biological sample of the subject as having an alteration in the level of a biomarker relative to a reference, wherein the biomarker is selected from the group consisting of Apolipoprotein A1 (ApoA1), β 2-microglobulin (B2M), Cancer Antigen 125 (CA125), Transferrin (TRF), Transthyretin (TT)/Prealbumin (PREA), Human Epididymis Protein 4 (HE4), Follicle Stimulating Hormone (FSH), and one or more of the following polypeptide markers: Chemokine 4 (CCL4, MIP-1 β), Immunoglobulin M (IgM), Luteinizing Hormone (LH), Macrophage Derived Chemokine (MDC, CCL22), and Progesterone (P4).
14. Use of a gonadotropin-releasing hormone (GnRH) antagonist or a GnRH agonist in the preparation of a medicament for the treatment of endometriosis in a selected subject, wherein the subject is selected by characterizing a biological sample of the subject as having an alteration in the level of a biomarker relative to a reference, wherein the biomarker is

selected from the group consisting of β 2-microglobulin (B2M), Cancer Antigen 125 (CA125), Follicle Stimulating Hormone (FSH), Chemokine 4 (CCL4, MIP-1 β), Immunoglobulin M (IgM), Luteinizing Hormone (LH), Macrophage Derived Chemokine (MDC, CCL22), and Progesterone (P4).

15. Use of a gonadotropin-releasing hormone (GnRH) antagonist or a GnRH agonist in the preparation of a medicament for the treatment of endometriosis in a selected subject, wherein the subject is selected by characterizing a biological sample of the subject as having an alteration in the level of a biomarker relative to a reference, wherein the biomarker is selected from the group consisting of Apolipoprotein A1 (ApoA1), β 2-microglobulin (B2M), Cancer Antigen 125 (CA125), Transferrin (TRF), Transthyretin (TT)/Prealbumin (PREA), Human Epididymis Protein 4 (HE4), Follicle Stimulating Hormone (FSH) and one or more of the following polypeptide markers: Alpha 1 Microglobulin (A1M), Alpha Fetoprotein (AFP), Angiopoietin 2 (Ang-2), Apolipoprotein B (ApoB), Apolipoprotein E (ApoE), Cystatin C (CST3), CD 40 Antigen (CD40), Chromogranin A (CgA), Chemokine 4 (CCL4, MIP-1 β), Clusterin (CLU, ApoJ), Eotaxin 1 (CCL11), Endostatin, EN-RAGE (S100A12), Fatty Acid Binding Protein (adipocyte)(FABP4), Fatty Acid Binding Protein (heart) (H-FABP, FABP3), Fas Ligand Receptor (Fas, FasR), Ferritin (FTL), Galectin 3 (Gal-3), Growth Hormone (GH, somatotropin, human growth hormone, HGH), Glutathione S Transferase alpha (GST α), Human Chorionic Gonadotropin (hCG), Hepatocyte Growth Factor (HGF), Haptoglobin (Hp), Immunoglobulin E (IgE), Insulin like Growth Factor Binding Protein 4 (IGFBP4), Insulin like Growth Factor I (IGF-I), Immunoglobulin M (IgM), Interleukin 8 (IL-8, CXCL8), Interferon gamma Induced Protein 10 (IP-10, CXCL10), Interferon inducible T cell alpha chemoattractant (I-TAC, CXCL11), Kallikrein 5 (KLK5), Leptin (LEP), Luteinizing Hormone (LH), Monocyte Chemotactic Protein 1 (MCP-1, CCL2), Monocyte Chemotactic Protein 4 (MCP-4, CCL13), Macrophage Derived Chemokine (MDC, CCL22), Monokine Induced by Gamma Interferon (Mig, CXCL9), Macrophage Inflammatory Protein 1 alpha (MIP-1 α , CCL3), Matrix Metalloproteinase 3 (MMP-3), Myoglobin (Mb), N terminal prohormone of brain natriuretic peptide (NT-proBNP), Osteoprotegerin (OPG, TNFRSF11B), Pulmonary and Activation Regulated Chemokine (PARC), Progesterone (P4), Prostatin (PRSS8), Phosphoserine Aminotransferase (PSAT), Stem Cell Factor (SCF), Thymus Expressed Chemokine (TECK), Trefoil Factor 3 (TFF3), Tumor Necrosis Factor alpha (TNF α , TNF), Tumor Necrosis Factor Receptor 1 (TNFR1), Tumor Necrosis Factor

Receptor 2 (TNFR2), Tissue type Plasminogen activator (tPA/PLAT), Urokinase type Plasminogen Activator (uPA), Urokinase type Plasminogen Activator Receptor (uPAR, CD87), Vascular Endothelial Growth Factor (VEGF), von Willebrand Factor (VWF), and YKL-40 (CHI3L1).

