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(57) Abstract: The invention relates to the surprising finding that biomarkers corresponding to ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1 R16A, RASSF7, RNF183, SIRT6, TJP3, EFEM-P2, SOCS2, and DCN are differentially expressed in control samples as compared to samples from patients having endometrial cancer and are therefore useful for detecting endometrial cancer. In particular these biomarkers having excellent sensitivity, specificity, and/or the ability to separate affected from non affected individuals. Furthermore, the inventors found that the differential expression of these biomarkers in primary endometrial cancer tumor tissue is correlated to their expression level in uterine fluid samples as compared to control values. Thus these biomarkers are robust in that they are found to be differentially expressed in several different types of samples from affected individuals.



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## MARKERS FOR ENDOMETRIAL CANCER

### FIELD OF THE INVENTION

The invention relates to the detection diagnosis, and prognosis of uterine cancer. The invention relates to the surprising finding that biomarkers corresponding to ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN are differentially expressed in control samples as compared to samples from patients having endometrial cancer and are therefore useful for detecting endometrial cancer. In particular these biomarkers having excellent sensitivity, specificity, and/or the ability to separate affected from non affected individuals. Furthermore, the inventors found that the differential expression of these biomarkers in primary endometrial cancer tumor tissue is correlated to their expression level in uterine fluid samples as compared to control values. Thus these biomarkers are robust in that they are found to be differentially expressed in several different types of samples from affected and individuals.

### BACKGROUND OF THE INVENTION

Each year in Europe there are about 150,000 new cases of endometrial cancer and about 46,000 women die from the disease (Ferlay *et al.* (2007) *Ann. Onc.* 18:581-592). In the United States, about 41,000 new case of endometrial carcinoma are diagnosed per year and 7,300 women die each year (see American Cancer Society statistics available on the internet). The incidence and death rate from endometrial cancer are increasing.

Endometrial cancer (EC) is the most frequent invasive tumors of the female genital tract and the fourth most common in women in western countries (Jemal *et al.* (2008) *CA Cancer J Clin* 58:71-96). New methods for the diagnosis, prognosis, and classification of endometrial cancer are needed to combat this deadly disease.

Often endometrial cancer is detected early, in its initial stages, by presentation of disease-related symptoms. Unfortunately, 20% of patients present with myometrial

invasion and/or lymph node affectation, which are main indicators related to poor prognosis, decrease in survival rate, and more advanced disease. The primary therapeutic modality for endometrial cancer is surgical treatment.

Common symptoms of uterine cancer (*e.g.*, endometrial cancer) include unusual vaginal bleeding or discharge, trouble urinating, pelvic pain, and pain during intercourse. Uterine cancer usually occurs after menopause. Other risk factors for endometrial cancer include being obese, taking estrogen-alone hormone replacement therapy, treatment with tamoxifen and having a genetic predisposition to cancer (*e.g.*, Lynch Syndrome). The standard treatment for endometrial cancer varies depending on the stage of the disease. Treatment usually involves surgery to remove the uterus which is called a hysterectomy, although other options include hormone therapy and radiotherapy.

Methods routinely used in the clinic for diagnosing endometrial cancer include biopsy followed by cytological analysis and/or trans-vaginal ultrasound. The diagnosis of endometrial carcinoma is usually done by pathology examination of an endometrial aspirate (20-30%), and by biopsy-guided hysteroscopy (70-80%). The rate of success of diagnosis with hysteroscopy is over 90%, with false positives in the case of precursor lesions of the endometrial adenocarcinoma (hyperplasias); endometrial polyps, that present a non-negligible degree of malignancy (0-4.8%) and must be removed although asymptomatic or benign appearance; or in the case of diffuse forms of endometrial adenocarcinomas that are difficult to differentiate from an endometrial hyperplasia. Thus, there is a need for a less invasive diagnostic test based on molecular markers. Such a less invasive test based on molecular markers would allow for more routine screening of uterine cancer. A diagnostic test based of molecular markers obtained in a less invasive manner and that has sensitivity and specificity comparable to that of the endometrial biopsy can preclude unnecessary hysteroscopy.

Endometrial carcinomas can be classified into low grade (type I) and high-grade (type 2). Type I endometrioid endometrial cancer (sometimes called estrogen dependent), which represent approximately 80% of new cases, are low grade tumors associated with estrogen stimulation, usually developed in peri- or post-menopausal



women and are usually preceded by endometrial hyperplasia with or without atypia. Type II non-endometrioid endometrial cancer usually affects older women, are less differentiated and of worse prognosis, not associated with estrogen stimulation, and are related to atrophic endometrium or, occasionally, with endometrial polyps.

Type I cancers are typically known to have alterations in PTEN, KRAS2, DNA mismatch repair defects, CTNNB1, and have near diploid karyotype. Type II cancers typically have TP53 mutations and ErBB2 overexpression and are mostly non-diploid. Sugiyama *et al.* ((2003) *Clin. Can. Res.* 9:5589-5600) reported that certain genes are selectively up or down regulated in type I versus type II endometrial cancers. For example, they found that MLH1 was down-regulated in type I cancers as well as other genes related to DNA damage signaling and repair like O<sup>6</sup>-methyl-guanine DNA methyltransferase, DNA polymerase  $\alpha$  catalytic subunit, and Ku (p70/p80) antigen. VEGF-C was found to be upregulated in type I cancers at the protein and mRNA level as compared to type II cancers. KRAS was found to be upregulated in type II cancers. STAT1 was upregulated in type I cancers and STAT2 was upregulated in type II cancers. Konecny *et al.* ((2009) *British Journal of Cancer* 100, 89–95) report that the rate HER2 gene amplification as measured by fluorescence in situ hybridization was greater in type II cancers whereas EGFR expression as measured by IHC techniques was significantly lower in type II cancers. Deng *et al.* ((2005) *Clin. Can. Res.* vol. 11, no 23:8258-8264) report that EIG121 is a marker for type I estrogen associated cancers.

Uterine cancers are also classified histologically according to cell-type. The most common cell-type is referred to as endometrioid and represents around 80% of the newly diagnosed cases. Other less common uterine cancers are referred to as serous and clear cell carcinomas. Most of the type I cancers are of the endometrioid cell-type whereas the type II cancers are more likely to be non-endometrioid uterine cancers. Type II cancers are more likely to metastasize and have a poorer prognosis than type I cancers. Type I cancers typically have a better prognosis and respond better to therapy.

A number of studies have examined gene-expression profiles for classifying uterine cancers. Sugiyama *et al.* ((2003) *Clin. Canc. Res.* 9:5589-5600) report that between

the type I and II cancers 45 gene were highly expressed in type I cancers and 24 highly expressed in type I cancers. Risinger *et al.* ((2003) *Canc. Res.* 63:6-11) report that microarray analysis of different histologic subtypes of endometrial cancer have distinct gene expression profiles. They found that 191 genes exhibited greater than 2-fold difference in expression between endometrioid and non-endometrioid endometrial cancers.

A number of endometrial cancer biomarkers for endometrial cancer have been identified. Elevated levels of CA 125, CA 15-3, and CA 19-9 are associated with shorter survival time. CA 125 correlates with tumor size and stage and is an independent predictor of the extrauterine spread.

Serum markers for the detection of uterine cancer have been reported in the literature. Yurkovetsky *et al.* ((2007) *Gyn. Onc.* 107:58-65) identified that prolactin is a serum biomarker with sensitivity and specificity for endometrial cancer. They found serum CA 125 CA 15-3 and CEA are higher in patients with Stage III disease as compared to stage I. A five-biomarker panel of prolactin, GH, eotaxin, E-selectin, and TSH discriminated endometrial cancer from ovarian and breast cancer.

Another important issue for clinicians for diagnosis of endometrial cancer relates to synchronous cancers. Guirguis *et al.* (*Gyn. Onc.* (2008) 108:370-376) have reported that 10% of ovarian cancer patients have a tumor in the endometrium and 5-25% of patients with endometrial cancer also have a tumor in the ovary. Determining the primary site of a cancer has important treatment implications. Stage III endometrial carcinoma is treated with surgery followed by chemotherapy and/or radiation; while dual primary stage I ovarian and endometrial cancers have a better prognosis and may not require adjuvant therapy.

