Claims

1. A method of diagnosis and/or for the prognosis of endometrial cancer, the method comprising determining, in a sample from the female genital tract part including one or more of the vulvae, vagina, cervix, uterus, fallopian tubes, and ovaries, and selected from a gynecologic sampling, including or selected from a cervical fluid, a cytology, a pap-smear sample, an endometrial biopsy, a uterine fluid, uterine washings and combinations thereof, the presence and/or the level of expression of one or more proteins selected from the group consisting of Agrin (AGR), Midkine (MDK), Apolipoprotein B (APOB), Complement C1q subcomponent subunit A (C1QA), Fibronectin 1 (FN1), Serpin Family D Member 1 (SERPIND1), apolipoprotein F precursor (APOF), Apolipoprotein C1 (APOC1), Chaperonin Containing TCP1 Subunit 6A (CCT6A), lipopolysaccharide-binding protein precursor (LBP), Serum Amyloid A4 (SAA4), Inter-Alpha-Trypsin Inhibitor Heavy Chain 2 (ITIH2), Lipocalin 2 (LCN2), Lecithin:cholesterol acyltransferase (LCAT), C4b-binding protein alpha chain (C4BPA), Complement *C1r (*C1R), Fibroblast Growth Factor Binding Protein 1 (FGFBP1), Small Proline Rich Protein 1B (SPRR1B), Small Proline Rich Protein 1A (SPRR1A), Tissue inhibitor of metalloproteinases 2 (TIMP2), Liopocalin-2 (LCN2), Phospholipase B Domain Containing 1 (PLBD1), CD44 antigen, Fc Fragment Of IgG Binding Protein (FCGBP), Epidermal growth factor receptor kinase substrate 8-like protein 1 (EPS8L1), Annexin A3 (ANXA3), matrix metalloproteinase-8 (MMP8), NEDD-8 protein, Cathelicidin Antimicrobial Peptide (CAMP), Heat Shock Protein Family E (Hsp10) Member 1 (HSPE1), Calumenin (CALU), Lactate Dehydrogenase A (LDHA), Polymeric Immunoglobulin Receptor (PIGR), Keratin 8 (KRT8), Periplakin (PPL), Stathmin 1 (STMN1), Calcyphosin (CAPS), Carbonic anhydrase 1 (CA1), Vimentin (VIM), T complex 1 (TCP1), Annexin A7 (ANXA7), Inositol Monophosphatase 1 (IMPA1), Syntaxin 7 (STX7), Inter-Alpha-Trypsin Inhibitor Heavy Chain 2 (ITIH2), Galectin 1 (LGALS1), ATPase H+ Transporting V1 Subunit G1 (ATP6V1G1), Pyruvate kinase isozymes M1/M2 (PKM), Glycogenin 1 (GYG1), Lymphocyte-specific protein 1 (LSP1), Hematopoietic Cell-Specific Lyn Substrate 1 (HCLS1), Proliferation And Apoptosis Adaptor Protein 15 (PEA15), S100 calcium-binding protein A9 (S100A9), Sciellin (SCEL), Serpin Family A Member 3 (SERPINA3), Integrin Subunit Beta 2 (ITGB2), Fc Fragment Of IgG Binding Protein (FCGBP), NEDD8-MDP1 protein (NEDD8-MDP1), Charged Multivesicular Body Protein 4B (CHMP4B), Exportin-2 (XPO2), A2ML1 (Alpha-2-macroglobulin-like protein 1), APP (Amyloid-beta precursor protein), BTD (Biotinidase), CD44 (CD44 antigen), COL12A1 (Collagen alpha-1(XII) chain), COL1A1 (Collagen alpha-1(I) chain), COL3A1 (Collagen alpha-1(III) chain), CTNNB1 (Catenin beta-1), FAM107B (Protein FAM107B), GPLD1 (Glycoprotein phospholipase D), GRN (Progranulin), IGFALS (Insulin-like growth factor-binding protein complex acid labile subunit), LMNB1 (Lamin-B1), LMO7 (LIM domain only protein 7), MUC4 (Mucin-4), NAMPT (Nicotinamide phosphoribosyltransferase), RAB21

(Ras-related protein), SERPINH1 (Serpin H1), SPP1 (Osteopontin), TMPRS11E (Transmembrane protease serine 11E), and VWF (von Willebrand factor).

2. The method according to claim 1, comprising determining the presence and/or the level of expression of AGRIN.

3. The method according to any one of claims 1-2, wherein the sample is a pap-smear, and specifically the fluid contained in a pap-smear and/or cervical fluid.

4. The method according to any of claims 1-3, comprising determining the presence and/or the level of expression of two, three, or four of the proteins.

5. The method according to claim 4, comprising determining in the isolated sample the presence and/or the level of expression of the proteins in at least one binary set listed on any of Tables 4 and 6.