16. Use of a gonadotropin-releasing hormone (GnRH) antagonist or a GnRH agonist in the preparation for the treatment of endometriosis in a selected subject, wherein the subject is selected by characterizing a biological sample of the subject as having an alteration in the level of a biomarker relative to a reference, wherein the biomarker is selected from the group consisting of Cancer Antigen 125 (CA125), Macrophage Derived Chemokine (MDC, CCL22), Progesterone (P4), and Apolipoprotein A1 (ApoA1).

17. Use of a gonadotropin-releasing hormone (GnRH) antagonist or a GnRH agonist in the preparation of a medicament for the treatment of endometriosis in a selected subject, wherein the subject is selected by characterizing a biological sample of the subject as having an alteration in the level of a biomarker relative to a reference, wherein the biomarker is selected from the group consisting of Cancer Antigen 125 (CA125), Apolipoprotein A1 (ApoA1), Transferrin (TRF), β 2-microglobulin (B2M), Follicle Stimulating Hormone (FSH), Human Epididymis Protein 4 (HE4), and Prealbumin (PREA) or polynucleotides encoding such polypeptides.

18. Use of a gonadotropin-releasing hormone (GnRH) antagonist or a GnRH agonist in the preparation of a medicament for the treatment of endometriosis in a selected subject, wherein the subject is selected by characterizing a biological sample of the subject as having an alteration in the level of a biomarker relative to a reference, wherein the biomarker is selected from the group consisting of Cancer Antigen 125 (CA125), Macrophage Derived Chemokine (MDC, CCL22), Progesterone (P4), EN-RAGE (S100A12), Immunoglobulin M (IgM), Chemokine 4 (CCL4, MIP-1 β), β 2-microglobulin (B2M), Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), and Cystatin C (CST3) or polynucleotides encoding such polypeptides.

19. Use of a gonadotropin-releasing hormone (GnRH) antagonist or a GnRH agonist in the preparation of a medicament for the treatment of endometriosis in a selected subject,

wherein the subject is selected by characterizing a biological sample of the subject as having an alteration in the level of a biomarker relative to a reference, wherein the biomarker is selected from the group consisting of Cancer Antigen 125 (CA125), Apolipoprotein A1 (ApoA1), Macrophage Derived Chemokine (MDC, CCL22), Progesterone (P4), EN-RAGE (S100A12), Immunoglobulin M (IgM), Chemokine 4 (CCL4, MIP-1 β , HCC4), β 2-microglobulin (B2M), Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), and or polynucleotides encoding such polypeptides.

20. The use of any one of claims 13-19, further comprising characterizing the age of the subject.

21. The use of any one of claims 13-20, further comprising characterizing the subject as pre-menopausal or post-menopausal.

22. The use of any one of claims 13-21, wherein the GnRH antagonist is elagolix, abarelix, cetrorelix, degarelix, ganirelix, or relugolix.

23. The use of any one of claims 13-22, wherein the GnRH antagonist is elagolix.

24. The use of any one of claims 13-23, wherein the GnRH agonist is goserelin, leuprolide, nafarelin, buserelin, gonadorelin, histrelin, or triptorelin.

25. The use of any one of claims 13-24, wherein an increase in the level of one or more of said markers distinguishes endometriosis from non-endometriosis.

26. The use of any one of claims 13-25, wherein a decrease in the level of one or more of said markers distinguishes endometriosis from non-endometriosis.

27. The use of any one of claims 13-26, wherein the reference is a corresponding biological sample derived from a healthy subject.

28. The use of any one of claims 13-26, wherein the reference is derived from the same subject at an earlier point in time.

29. The use of any one of claims 13-28, wherein the characterizing step is an immunoassay or affinity capture.
30. The use of claim 29, wherein the immunoassay comprises affinity capture assay, immunometric assay, heterogeneous chemiluminescence immunometric assay, homogeneous chemiluminescence immunometric assay, ELISA, western blotting, radioimmunoassay, magnetic immunoassay, real-time immunoquantitative PCR (iqPCR) and SERS label free assay.
31. A method for determining the marker profile of a biological sample, the method comprising quantifying the levels of a marker of Table 1 in the sample.
32. The use of any one of claims 13-30 or the method of claim 31, wherein the biological sample is a biological fluid selected from the group consisting of blood, blood serum, and plasma.
33. The use of any of claims 13-30 or the method of any one of claims 31-32, wherein the method is carried out in a plate, chip, beads, microfluidic platform, membrane, planar microarray, or suspension array.
34. The use of any of claims 13-30 or the method of any one of claims 31-33, wherein the method detects a CA125 glycoform.
35. A kit for detecting endometriosis in a biological sample, the kit comprising a set of capture molecules each of which specifically binds a marker of Table 1 or of any one of claims 1-7.