Current methods of diagnosing endometrial cancer often create discomfort to the patient and sometimes rely on subjective interpretation of visual images. There is a need for less invasive methods of screening for endometrial cancer which are less subjective in interpretation. In addition there is a need for new markers that are useful for the early detection of endometrial cancer. Current methods for detecting endometrial cancer include the dilation and curettage method which is considered the

gold standard, but this method is invasive, can cause significant discomfort, and may require a trained pathologist for interpretation, and therefore is not suitable as a general screening tool. Another less invasive method for diagnosing endometrial cancer involves transvaginal ultrasound which measures the thickness of the endometrium. In a study of patients having post-menopausal bleeding, using a cutoff of 4 mm, it was found that transvaginal ultrasound had 100% sensitivity and 60% specificity (Gull *et al.* (2003) *Am. J. Obstet. Gynecol.* 188(2):401-408). In women without vaginal bleeding, the sensitivity of the endometrial thickness measurement was 17% for a threshold 6 mm and 33% for a threshold of 5 mm (Fleischer *et al.* (2001) *Am. J. Obstet. Gynecol.* 184:70-75). TVS has a high rate of false positives since other conditions besides endometrial cancer can produce a thicker endometrium. One potential problem with the use of TVS in pre- and peri-menopausal women is that the thickness of the endometrium varies as a function of the phase of the menstrual cycle. Furthermore, women taking tamoxifen also have thicker endometrium. Therefore there is a need for techniques and markers that can complement and/or improve the ability of TVS in the diagnosis of endometrial cancer.

Clearly there is room for improvement in the tools currently available for screening for endometrial cancer.

#### BRIEF SUMMARY OF THE INVENTION

The invention relates to the surprising finding that biomarkers corresponding to ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN are differentially expressed in control samples as compared to samples from patients having endometrial cancer and are therefore useful for detecting endometrial cancer. In particular these biomarkers having excellent sensitivity, specificity, and/or the ability to separate affected from non affected individuals. Furthermore, the inventors found that the differential expression of these biomarkers in primary endometrial cancer tumor tissue is correlated to their expression level in uterine fluid samples as compared to control values. Thus, these biomarkers are robust in that they are found to be differentially expressed in several different types of samples from affected individuals as compared to non-affected individuals.

Therefore, the present invention relates to an in vitro diagnostic method for the diagnosis of endometrial cancer or an increased likelihood of endometrial comprising detecting the level of

(1) from 1 to 17 biomarker(s) chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, and TJP3 in a sample from a patient wherein an increased level of said from 1 to 17 biomarkers compared to a control value indicates a diagnosis of endometrial cancer or increased likelihood of endometrial cancer and/or

(2) detecting the level of from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN, wherein a decreased level of EFEMP2, SOCS2, and/or DCN compared to a control value indicates a diagnosis of endometrial cancer or increased likelihood of endometrial cancer.

Accordingly, the present invention relates to an in vitro diagnostic method for the diagnosis of endometrial cancer comprising

(1) detecting the level of from 1 to 17 biomarker(s) chosen from P4HB, GMIP, IKBKE, FASTKD1, DDR1, SIRT6, PHKG2, ACAA1, AP1M2, EPS8L2, P2RX4, PPFIBP2, PPP1R16A, CGN, RASSF7, RNF183, and TJP3 in a sample from a patient wherein an increased level of said from 1 to 17 biomarkers compared to a control value indicates the existence of endometrial cancer and/or

(2) detecting the level of from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN, wherein a decreased level of EFEMP2, SOCS2, and/or DCN compared to a control value indicates the existence of endometrial cancer.

The biomarkers of Table 1 were found to be differential expressed between endometrial cancer samples and normal samples as determined by microarray studies (see Table 1 in the Detailed Description of the Invention). The inventors have found that individually each of the biomarkers of Table 1 have predictive value for the diagnosis of endometrial cancer. Furthermore, the levels of combinations of markers of Table 1 have additional predictive value for the diagnosis of endometrial cancer (See Example 5). For example, the inventors have surprisingly found that subgroups of the biomarkers of Table 1 having from 2-20 biomarkers in various combinations to give fingerprint patterns have excellent predictive value for diagnosis or detection of endometrial cancer. Generally, if more than one of the

biomarkers of Table 1 are differentially expressed in a sample, this increases the likelihood that the individual has endometrial cancer. Moreover, the inventors have also found that addition of other biomarkers besides those listed in Table 1, to the fingerprint pattern also can increase predictive value, and can be useful for classifying endometrial cancers, for differential diagnosis of diseases other than endometrial cancer, and for endometrial cancer prognosis. Table 1 lists the ENSEMBL accession numbers for the genes, mRNA, and proteins corresponding to the biomarkers of the invention. Some of the biomarkers have alternative transcripts. The invention relates to determining the differential expression of any of these alternative transcripts (or protein isoforms) as long as its expression is correlated with the absence or presence of endometrial cancer. Preferred transcripts (or protein isoforms) for detecting endometrial cancer are those which were detected with the array probes as indicated in the Examples.

The inventors have also found that the markers of Table 1 can be detected in uterine fluid samples and that the level of expression of these markers are correlated in primary tumor and uterine fluid (*e.g.*, obtained by a uterine wash or aspiration).

The invention therefore provides methods for determining the level of from 1 to 20 of the biomarkers listed in Table 1 in a test sample. The method can comprise providing or obtaining a test sample from the patient; determining the level of from 1 to 20 of the biomarkers of Table 1 in the sample; and comparing the level of the biomarker(s) in the test sample(s) to a control value (*e.g.*, control sample, control value, or control score). A higher level of biomarker(s) which was found to be overexpressed in endometrial cancer as shown in Table 1 in the test sample obtained from the patient compared to the control value (*e.g.*, control sample, control value, and/or control score) indicates endometrial cancer, an increased likelihood of endometrial cancer, and/or a precancerous condition (*e.g.*, endometrial hyperplasia). A lower level of biomarker(s) which was found to be underexpressed in endometrial cancer as shown in Table 1 in the test sample obtained from the patient compared to level in the control value (*e.g.*, control sample, control value, and/or control score) indicates endometrial cancer, an increased likelihood of endometrial cancer, and/or a precancerous condition (*e.g.*, endometrial hyperplasia). The level of the biomarker(s) can be determined using appropriate assays, including RT-PCR, quantitative PCR,

multiplex PCR, Northern hybridization, microarray analysis, two-hybrid assays such as GAL4 DNA binding domain based assays, antibody based assays, EIA, blot assays, sandwich assays, and the like. The level of the biomarkers of Table 1 can be determined in body fluids and tissues for the diagnosis of endometrial cancer. The level of the biomarkers of Table 1 can be determined in tumor tissue obtained by biopsy for example. The level of the biomarkers of Table 1 can be determined in samples obtained from uterine aspirates and/or fluid. The level of the biomarkers of Table 1 can be determined in blood, serum, or plasma.

The biomarkers of Table 1 include ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, and TJP3, which were found to be upregulated in endometrial cancer and DCN, SOCS2, and EFEMP2 which were found to be down regulated in endometrial cancer in these studies. In one embodiment, the biomarkers for use in the method of the invention for detecting endometrial cancer or an increased likelihood of endometrial cancer include from 1 to 17 of the upregulated biomarkers listed in Table 1 and from 1 to 3 of the downregulated markers listed in Table 1.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of one or more biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

Accordingly, the present invention relates to an in vitro diagnostic method for the diagnosis of endometrial cancer comprising

- (1) detecting the level of one or more biomarker(s) chosen from P4HB, GMIP, IKBKE, FASTKD1, DDR1, SIRT6, PHKG2, ACAA1, AP1M2, EPS8L2, P2RX4, PPFIBP2, PPP1R16A, CGN, RASSF7, RNF183, and TJP3 in a sample from a patient wherein an increased level of said one or more biomarkers compared to a control value indicates the existence of endometrial cancer and/or
- (2) detecting the level of one or more biomarkers chosen from EFEMP2, SOCS2, and DCN, wherein a decreased level of EFEMP2, SOCS2, and/or DCN compared to a control value indicates the existence of endometrial cancer.

In a further embodiment, the present invention relates to an in vitro diagnostic method for the diagnosis of endometrial cancer comprising

- (1) detecting the level of from 1 to 17 biomarker(s) chosen from P4HB, GMIP, IKBKE, FASTKD1, DDR1, SIRT6, PHKG2, ACAA1, AP1M2, EPS8L2, P2RX4, PPFIBP2, PPP1R16A, CGN, RASSF7, RNF183, and TJP3 in a sample from a patient wherein an increased level of said from 1 to 17 biomarkers compared to a control value indicates the existence of endometrial cancer and/or
- (2) detecting the level of from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN, wherein a decreased level of EFEMP2, SOCS2, and/or DCN compared to a control value indicates the existence of endometrial cancer.

In one embodiment, the in vitro diagnostic method comprises detecting the level of P4HB. In another embodiment, the in vitro diagnostic method comprises detecting the level of EFEMP2. In a further embodiment the in vitro method comprises detecting the level of IKBKE. In a further embodiment the in vitro diagnostic method comprises detecting the level of GMIP.