6. The method according to claim 4, comprising determining in the isolated sample the presence and/or the level of expression of the proteins in at least one ternary set listed on any of Tables 5 and 7.

7. The method according to claim 6, comprising determining in the isolated sample the presence and/or the level of expression of at least one binary set selected from the group consisting of AGRN and LCN2, AGRN and PLBD1, AGRN and GYG1, AGRN and FCGBP, AGRN and ANXA3, AGRN and GRN, AGRN and TIMP2, AGRN and ITGB2, AGRN and A2ML1, AGRN and SPRR1A, AGRN and TMPRSS11E, AGRN and GYG1, AGRN and COL1A1, AGRN and SPP1, and AGRN and APP.

8. The method according to any of the claims 1-7, comprising:
a) determining, *in vitro*, the level of expression of one or more of the following proteins: AGRIN, MDK, APOB, C1QA, FN1, SERPIND1, APOF, APOC1, CCT6A, LBP, SAA4, ITIH2, LCN2, LCAT, C4BPA, C1R, FGFBP1, SPRR1B, SPRR1A, TIMP2, LCN2, PLBD1, CD44 antigen, FCGBP, EPS8L1, ANXA3, MMP8, NEDD-8 protein, CAMP, HSPE1, CALU, LDHA, PIGR, KRT8, PPL, STMN1, CAPS, CA1, VIM, TCP1, ANXA7, IMPA1, STX7, ITIH2, LGALS1, ATP6V1G1, PKM, GYG1, LSP1, HCLS1, PEA15, S100A9, SCEL, SERPINA3, ITGB2, FCGBP, NEDD8-MDP1, CHMP4B, XPO2, A2ML1, APP, BTD, CD44, COL12A1, COL1A1, COL3A1, CTNNB1, FAM107B, GPLD1, GRN, IGFALS, LMNB1, LMO7, MUC4, NAMPT, RAB21, SERPINH1, SPP1, TMPRS11E, and VWF, in the isolated sample from the genital tract of the female;
b) comparing the level of the one or more of the proteins of step (a) with a corresponding

reference value or reference interval for each protein, said reference value or interval selected from a value or interval of values from a subject suffering from endometrial cancer, and/or comparing with a cut-off value discriminating among endometrial cancer and other endometriod disorders or conditions of (i.e., a healthy) endometrium, and wherein the subject is diagnosed of endometrial cancer if at least the level of the one or more of the proteins of step (a) is within the corresponding value or interval of values from a subject suffering from this cancer, and/or if at least the level of the one or more of the proteins of step (a) in relation to the corresponding cut-off value is classified to the endometrial cancer group.

9. The method according to any of claims 1-8, which is a method for the diagnosis of recurrence or risk of recurrence of endometrial cancer, which further comprises determining in the isolated sample of the female the presence and/or the level of expression of one or more of the proteins selected from the group consisting of: MUC1, PRSS8, PNP, APEH, MUC16, C9, SERPINC1, SERPINA1, F2, AMBP, HP, SERPINA3, CFB, ORM2, CAT, GNAI2, A1BG, FN1, C7. ASTRGL1, B4GALT1, CAPS, CBX3, CD163, CDV3, DMBT1, DSG3, EHD1, GOLM1, MUC5AC, NME1, NT5E, PDLIM5, RDX, and VASP.

10. The method according to any of claims 1-9, which is a method for the diagnosis of endometrial cancer subtype, and which further comprises determining in the isolated sample of the female the presence and/or the level of expression of one or more of the proteins selected from the group consisting of: LBP, VWF, GPLD1, SAA4, APOF, C4BPA, SPRR1A, SERPIND1, APOB, SCEL, LCAT, SERPINA3, LMO7, C1R, MUC4, FN1, SPRR1B, C1QA, ITIH2, TIMP2, APOC1, GRN, ANXA3, S100A9, PLBD1, PIGR, SERPINH1, HSPE1

11. The method according to any of claims 1-10, wherein the level of expression is determined at the protein level.

12. The method according to any of claims 1-11, wherein the protein level is determined by an assay or technology selected from the group consisting of an immunoassay, a bioluminescence assay, a fluorescence assay, a chemiluminescence assay, electrochemistry assay, mass spectrometry, and combinations thereof.

13. The method according to any of claims 11-12, wherein the level of expression of protein is determined using an antibody or a fragment thereof able to bind to the protein.

14. The method according to claim 13, wherein said antibody or fragment o thereof forms

part of a kit.

