Claims

1. A method of diagnosis and/or for the prognosis of endometrial cancer, the method comprising determining, in a cervical fluid sample and/or a pap-smear sample, the presence and/or the level of expression of Agrin (AGRN).

2. The method according to claim 1, further comprising determining in the cervical fluid sample and/or a pap-smear sample the presence and/or the level of expression of one or more proteins selected from the group consisting of 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), , 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), 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), , 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), TMPRSS11E (Transmembrane

protease serine 11E), and VWF (von Willebrand factor).

3. The method according to claim 2, comprising determining the presence and/or the level of expression of two, three, or four of the proteins.

4. The method according to any one of claims 1-3, comprising determining in the isolated sample the presence and/or the level of expression of at least one set selected from the group consisting of AGRN and MDK; AGRN and MUC4; AGRN, MDK and MUC4; AGRN and PIGR; and AGRN, PIGR and CD44.

5. The method according to any of the claims 1-4, comprising:
a) determining, *in vitro*, the level of expression of AGRIN in the isolated cervical fluid sample and/or a pap-smear sample;
b) comparing the level of AGRN with a reference value or reference interval, said reference value or interval selected from a value or interval of values of AGRN from a subject suffering from endometrial cancer, and/or comparing with a cut-off value of AGRN that discriminates 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 the level of AGRN is within the reference value or interval of values from a subject suffering from this cancer, and/or if at least the level of AGRN in relation to the cut-off value of AGRN is classified to the endometrial cancer group.

6. The method according to claim 5, further comprising:
in step (a) determining the presence and/or the level of expression of one or more proteins selected from the group consisting of 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), Phospholipase B Domain Containing 1 (PLBD1), CD44 antigen, , 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), 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), 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), TMPRSS11E (Transmembrane protease serine 11E), and VWF (von Willebrand factor), and

in step (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 of each protein from a subject suffering from endometrial cancer, and/or comparing with a cut-off value for each protein that discriminates 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.

7.The method according to any of claims 1-6, 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.

8.The method according to any of claims 1-7, 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

9. The method according to any of claims 1-8, wherein the level of expression is determined at the protein level.

10. The method according to any of claims 1-9, 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.

11. The method according to any of claims 9-10, wherein the level of expression of protein is determined using an antibody or a fragment thereof able to bind to the protein.

12. The method according to claim 11, wherein said antibody or fragment o thereof forms part of a kit.

13. Use of AGRN as *in vitro* marker for the diagnosis and/or for the prognosis of endometrial cancer in a cervical fluid sample and/or a pap-smear sample.

14. The use according to claim 13, wherein AGRN is used in combination with MDK, MUC4, MDK and MUC4, PIGR, or PIGR and CD44.

15. A kit comprising a solid support and means for detecting the presence and/or for determining the level of expression of one or more sets of proteins selected from the group consisting of AGRN and MDK; AGRN and MUC4; AGRN, MDK and MUC4; AGRN and PIGR; and AGRN, PIGR and CD44.

16. A computer-implemented method for carrying out the method as defined in any of claims 1-12, in which after the determination of the level of expression of AGRN or AGRN and 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 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.