In accordance with the in vitro diagnostic method of the invention, the the level of one or more of GMIP, IKBKE, or EFEMP2 may be detected in addition to P4HB. The in vitro diagnostic method may further comprise detecting the level of one or more of P4HB, IKBKE, or GMIP in addition to EFEMP2. The in vitro diagnostic method may further comprise detecting the level of one or more of GMIP, EFEMP2, or P4HB in addition to IKBKE. It is also envisaged that the in vitro diagnostic method may further comprise detecting the level of FASTKD1, DDR1, SIRT6, and/or PHKG2. The in vitro diagnostic method may further comprise detecting the level of

from 1 to 12 biomarkers chosen from ACAA1, AP1M2, EPS8L2, P2RX4, PPFIBP2, PPP1R16A, CGN, RASSF7, RNF183, TJP3, SOCS2, and DCN.

In one embodiment, the patient has a risk factor for endometrial cancer or is being screened for endometrial cancer. Further, the sample from the patient may be (obtained) from a patient with abnormal uterine bleeding. In other words, the patient may suffer from abnormal uterine bleeding. The sample from said patient may also be (obtained) from a patient having an endometrium with increased thickness. The patient may, accordingly, have an endometrium with increased thickness.

The sample from the patient may be (obtained) from a pre-menopausal, peri-menopausal, or post-menopausal patient. Accordingly, the patient is a pre-menopausal, peri-menopausal, or post-menopausal patient. In one embodiment, the patient is pre-menopausal. In another embodiment, the patient is peri-menopausal. In a further embodiment, the patient is post-menopausal.

The sample may be a tissue sample, blood and/or serum, and/or uterine fluid.

In one embodiment, the sample is a uterine fluid sample. The uterine fluid sample may be obtained by aspiration.

In one embodiment, the level of the biomarkers is determined with an antibody in accordance with the present invention. The level of the biomarker(s) may also be determined by RT-PCR.

The following markers may be detected in accordance with the in vitro diagnostic method of the present invention: P4HB, IKBKE, EFEMP2, SOCS2, FASTKD1, GMIP, DDR1, SIRT6, PHKG2, EPS8L2, PPP1R16A, P2RX4, RASSF7, and/or TJP3. Also the following markers may be detected in accordance with the in vitro diagnostic method of the present invention: P4HB, IKBKE, SOCS2, GMIP, DDR1, SIRT6, PHKG2, EPS8L2, PPP1R16A, P2RX4, RASSF7, and/or TJP3.



The markers to be detected may be P2RX4, P4HB, PHKG2, PPFIBP2, and/or SOCS2. The markers to be detected may also be P4HB, RASSF7, RNF183 and/or IKBKE.

In one embodiment, the in vitro diagnostic method comprises the detection of from 2 to 20 markers.

Preferably, the combination of the following markers is detected: P4HB, EFEMP2, SIRT6, GMIP, FASTKD1 and DDR1. Also preferred is the detection of a combination of the following markers: P4HB, EFEMP2, SIRT6, GMIP, FASTKD1 and PHKG2. Also preferred is the detection of a combination of the following markers: P4HB, EFEMP2, SIRT6, ACAA1, AP1M2, EPS8L2, IKBKE, P2RX4, PPFIBP2 and PPP1R16A.

The following marker combinations are also preferably detected in accordance with the present invention:

GMIP, IKBKE, PFHB, EFEMP2;  
DDR1, FASTKD1, GMIP, IKBKE, P4HB, PHKG2, SIRT6, EFEMP2;  
P4HB, EFEMP2, IKBKE, GMIP, FASTKD1.

In context of the present invention combinations of markers which include a combination with P4HB (i.e. set of markers including P4HB) are particularly preferred.

Also envisaged herein is the detection of the following combination of markers:  
DDR1, FASTKD1, GMIP, IKBKE, P4HB, PHKG2, SIRT6, EFEMP2; SOCS2;  
P4HB, SOCS2;  
GMIP, IKBKE, P4HB, SOCS2;  
GMIP, IKBKE, P4HB, SOCS2, FASTKD1;  
GMIP, IKBKE, P4HB, SOCS2, DDR1;  
GMIP, IKBKE, P4HB, SOCS2, PHKG2;  
GMIP, IKBKE, P4HB, SOCS2, SIRT6;  
GMIP, IKBKE, P4HB, SOCS2, ACAA1;

GMIP, IKBKE, P4HB, SOCS2, AP1M2;  
GMIP, IKBKE, P4HB, SOCS2, EFEMP2;  
GMIP, IKBKE, P4HB, SOCS2, EPS8L2;  
GMIP, IKBKE, P4HB, SOCS2, P2RX4;  
GMIP, IKBKE, P4HB, SOCS2, PPFIB2;  
GMIP, IKBKE, P4HB, SOCS2, PPP1R16A;  
GMIP, IKBKE, P4HB, SOCS2, ACAA1, FASTKD1;  
GMIP, IKBKE, P4HB, SOCS2, FASTKD1, PHKG2;  
GMIP, IKBKE, P4HB, SOCS2, FASTKD1, SIRT6;  
GMIP, IKBKE, P4HB, SOCS2;

One or more additional biomarkers may be detected in accordance with the herein disclosed in vitro diagnostic method. The one or more additional biomarkers may be chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one embodiment, the one or more additional biomarkers are chosen from differential diagnosis biomarkers.

The one or more auxiliary biomarkers may be chosen from prognostic markers. The one or more auxiliary biomarkers may be chosen from endometrial cancer classification markers.

In a further embodiment, the present invention relates to a nucleic acid chosen from IKBKE mRNA, cDNA, or a complement thereof;  
P4HB mRNA, cDNA, or a complement thereof;  
SOCS2 mRNA, cDNA, or a complement thereof;  
GMIP mRNA, cDNA, or a complement thereof;  
DDR1 mRNA, cDNA, or a complement thereof;  
EPS8L2 mRNA, cDNA, or a complement thereof; and  
PPP1R16A mRNA, cDNA, or a complement thereof,  
for use in diagnosing endometrial cancer.

The invention also relates to a nucleic acid chosen from  
Primers for IKBKE;

Primers for P4HB;  
Primers for SOCS2;  
Primers for GMIP;  
Primers for DDR1;  
Primers for EPS8L2; and  
Primers for PPP1R16A;  
for use in diagnosing endometrial cancer.

In one embodiment, the invention relates to a nucleic acid chosen from  
probe for IKBKE;  
probe for P4HB;  
probe for SOCS2;  
probe for GMIP;  
probe for DDR1;  
probe for EPS8L2; and  
probe for PPP1R16A,  
for use in diagnosing endometrial cancer.

Also a kit comprising two or more of the herein described probes for use in diagnosing endometrial cancer is envisaged in context of the present invention. Further, a kit comprising primers for two or more herein disclosed primers/primer pairs for use in diagnosing endometrial cancer is envisaged in context of the present invention.

In a further embodiment, the present invention relates to an antibody chosen from  
an antibody to IKBKE;  
an antibody to P4HB;  
an antibody to SOCS2;  
an antibody to GMIP;  
an antibody to DDR1;  
an antibody to EPS8L2; and  
an antibody to PPP1R16A,  
for use in diagnosing endometrial cancer.

Accordingly, a kit comprising antibodies to two or more herein disclosed antibodies for use in diagnosing endometrial cancer is envisaged. The invention further relates to a kit for obtaining uterine fluid for use in diagnosing endometrial cancer by assessing the levels of from 1-20 biomarkers as defined and described herein.

The in vitro diagnostic method of the present invention may comprise determining/detecting the level of 2 biomarkers, 3 biomarkers, 4 biomarkers, 5 biomarkers, 7 biomarkers, 10 biomarkers, 15 biomarkers or 20 biomarkers.

In one embodiment, the present invention relates to an in vitro diagnostic method for diagnosing endometrial cancer comprising obtaining a uterine fluid aspirate sample from a patient having a symptom or risk factor for endometrial cancer and determining the level of from 1 to 100 biomarkers markers that are differentially expressed in endometrial cancer as compared to control values representative of individuals not affected by endometrial cancer, wherein (1) if the levels of 1 to 100 biomarkers are upregulated in the endometrial aspirate sample in the patient and in the control value then the patient has an increased likelihood of having endometrial cancer and wherein (2) if the level of the 1 to 100 biomarkers are downregulated in the aspirate sample and then the patient has an increased likelihood of having endometrial cancer.

The present invention further relates to a nucleic acid chosen from

ACAA1 mRNA, cDNA, or a complement thereof;  
AP1M2 mRNA, cDNA, or a complement thereof;  
CGN mRNA, cDNA, or a complement thereof;  
FASTKD1 mRNA, cDNA, or a complement thereof;  
P2RX4 mRNA, cDNA, or a complement thereof;  
RASSF7 mRNA, cDNA, or a complement thereof;  
RNF183 mRNA, cDNA, or a complement thereof;  
PHKG2 mRNA, cDNA, or a complement thereof;  
PPFIBP2 mRNA, cDNA, or a complement thereof;  
SIRT6 mRNA, cDNA, or a complement thereof;  
TJP3 mRNA, cDNA, or a complement thereof;  
EFEMP2 mRNA, cDNA, or a complement thereof; and

DCN mRNA, cDNA, or a complement thereof,  
for use in diagnosing endometrial cancer.