15. Use of one or more proteins selected from the group consisting of AGRIN, MDK, APOB, C1QA, FN1, SERPIND1, APOF, APOC1, CCT6A, LBP, SAA4, ITIH2, LCN2, LCAT, C4BPA, C1R, FGFBP1, SPRR1B, SPRR1A, TIMP2, LCN2, PLBD1, CD44 antigen, FCGBP, EPS8L1, ANXA3, MMP8, NEDD-8 protein, CAMP, HSPE1, CALU, LDHA, PIGR, KRT8, PPL, STMN1, CAPS, CA1, VIM, TCP1, ANXA7, IMPA1, STX7, ITIH2, LGALS1, ATP6V1G1, PKM, GYG1, LSP1, HCLS1, PEA15, S100A9, SCEL, SERPINA3, ITGB2, FCGBP, NEDD8-MDP1, CHMP4B, XPO2, A2ML1, APP, BTD, CD44, COL12A1, COL1A1, COL3A1, CTNNB1, FAM107B, GPLD1, GRN, IGFALS, LMNB1, LMO7, MUC4, NAMPT, RAB21, SERPINH1, SPP1, TMPRS11E, and VWF, as *in vitro* marker for the diagnosis and/or for the prognosis of endometrial cancer in a sample from the female genital tract part including one or more of the vulvae, vagina, cervix, uterus, fallopian tubes, and ovaries and selected from a gynecologic sampling, including one or more of a cervical fluid, a cytology, a pap-smear sample, an endometrial biopsy, a uterine fluid, uterine washings.

16. A kit comprising a solid support and means for detecting the presence and/or for determining the level of expression of one or more proteins selected from the group consisting of AGRIN, MDK, APOB, C1QA, FN1, SERPIND1, APOF, APOC1, CCT6A, LBP, SAA4, ITIH2, LCN2, LCAT, C4BPA, C1R, FGFBP1, SPRR1B, SPRR1A, TIMP2, LCN2, PLBD1, CD44 antigen, FCGBP, EPS8L1, ANXA3, MMP8, NEDD-8 protein, CAMP, HSPE1, CALU, LDHA, PIGR, KRT8, PPL, STMN1, CAPS, CA1, VIM, TCP1, ANXA7, IMPA1, STX7, ITIH2, LGALS1, ATP6V1G1, PKM, GYG1, LSP1, HCLS1, PEA15, S100A9, SCEL, SERPINA3, ITGB2, FCGBP, NEDD8-MDP1, CHMP4B, XPO2, A2ML1, APP, BTD, CD44, COL12A1, COL1A1, COL3A1, CTNNB1, FAM107B, GPLD1, GRN, IGFALS, LMNB1, LMO7, MUC4, NAMPT, RAB21, SERPINH1, SPP1, TMPRS11E, and VWF.

17. A computer-implemented method for carrying out the method as defined in any of claims 1-14, in which after the determination of the level of expression of the one or more proteins for the diagnosis and/or for the prognosis of endometrial cancer, said level(s) are given a value and/or a score, and optionally are computed in a mathematical formula to obtain a computed value; wherein in function of the said level(s), score(s) and or computed value(s), a decision is taken between the options of suffering or not from EC and/or between the options of suffering among different EC presenting different prognosis, including different histological subtypes and grades and different molecular features.

18. A method for the diagnosis of recurrence or risk of recurrence of endometrial cancer, which comprises determining in an isolated sample of a female the presence and/or the level of expression of one or more of the proteins selected from the group consisting of: MUC1, PRSS8, PNP, APEH, MUC16, C9, SERPINC1, SERPINA1, F2, AMBP, HP, SERPINA3, CFB, ORM2, CAT, GNAI2, A1BG, FN1, C7. ASTRGL1, B4GALT1, CAPS, CBX3, CD163, CDV3, DMBT1, DSG3, EHD1, GOLM1, MUC5AC, NME1, NT5E, PDLIM5, RDX, and VASP, wherein the sample is a sample from the female genital tract part including one or more of the vulvae, vagina, cervix, uterus, fallopian tubes, and ovaries, and selected from a gynecologic sampling, including or selected from a cervical fluid, a cytology, a pap-smear sample, an endometrial biopsy, a uterine fluid, uterine washings and combinations thereof.

19. A method for the diagnosis of endometrial cancer subtype, and/or endometrial cancer molecular classification, which comprises determining in the isolated sample of a female the presence and/or the level of expression of one or more of the proteins selected from the group consisting of: LBP, VWF, GPLD1, SAA4, APOF, C4BPA, SPRR1A, SERPIND1, APOB, SCEL, LCAT, SERPINA3, LMO7, C1R, MUC4, FN1, SPRR1B, C1QA, ITIH2, TIMP2, APOC1, GRN, ANXA3, S100A9, PLBD1, PIGR, SERPINH1, HSPE1, wherein the sample is a sample from the female genital tract part including one or more of the vulvae, vagina, cervix, uterus, fallopian tubes, and ovaries, and selected from a gynecologic sampling, including or selected from a cervical fluid, a cytology, a pap-smear like sample, a pap-smear sample, an endometrial biopsy, a uterine fluid, uterine washings and combinations thereof.