Also subject of the present invention is a nucleic acid chosen from

Primers for ACAA1;

Primers for AP1M2;

Primers for CGN;

Primers for FASTKD1;

Primers for P2RX4;

Primers for RASSSF7;

Primers for RNF183;

Primers for SIRT6;

Primers for PPFIBP2;

Primers for PHKG2;

Primers for TJP3;

Primers for EFEMP2; and

Primers for DCN;

for use in diagnosing endometrial cancer.

In a further embodiment, the present invention relates to a nucleic acid chosen from

probe for ACAA1;

probe for AP1M2;

probe for CGN;

probe for FASTKD1;

probe for P2RX4;

probe for RASSF7;

probe for RNF183;

probe for SIRT6;

probe for PPFIBP2;

probe for PKHG2;

probe for TJP3;

probe for EFEMP2; and

probe for DCN,

for use in diagnosing endometrial cancer.

In another embodiment, the invention relates to an antibody chosen from  
an antibody to ACAA1;  
an antibody to AP1M2;  
an antibody to CGN;  
an antibody to FASTKD1;  
an antibody to P2RX4;  
an antibody to RASSF7;  
an antibody to RNF183;  
an antibody to SIRT6;  
an antibody to PPFIBP2;  
an antibody to PKHG2;  
an antibody to TJP3;  
an antibody to EFEMP2; and  
an antibody to DCN,  
for use in diagnosing endometrial cancer.

The antibody/antibodies, nucleic acid(s), probes, primer(s)/primer pair(s), and/or kit(s) described and defined herein are useful in the in diagnosis of endometrial cancer in accordance with the present invention. Therefore the antibody/antibodies, nucleic acid(s), probes, primer(s)/primer pair(s), and/or kit(s) described and defined herein are for use in diagnosing endometrial cancer. Similarly, also the use of the antibody/antibodies, nucleic acid(s), probes, primer(s)/primer pair(s), and/or kit(s) for the preparation of a diagnostic composition for diagnosing endometrial cancer is envisaged. Also a diagnostic composition for use in diagnosing endometrial cancer and comprising the herein described and defined antibody/antibodies, nucleic acid(s), probes, primer(s)/primer pair(s), and/or kit(s) is envisaged in context of the present invention.

Diagnosing endometrial cancer may, in this context, comprise or relate to a diagnostic method practised on the human or animal body which comprises or includes the features relating to

(i) the diagnosis for curative purposes *stricto sensu* representing the deductive medical or veterinary decision phase as a purely intellectual exercise,

- (ii) the preceding steps which are constitutive for making that diagnosis, and
- (iii) the specific interactions with the human or animal body which occur when carrying those out among these preceding steps which are of a technical nature.

In a further embodiment, the present invention relates to an in vitro diagnostic method for diagnosing endometrial cancer comprising providing or obtaining a uterine fluid sample from a human patient having a symptom or risk factor for a gynecological cancer and determining the level of RNA expression of from 2 to 9 biomarkers chosen from P4HB, EFEMP2, GMIP, IKBKE, DDR1, FASTKD1, SIRT6, PKHG2, and SOCS2 by quantitative PCR wherein an increased level of from 1 to 7 biomarkers chosen from P4HB, GMIP, IKBKE, DDR1, FASTKD1, SIRT6, and PKHG2 and/or a decreased level of EFEMP2 or SOCS2 as compared to control indicates the existence of endometrial cancer. Preferably, the gynecological cancer is endometrial cancer.

In one embodiment, the expression level of 2 to 8 biomarkers chosen from P4HB, EFEMP2, GMIP, IKBKE, DDR1, FASTKD1, SIRT6, and PKHG2 may be determined. The 2 to 8 biomarkers may also be chosen from P4HB, GMIP, IKBKE, DDR1, FASTKD1, SIRT6, PKHG2, and SOCS2.

The detection of the level may comprise contacting said one or more biomarkers with primers and reagents capable of amplifying specifically said one or more biomarkers and detecting the level of said amplified one or more biomarkers with a probe or probes that hybridize to said amplified biomarker. The probe hybridizes specifically to said amplified biomarker.

The following combinations of biomarkers may, in particular, be detected in accordance with the method of the present invention: P4HB and EFEMP2; P4HB and IKBKE; P4HB and GMIP; EFEMP2 and IKBKE; EFEMP2 and P4HB; P4HB, GMIP, and IKBKE; P4HB, GMIP, and IKBKE.

Also the following combination of markers may be detected in accordance with the present method, wherein said combination comprises IKBKE and P4HB; IKBKE and SOCS2; P4HB and SOCS2; GMIP and IKBKE; GMIP and P4HB; GMIP and SOCS2;

GMIP, SOCS2, and IKBKE; GMIP, SOCS2, and P4HB; GMIP, IKBKE, and P4HB; IKBKE, P4HB, and SOCS2; GMIP, IKBKE, P4HB, and SOCS2; GMIP, SOCS2, IKBKE, and EPS8L2; GMIP, SOCS2, P4HB, and EPS8L2; GMIP, IKBKE, P4HB, and EPS8L2; IKBKE, P4HB, SOCS2, and EPS8L2; GMIP, IKBKE, P4HB, SOCS2, and DDR1; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, and PPP1R16A; GMIP, IKBKE, P4HB, SOCS2, PHKG2, and RASSF7; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, and DDR1; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, PPP1R16A, and DDR1; DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, RASSF7, SIRT6, TJP3, and SOCS2; or DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, RASSF7, SIRT6, TJP3, RNF183 and SOCS2.

Further, the following combination of markers may be detected in accordance with the present method, wherein said combination comprises GMIP, IKBKE, P4HB, SOCS2 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2 and DDR1; GMIP, IKBKE, P4HB, SOCS2 and PHKG2; GMIP, IKBKE, P4HB, SOCS2 and SIRT6; GMIP, IKBKE, P4HB, SOCS2 and ACAA1; GMIP, IKBKE, P4HB, SOCS2 and EFEMP2; GMIP, IKBKE, P4HB, SOCS2 and EPS8L2; GMIP, IKBKE, P4HB, SOCS2 and P2RX4; GMIP, IKBKE, P4HB, SOCS2 and PPFIBP2; GMIP, IKBKE, P4HB, SOCS2 and PPP1R16A; GMIP, IKBKE, P4HB, SOCS2, ACAA1 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2, PHKG2 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2, SIRT6 and FASTKD1; ACAA1, AP1M2, EPS8L2, IKBKE, P2RX4, P4HB, PPFIBP2, PPP1R16A, SIRT6, and EFEMP2; GMIP, IKBKE, P4HB, and EFEMP2; DDR1, FASTKD1, PHKG2, SIRT6, SOCS2, GMIP, IKBKE, P4HB, and EFEMP2; DDR1, FASTKD1, PHKG2, SIRT6, GMIP, IKBKE, P4HB, and EFEMP2; or P4HB, EFEMP2, IKBKE, GMIP, and FASTKD1.

Further, the following combination of markers may be detected in accordance with the present method, wherein said combination comprises GMIP, IKBKE, P4HB, EFEMP2 and FASTKD1; GMIP, IKBKE, P4HB, EFEMP2 and DDR1; GMIP, IKBKE, P4HB, EFEMP2 and PHKG2; GMIP, IKBKE, P4HB, EFEMP2 and SIRT6; GMIP, IKBKE, P4HB, EFEMP2 and ACAA1; GMIP, IKBKE, P4HB, SOCS2 and EFEMP2; GMIP, IKBKE, P4HB, EFEMP2 and EPS8L2; GMIP, IKBKE, P4HB, EFEMP2 and P2RX4; GMIP, IKBKE, P4HB, EFEMP2 and PPFIBP2; GMIP, IKBKE, P4HB,



EFEMP2 and PPP1R16A; GMIP, IKBKE, P4HB, EFEMP2, ACAA1 and FASTKD1; GMIP, IKBKE, P4HB, EFEMP2, PHKG2 and FASTKD1; or GMIP, IKBKE, P4HB, EFEMP2, SIRT6 and FASTKD1.

The methods of the present invention may further comprise providing a uterine fluid sample obtained from a patient with a pipelle device or syringe wherein the patient has a risk factor or symptom of endometrial cancer; contacting said sample with an agent capable of preserving, preventing, or lessening the degradation of RNA in said uterine fluid sample; determining in said sample the expression level of mRNA corresponding to from 1 to 20 herein described markers (preferably 2 to 8 markers) and one or more endogenous genes using quantitative PCR; normalizing the expression level of from 1 to 20 (preferably 2 to 8 markers) herein described biomarkers with the one or more endogenous genes; comparing the normalized level of the from 1 to 20 (preferably 2 to 8 markers) biomarkers to a control value wherein differential expression of from 1 to 20 (preferably 2 to 8 markers) of the biomarkers indicates endometrial cancer or an increased likelihood of endometrial cancer.

The present invention relates further to an in vitro diagnostic method comprising providing a uterine fluid sample obtained from a patient with a pipelle device or syringe wherein the patient has a risk factor or symptom of endometrial cancer; contacting said sample with an agent capable of preserving, preventing, or lessening the degradation of RNA in said uterine fluid sample; determining in said sample the expression level of mRNA corresponding to from 1 to 20 herein described markers (preferably 2 to 8 markers) and one or more endogenous genes using quantitative PCR; normalizing the expression level of from 1 to 20 (preferably 2 to 8 markers) herein described biomarkers with the one or more endogenous genes; comparing the normalized level of the from 1 to 20 (preferably 2 to 8 markers) biomarkers to a control value wherein differential expression of from 1 to 20 (preferably 2 to 8 markers) of the biomarkers indicates endometrial cancer or an increased likelihood of endometrial cancer.

The one or more endogenous genes may be chosen from POLR2A, B2M, PFN1, HMBS, G6PD, and PABPN1.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of from 1-17 biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, and/or from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. In a specific aspect of this embodiment, when the level of from 1 to 17 biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, are increased relative to a control value and/or the level from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN are decreased relative to control value then this indicates endometrial cancer or an increased chance of having endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to another aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

Amongst the biomarkers of Table 1, the levels of CGN, P4HB, PPP1R16A, IKBKE, RASSF7, RNF183, and TJP3, were found to have the highest mean level of overexpression in the RT-PCR studies as compared to their expression in normal samples (*e.g.*, not having endometrial cancer). Thus, given that the RT-PCR experiments demonstrated a high level of overexpression in a statistically significant manner (all p-values are less than 0.0001 for the sample set studied) for these markers, they represent preferred markers for diagnosis of endometrial cancer and/or an increased likelihood of having endometrial cancer. Therefore, the levels of CGN, P4HB, PPP1R16A, IKBKE, RASSF7, RNF183, and TJP3 are excellent predictors of endometrial cancer and/or an increased likelihood of having endometrial cancer. The levels of these markers are less likely to give a false positive as compared to other markers whose expression levels are not as high and/or as significant. In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of one

or more biomarkers chosen from CGN, P4HB, PPP1R16A, IKBKE, RASSF7, RNF183, and TJP3 wherein if one or more of said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of cancer. Fingerprint patterns/expression profiles having from 1-7 biomarkers chosen from CGN, P4HB, PPP1R16A, IKBKE, RASSF7, RNF183, and TJP3 and from 1-13 biomarkers chosen from ACAA1, AP1M2, DDR1, EPS8L2, FASTKD1, GMIP, P2RX4, PHKG2, PPFIBP2, SIRT6, EFEMP2, SOCS2, and DCN, are one example of a set preferred profiles for diagnosing and/or predicting an increased likelihood of endometrial cancer. Specific examples of such profiles are described below. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

Amongst the biomarkers of Table 1, the level of some biomarkers were found to be able to differentiate samples from patients having cancer as compared to normal samples (or control) and samples from patients in the secretory phase of the menstrual cycle. Therefore, the levels of ACAA1, DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, RASSF7, SIRT6, TJP3, SOCS2, and DCN are excellent predictors of endometrial cancer in pre- and post-menopausal women and in peri-menopausal women, the levels of these markers are less likely to give a false positive as compared to other markers who expression level varies as a function of cycle. In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of one or more biomarkers chosen from ACAA1, DDR1, EPS8L2, GMIP, IKBKE, LSR, P2RX4, P4HB, PHKG2, PPFIBP2, RASSF7, SIRT6, TJP3, SOCS2, and DCN wherein if one or more of said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. Fingerprint patterns/expression profiles having from 1-15 markers chosen from ACAA1, DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, SIRT6, TJP3, SOCS2, and DCN and from 1 to 5 markers chosen from AP1M2, CGN,

FASTKD1, RNF183, and EFEMP2 are one example of a set preferred profiles for diagnosing and/or predicting an increased likelihood of endometrial cancer since the expression level of at least one of the markers in the profile does not vary as a function of menstrual cycle phase. Specific examples of such profiles are described below. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of one or more biomarkers chosen from IKBKE, P4HB, SOCS2, GMIP, DDR1, EPS8L2, PPP1R16A, P2RX4, PHKG2, RASSF7, SIRT6, TJP3, AP1M2, RNF183, and DCN wherein if one or more of said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of one or more biomarkers chosen from IKBKE, P4HB, SOCS2, GMIP, DDR1, EPS8L2, PPP1R16A, P2RX4, PHKG2, RASSF7, SIRT6, and TJP3, wherein if one or more of said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one

aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In one embodiment of the invention, preferred biomarkers for diagnosing endometrial cancer and/or diagnosing an increased likelihood of endometrial cancer are IKBKE, P4HB, SOCS2, GMIP, DDR1, EPS8L2, and PPP1R16A. In one aspect, the level of the biomarker in primary tumor is determined. In one aspect, the level of the biomarker in blood, plasma, or serum is determined. In one aspect, the level of the biomarker in uterine fluid is determined. Thus, the method according to this embodiment, comprise obtaining a sample and determining the level of from 1 to 7 biomarkers chosen from IKBKE, P4HB, SOCS2, GMIP, DDR1, EPS8L2, and PPP1R16A wherein differential expression of one or more of these biomarkers as compared to a control value indicates endometrial cancer and/or an increased risk of having endometrial cancer. In one aspect of this invention, the protein level of the biomarker is determined and/or estimated. In another aspect, the mRNA expression level is determined and/or estimated.

In one embodiment of the invention, preferred biomarkers for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer include GMIP, IKBKE, P4HB, RASSF7, DDR1, RNF183, EFEMP2 and SOCS2. GMIP, IKBKE, P4HB, RASSF7, DDR1, RNF183, EFEMP2 and SOCS2 were found to have excellent AUROC values and therefore are unexpectedly good classifiers in the sample set studied. In one aspect, the level of the biomarker in primary tumor is determined. In one aspect, the level of the biomarker in blood, plasma, or serum is determined. In one aspect, the level of the biomarker in uterine fluid is determined. Thus, the method according to this embodiment, comprise obtaining a sample and determining the level of from 1 to 8 biomarkers chosen from GMIP, IKBKE, P4HB, RASSF7, DDR1, RNF183, EFEMP2 and SOCS2 wherein differential expression of one or more of these biomarkers as compared to a control value indicates endometrial cancer and/or an increased risk of having endometrial cancer. In one aspect of this invention, the protein level of the biomarker is determined and/or estimated. In another aspect, the mRNA expression level is determined and/or estimated.

In one embodiment of the invention, preferred biomarkers for diagnosing endometrial cancer and/or diagnosing an increased likelihood of endometrial cancer include P2RX4, P4HB, PHKG2, PPFIBP2 and SOCS2. As a result of these studies it was found that P2RX4, P4HB, PHKG2, PPFIBP2 and SOCS2 have excellent specificity for endometrial cancer diagnosis. In one aspect, the level of the biomarker in primary tumor is determined. In one aspect, the level of the biomarker in blood, plasma, or serum is determined. In one aspect, the level of the biomarker in uterine fluid is determined. Thus, the method according to this embodiment, comprise obtaining a sample and determining the level of from 1 to 5 biomarkers chosen from P2RX4, P4HB, PHKG2, PPFIBP2 and SOCS2 wherein differential expression of one or more of these biomarkers as compared to a control value indicates endometrial cancer and/or an increased risk of having endometrial cancer. In one aspect of this invention, the protein level of the biomarker is determined and/or estimated. In another aspect, the mRNA expression level is determined and/or estimated.

In one embodiment of the invention, preferred biomarkers for diagnosing endometrial cancer and/or diagnosing an increased likelihood of endometrial cancer include IKBKE, P4HB, RASSF7, and RNF183. As a result of these studies it was found that IKBKE, P4HB, RASSF7, and RNF183 have excellent sensitivity for endometrial cancer diagnosis. In one aspect, the level of the biomarker in primary tumor is determined. In one aspect, the level of the biomarker in blood, plasma, or serum is determined. In one aspect, the level of the biomarker in uterine fluid is determined. Thus, the method according to this embodiment, comprise obtaining a sample and determining the level of from 1 to 4 biomarkers chosen from IKBKE, P4HB, RASSF7, and RNF183 wherein differential expression of one or more of these biomarkers as compared to a control value indicates endometrial cancer and/or an increased risk of having endometrial cancer. In one aspect of this invention, the protein level of the biomarker is determined and/or estimated. In another aspect, the mRNA expression level is determined and/or estimated.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of from 2 to 7 biomarkers chosen from GMIP, IKBKE, P4HB, SOCS2, EPS8L2,

PPP1R16A, and TJP3 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. As result of the studies disclosed herein, it was surprisingly found that combinations (*e.g.*, profiles and/or fingerprint patterns) of biomarkers chosen from GMIP, IKBKE, P4HB, SOCS2, EPS8L2, PPP1R16A, and TJP3 have excellent sensitivity and specificity for endometrial cancer and the AUROC values for various combinations of these markers are indicative of the ability of these markers to separate patients having endometrial cancer from those not having endometrial cancer.

According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of from 2 to 9 biomarkers chosen from GMIP, IKBKE, P4HB, SOCS2, EFEMP2, PHKG2, SIRT6, DDR1, and FASTKD1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. As result of the studies disclosed herein, it was surprisingly found that combinations (*e.g.*, profiles and/or fingerprint patterns) of biomarkers chosen from GMIP, IKBKE, P4HB, SOCS2, EFEMP2, PHKG2, SIRT6, DDR1, and FASTKD1 have excellent sensitivity and specificity for endometrial cancer and the AUROC values for various combinations of these markers are indicative of the ability of these markers to separate patients having endometrial cancer from those not having endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined. In one specific aspect of this embodiment, the in vitro diagnostic method comprises

providing a uterine fluid sample obtained from a patient with a pipelle device or syringe wherein the patient has a risk factor or symptom of endometrial cancer; contacting said sample with an agent capable of preserving, preventing, or lessening the degradation of RNA in said uterine fluid sample; determining in said sample the expression level of mRNA corresponding to said from 2 to 9 markers and one or more endogenous genes using quantitative PCR; normalizing the expression level of said from 2 to 9 biomarkers with the one or more endogenous genes; comparing the normalized level of the from 2 to 9 biomarkers to a control value wherein differential expression of from 2 to 9 of the biomarkers indicates endometrial cancer or an increased likelihood of endometrial cancer. In one specific aspect of this method, said one or more endogenous genes are chosen from POLR2A, B2M, PFN1, HMBS, G6PD, and PABPN1.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of from 2 to 8 biomarkers chosen from GMIP, IKBKE, P4HB, EFEMP2, PHKG2, SIRT6, DDR1, and FASTKD1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. As result of the studies disclosed herein, it was surprisingly found that combinations (*e.g.*, profiles and/or fingerprint patterns) of biomarkers chosen from GMIP, IKBKE, P4HB, EFEMP2, PHKG2, SIRT6, DDR1, and FASTKD1 have excellent sensitivity and specificity for endometrial cancer and the AUROC values for various combinations of these markers are indicative of the ability of these markers to separate patients having endometrial cancer from those not having endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of 2 to 8 biomarkers are determined by quantitative PCR. In one specific aspect of this embodiment, the in vitro diagnostic method comprises providing a uterine fluid sample obtained from a patient with a pipelle device or syringe wherein the patient has a risk factor or symptom of endometrial cancer;



contacting said sample with an agent capable of preserving, preventing, or lessening the degradation of RNA in said uterine fluid sample; determining in said sample the expression level of mRNA corresponding to said from 2 to 9 markers and one or more endogenous genes using quantitative PCR; normalizing the expression level of said from 2 to 8 biomarkers with the one or more endogenous genes; comparing the normalized level of the from 2 to 8 biomarkers to a control value wherein differential expression of from 2 to 8 of the biomarkers indicates endometrial cancer or an increased likelihood of endometrial cancer. In one specific aspect of this method, said one or more endogenous genes are chosen from POLR2A, B2M, PFN1, HMBS, G6PD, and PABPN1.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising obtaining a sample from an individual and determining the level of from 2 to 8 biomarkers chosen from GMIP, IKBKE, P4HB, SOCS2, PHKG2, SIRT6, DDR1, and FASTKD1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. As result of the studies disclosed herein, it was surprisingly found that combinations (*e.g.*, profiles and/or fingerprint patterns) of biomarkers chosen from GMIP, IKBKE, P4HB, SOCS2, PHKG2, SIRT6, DDR1, and FASTKD1 have excellent sensitivity and specificity for endometrial cancer and the AUROC values for various combinations of these markers are indicative of the ability of these markers to separate patients having endometrial cancer from those not having endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of 2 to 8 biomarkers are determined by quantitative PCR. In one specific aspect of this embodiment, the in vitro diagnostic method comprises providing a uterine fluid sample obtained from a patient with a pipelle device or syringe wherein the patient has a risk factor or symptom of endometrial cancer; contacting said sample with an agent capable of preserving, preventing, or lessening the degradation of RNA in said uterine fluid sample; determining in said sample the

expression level of mRNA corresponding to said from 2 to 8 markers and one or more endogenous genes using quantitative PCR; normalizing the expression level of said from 2 to 8 biomarkers with the one or more endogenous genes; comparing the normalized level of the from 2 to 8 biomarkers to a control value wherein differential expression of from 2 to 8 of the biomarkers indicates endometrial cancer or an increased likelihood of endometrial cancer. In one specific aspect of this method, said one or more endogenous genes are chosen from POLR2A, B2M, PFN1, HMBS, G6PD, and PABPN1.

In one embodiment, the present invention provides a method for characterizing a sample obtained from a patient for prognostic, diagnostic and/or pharmacogenomic uses. Characterization of a sample obtained from a patient by determining the levels of one or more of the biomarkers of Table 1 can be used to provide information regarding diagnosis of endometrial cancer, disease progression, diagnosis of endometrial cancer type (and/or subtype), and selection of an appropriate therapeutic treatment. According to the method of the invention, a sample is obtained from an individual. The individual can be a healthy person, an individual diagnosed with cancer, an individual suspected of having cancer, an individual displaying one or more symptoms of cancer and/or an individual desiring screening for cancer. The method comprises the step of determining the level of the biomarker(s) of Table 1 in a sample obtained from a patient. Alternative methods for determining the biomarkers at the RNA and/or protein (IHC, mRNA expression analysis, etc) can be used in these methods. Detection of increased levels of from 1 to 17 the biomarkers of Table 1 that were found to be upregulated in endometrial cancer and/or detection of decreased levels of from 1 to 3 biomarkers that were found to be downregulated in endometrial cancer, compared to a control value, indicates that the patient has increased likelihood of having endometrial cancer.

In one embodiment, the invention provides a method for diagnosing a gynecological cancer comprising the use of diagnostic reagents for assaying for or detecting from 1 to 20 of the biomarkers listed in Table 1. In a more specific aspect of this embodiment, the diagnostic reagents are used for detecting the level of from 1 to 20 of the biomarkers listed in Table 1, for the diagnosis of endometrial cancer. In a more specific aspect of this embodiment, the diagnostic reagents are used for

detecting the level of from 1 to 20 of the biomarkers listed in Table 1, for the detection of endometrial cancer. In one aspect of this embodiment, the level of the mRNA corresponding to from 1 to 20 biomarkers is determined. In one aspect of this embodiment, the level of the mRNA corresponding to from 2 to 17 biomarkers is determined. In one aspect of this embodiment, the level of the mRNA corresponding to from 3 to 15 biomarkers is determined. In one aspect of this embodiment, the level of a protein or polypeptide corresponding to from 1 to 20 biomarkers is determined. In one aspect of this embodiment, the level of a protein or polypeptide corresponding to from 2 to 17 biomarkers is determined. In one aspect of this embodiment, the level of a protein or polypeptide corresponding to from 3 to 15 biomarkers is determined. In one aspect of this embodiment, the sample that is analyzed is a tumor sample. In one aspect of this embodiment, the sample is analyzed is a uterine fluid sample. In one aspect of this embodiment, the sample that is analyzed is a serum, blood, or plasma sample. In one aspect, the sample is that is used is obtained by using a soft, straw-like device (pipelle) that is used to suction off a small sample of lining from the uterus (*e.g.*, uterine fluid). In one aspect, the sample is obtained by using a sharp-edged tool called a curette by scraping a small sample and collecting it with a syringe or suction (*e.g.*, dilation and curettage). In one aspect, the sample is obtained by using an electronic suction device (*e.g.*, Vabra aspiration). In one aspect, the sample is obtained by using a spray of liquid (jet irrigation) to wash off some of the tissue that lines the uterus. In some aspects, a brush may be used to remove some of the lining before the washing is done. In one aspect, a blood, serum, or plasma sample is analyzed for from 1 to 20 of the biomarkers of the invention.

In microrarray studies, GMIP was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of GMIP was also found to be correlated in primary tumor and uterine fluid. Thus, GMIP is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having GMIP are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a

method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of GMIP and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, GMIP alone has AUROC value in Table 6 of 0.88 IKBKE alone has an AUROC value of 0.90, when these two markers are combined together in a profile the AUROC value 0.92 with a substantial increase in specificity (increased AUROC value indicate increased ability to separate the population). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, IKBKE was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of IKBKE was also found to be correlated in primary tumor and uterine fluid. Thus, IKBKE is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having IKBKE are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of IKBKE and from 2 to 19 biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, IKBKE alone has AUROC value in Table 6 of 0.90, P4HB alone has an AUROC value of 0.97, when these two markers are combined together in a profile the AUROC value 0.98 with a substantial increase in specificity to 100% (increased AUROC value indicate increased ability to separate

the population). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, P4HB was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of P4HB was also found to be correlated in primary tumor and uterine fluid. Thus, P4HB is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having P4HB are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of P4HB and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, P4HB alone has AUROC value in Table 6 of 0.97, SOCS2 alone has an AUROC value of 0.93, when these two markers are combined together in a profile the AUROC value 1 with a substantial increase in specificity to 100% (increased AUROC value indicate increased ability to separate the population). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, SOCS2 was found to be underexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of SOCS2 was also found to be correlated in primary tumor and uterine fluid. Thus, SOCS2 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having SOCS2 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of SOCS2 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, SOCS2 alone has AUROC value in Table 6 of 0.93, GMIP alone has an AUROC value of 0.88, when these two markers are combined together in a profile the AUROC value 0.999 with a substantial increase in sensitivity to 100% (increased AUROC value indicate increased ability to separate the population). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, EPS8L2 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.002 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of EPS8L2 was also found to be correlated in primary tumor and uterine fluid. Thus, EPS8L2 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having EPS8L2 are

expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of EPS8L2 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when EPS8L2 is combined with GMIP, IKBKE, P4HB, SOCS2, and DDR1 the AUROC value is 1 and the sensitivity is nearly 96% and the specificity is 100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, RASSF7 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0005 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of RASSF7 was also found to be correlated in primary tumor and uterine fluid. Thus, RASSF7 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having RASSF7 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of RASSF7 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when RASSF7 is combined with DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, SIRT6, TJP3 and SOCS2 the AUROC value is 1 and the sensitivity is 100% and the specificity is

100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, DDR1 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.02 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of DDR1 was also found to be correlated in primary tumor and uterine fluid. Thus, DDR1 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having DDR1 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of DDR1 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when DDR1 is combined with EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, SIRT6, TJP3, SOCS2, and RNF183 the AUROC value is 1 and the sensitivity is 100% and the specificity is 100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, PPP1R16A was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In



RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of PPP1R16A was also found to be correlated in primary tumor and uterine fluid. Thus, PPP1R16A is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having PPP1R16A are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of PPP1R16A and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when PPP1R16A is combined with GMIP, IKBKE, P4HB, SOCS2, and EPS8L2 the AUROC value is nearly 1 and the sensitivity is nearly 92% and the specificity is 100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, PHKG2 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of PHKG2 was also found to be correlated in primary tumor and uterine fluid. Thus, PHKG2 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having PHKG2 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and

determining the level of PHKG2 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when PHKG2 is combined with DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PPP1R16A, SIRT6, TJP3, SOCS2, and RNF183 the AUROC value is 1 and the sensitivity is 100% and the specificity is 100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, P2RX4 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0005 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of P2RX4 was also found to be correlated in primary tumor and uterine fluid. Thus, P2RX4 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having P2RX4 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of P2RX4 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when P2RX4 is combined with DDR1, EPS8L2, GMIP, IKBKE, P4HB, PHKG2, PPP1R16A, SIRT6, TJP3, SOCS2, and RNF183 the AUROC value is 1 and the sensitivity is 100% and the specificity is 100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment,

the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, ACAA1 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of ACAA1 was also found to be correlated in primary tumor and uterine fluid. Thus, ACAA1 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having ACAA1 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of ACAA1 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to one aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In microrarray studies, AP1M2 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of AP1M2 was also found to be correlated in primary tumor and uterine fluid. Thus, AP1M2 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having AP1M2 are

expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of AP1M2 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microarray studies, CGN was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of CGN was also found to be correlated in primary tumor and uterine fluid. Thus, CGN is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having CGN are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of CGN and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microarray studies, FASTKD1 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In

RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of FASTKD1 was also found to be correlated in primary tumor and uterine fluid. Thus, FASTKD1 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having FASTKD1 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of FASTKD1 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microarray studies, PPFIBP2 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.02 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of PPFIBP2 was also found to be correlated in primary tumor and uterine fluid. Thus, PPFIBP2 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having PPFIBP2 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of PPFIBP2 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the

sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microrarray studies, RNF183 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of RNF183 was also found to be correlated in primary tumor and uterine fluid. Thus, RNF183 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having RNF183 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of RNF183 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when RNF183 is combined with DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, SIRT6, TJP3, and SOCS2 the AUROC value is 1 and the sensitivity is 100% and the specificity is 100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microrarray studies, SIRT6 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of SIRT6 was also found to be correlated in primary tumor and uterine fluid. Thus, SIRT6 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood

of endometrial cancer. Furthermore, fingerprint patterns/profiles having SIRT6 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of SIRT6 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when SIRT6 is combined with DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, TJP3, SOCS2, and RNF183 the AUROC value is 1 and the sensitivity is 100% and the specificity is 100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microrarray studies, TJP3 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of TJP3 was also found to be correlated in primary tumor and uterine fluid. Thus, TJP3 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having TJP3 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of TJP3 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. For example, when TJP3 is combined with DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, SIRT6, SOCS2, and RNF183 the AUROC value is 1 and the sensitivity is 100% and the specificity is

100% (see Table 11). According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microrarray studies, EFEMP2 was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.0001 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of EFEMP2 was also found to be correlated in primary tumor and uterine fluid. Thus, EFEMP2 is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having EFEMP2 are expected to be useful for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of EFEMP2 and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In microrarray studies, DCN was found to be overexpressed in samples from patients having endometrial cancer as compared to normal values (non-affected). In RT-PCR studies this result was confirmed and a p-value of less than 0.005 was obtained for aspirate samples from non-affected individuals versus aspirates from individuals having endometrial cancer comparisons. The expression of DCN was also found to be correlated in primary tumor and uterine fluid. Thus, DCN is an excellent biomarker for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer. Furthermore, fingerprint patterns/profiles having DCN are expected to be useful for diagnosing endometrial cancer and/or an increased



likelihood of endometrial cancer. In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer comprising obtaining a sample from an individual and determining the level of DCN, and from 2 to 19 other biomarkers chosen from Table 1 wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined.

In one embodiment, the invention provide an in vitro diagnostic method for the diagnosis of endometrial cancer or an increased likelihood of endometrial comprising detecting the level of (1) from 1 to 17 biomarker(s) chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, and TJP3 in a sample from a patient wherein an increased level of said from 1 to 17 biomarkers compared to a control value indicates a diagnosis of endometrial cancer or increased likelihood of endometrial cancer and/or (2) detecting the level of from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN, wherein a decreased level of EFEMP2, SOCS2, and/or DCN compared to a control value indicates a diagnosis of endometrial cancer or increased likelihood of endometrial cancer. In one preferred aspect, the method of diagnosing endometrial cancer or an increased likelihood of endometrial cancer involves using one or more upregulated biomarkers and one or more downregulated biomarkers according to Table 1.

In one aspect of this embodiment, the patient has a risk factor for endometrial cancer or is being screened for endometrial cancer.

In one aspect of this embodiment, the sample from said patient is obtained from a patient with abnormal uterine bleeding.

In one aspect of this embodiment, the sample is from said patient is obtained from a patient having an endometrium with increased thickness.

In one aspect of this embodiment, the sample from said patient is obtained from a pre-menopausal, peri-menopausal, or post-menopausal patient.

In one aspect of this embodiment, the patient is pre-menopausal.

In one aspect of this embodiment, the patient is peri-menopausal.

In one aspect of this embodiment, the patient is post-menopausal.

In one aspect of this embodiment, the sample is chosen from a tissue sample, blood and/or serum, and uterine fluid.

In one aspect of this embodiment, the sample is a uterine fluid sample.

In one aspect of this embodiment, the uterine fluid sample is obtained by aspiration.

In one aspect of this embodiment, the level of the biomarker(s) is determined with an antibody.

In one aspect of this embodiment, the level of the biomarker(s) is determined by RT-PCR. In one specific aspect, the level of the biomarker is determined by quantitative RT-PCR.

In one aspect of this embodiment, the markers are chosen from IKBKE, P4HB, SOCS2, GMIP, DDR1, EPS8L2, PPP1R16A, P2RX4, PHKG2, RASSF7, SIRT6, and TJP3.

In one aspect of this embodiment, the marker(s) is chosen from P2RX4, P4HB, PHKG2, PPFIBP2, and SOCS2.

In one aspect of this embodiment, the markers are chosen from P4HB, RASSF7, RNF183, and IKBKE.

In one aspect of this embodiment, from 2 to 20 markers are detected.

In one aspect of this embodiment, one or more additional auxiliary biomarkers are detected.

In one aspect of this embodiment, the one or more auxiliary biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and additional biomarkers for detecting endometrial cancer.

In one aspect of this embodiment, the one or more auxiliary biomarkers are chosen from differential diagnosis biomarkers.

In one aspect of this embodiment, the one or more auxiliary biomarkers are chosen from prognostic markers.

In one aspect of this embodiment, the one or more auxiliary biomarkers are chosen from endometrial cancer classification markers.

In one aspect of this embodiment, the invention provides a nucleic acid chosen from IKBKE mRNA, cDNA, or a complement thereof; P4HB mRNA, cDNA, or a complement thereof; SOCS2 mRNA, cDNA, or a complement thereof; GMIP mRNA, cDNA, or a complement thereof; DDR1 mRNA, cDNA, or a complement thereof; EPS8L2 mRNA, cDNA, or a complement thereof; and PPP1R16A mRNA, cDNA, complement thereof, for use for diagnosing endometrial cancer or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides a nucleic acid chosen from ACAA1 mRNA, cDNA, or a complement thereof; AP1M2 mRNA, cDNA, or a complement thereof; CGN mRNA, cDNA, or a complement thereof; P2RX4 mRNA, cDNA, or a complement thereof; PPFIBP2 mRNA, cDNA, or a complement thereof; RASSF7 mRNA, cDNA, or a complement thereof; TJP3 mRNA, cDNA, or a complement thereof; DCN mRNA, cDNA, or a complement thereof; and RNF183

mRNA, cDNA, or a complement thereof, for use for diagnosing endometrial cancer or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides a nucleic acid chosen from EFEMP2 mRNA, cDNA, or a complement thereof; PHKG2 mRNA, cDNA, or a complement thereof; SIRT6 mRNA, cDNA, or a complement thereof; and FASTKD1 mRNA, cDNA, or a complement thereof, for use for diagnosing endometrial cancer or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides primers chosen from primers for IKBKE; primers for P4HB; primers for SOCS2; primers for GMIP; primers for DDR1; primers for EPS8L2; and primers for PPP1R16A; for use for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides primers chosen from primers for ACAA1; primers for AP1M2; primers for CGN; primers for P2RX4; primers for PPFIBP2; primers for RASSF7; primers for RNF183; primers for TJP3; and primers for DCN; for use for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides primers chosen from primers for EFEMP2; primers for SIRT6; primers for PHKG2; and primers for FASTKD1; for use for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides a nucleic acid chosen from probe for IKBKE; probe for P4HB; probe for SOCS2; probe for GMIP; probe for DDR1; probe for EPS8L2; and probe for PPP1R16A, for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides a nucleic acid chosen from probe for ACAA1; probe for AP1M2; probe for CGN; probe for P2RX4; probe for

PPFIBP2; probe for RASSF7; probe for RNF183; probe for TJP3; and probe for DCN, for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides a nucleic acid chosen from probe for EFEMP2; probe for FASTKD1; probe for SIRT6; probe for GMIP; and probe for PHKG2, for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides a kit comprising two or more probes to the 1-20 biomarkers of the invention, for diagnosing endometrial cancer and/or an increased likelihood of cancer.

In one aspect of this embodiment, the invention provides a kit comprising primers for two or more of the 1-20 biomarkers of the invention for diagnosing endometrial cancer and/or an increased likelihood of cancer.

In one aspect of this embodiment, the invention provides an antibody chosen from an antibody to IKBKE; an antibody to P4HB; an antibody to SOCS2; an antibody to GMIP; an antibody to DDR1; an antibody to EPS8L2; and an antibody to PPP1R16A, for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides an antibody chosen from an antibody to ACAA1; an antibody to AP1M2; an antibody to CGN; an antibody to P2RX4; an antibody to PPFIBP2; an antibody to RASSF7; an antibody to RNF183; an antibody to TJP3; and an antibody to DCN, for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides an antibody chosen from an antibody to EFEMP2; an antibody to FASTKD1; an antibody to SIRT6; an antibody to GMIP; and an antibody to PHKG2; for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer.

In one aspect of this embodiment, the invention provides a kit comprising antibodies to two or more biomarkers of Table 1 for diagnosing endometrial cancer and/or an increased likelihood of cancer.

In aspect of this embodiment, the invention provides a kit for obtaining uterine fluid for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer by assessing the levels of from 1-20 biomarkers of Table 1.

In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 2 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 3 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 4 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 5 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 5 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 7 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 10 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 15 biomarkers of the invention. In one aspect of this embodiment, the in vitro diagnostic method comprises determining the level of 20 biomarkers of the invention.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description, and from the claims.

### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows correlation of the expression level of biomarkers in primary tumor and in uterine fluid for the biomarkers including those of the invention. See Example 3 for details.

FIG. 2A and 2B is a box and whiskers plots represent the relative amount of RNA (RQ) present in the aspirate samples from patients having endometrial cancer as compared with the control samples for each gene as determined by RT-PCR. 30 tumor samples and 24 controls were considered in the plots. Boxes represent the interquartile range for each gene and the whiskers go from percentile 10 to 90 of the RQ values for each gene. The bar in the boxes represents the median RQ. The white boxes represent the values for the tumour samples of each gene and the shaded boxes the values for the control samples. See Example 4 for details.

FIG. 3 shows an example of the expression level of RNF183 as determined by RT-PCR in aspirates obtained from patients having endometrial cancer (RNF183\_T), normals in secretory phase (RNF183\_S), normals not having endometrial cancer (RNF183\_N), and all normals together (RNF183\_Nt).

FIG. 4 shows an example of the expression level of AP1M2 as determined by RT-PCR in aspirates obtained from patients having endometrial cancer (AP1M2\_T), normals in secretory phase (AP1M2\_S), normals not having endometrial cancer (AP1M2\_N), and all normals together (AP1M2\_Nt).

FIG. 5 shows an example of the expression level of CGN as determined by RT-PCR in aspirates obtained from patients having endometrial cancer (CGN\_T), normals in secretory phase (CGN\_S), normals not having endometrial cancer (CGN\_N), and all normals together (CGN\_Nt).

FIG. 6 shows an example of the expression level of FASTKD1 as determined by RT-PCR in aspirates obtained from patients having endometrial cancer (FASTKD1\_T),

normals in secretory phase (FASTKD1\_S), normals not having endometrial cancer (FASTKD1\_N), and all normals together (FASTKD1\_Nt).

FIG. 7 shows an example of the expression level of IKBKE as determined by RT-PCR in aspirates obtained from patients having endometrial cancer (IKBKE\_T), normals in secretory phase (IKBKE\_S), normals not having endometrial cancer (IKBKE\_N), and all normals together (IKBKE\_Nt).

FIG. 8 shows an example of the expression level of P4HB as determined by RT-PCR in aspirates obtained from patients having endometrial cancer (P4HB\_T), normals in secretory phase (P4HB\_S), normals not having endometrial cancer (P4HB\_N), and all normals together (P4HB\_Nt).

FIG. 9 shows an example of the expression level of SOCS2 as determined by RT-PCR in aspirates obtained from patients having endometrial cancer (SOCS2\_T), normals in secretory phase (SOCS2\_S), normals not having endometrial cancer (SOCS2\_N), and all normals together (SOCS2\_Nt).

FIG. 10 shows a western blot of endometrial cancer tissue with antibody against a Biomarker of the invention: P4HB. The samples tested include four normal tissues (N) and four tumor tissues (T). Normal and tumors tissues were obtained from the same patient. As a positive control: total protein extract from the endometrial tumour cell line Isikawa. See Example 6.

FIG. 11 shows a western blot of endometrial cancer tissue with antibody against a Biomarker of the invention: AP1M2. The samples tested include four normal tissues (N) and four tumor tissues (T) from 4 different patients. Matched normal and tumors tissues were obtained from the same patient. As a positive control: total protein extract from the endometrial tumor cell line Isikawa. See Example 6.

FIG. 12 shows a western blot of endometrial cancer tissue with antibody against a Biomarker of the invention: IKBKE. The samples tested include a normal tissue (N) and a tumor tissue (T). Matched normal and tumors tissue were obtained from the same patient. As a positive control: total protein extract from the endometrial tumor cell line Isikawa. See Example 6.



FIG. 13 shows a western blot of endometrial cancer tissue with antibody against a Biomarker of the invention: EPS8L2. The samples tested include 3 normal tissues (N) and 3 tumor tissues (T) from 3 different patients. As a positive control: total protein extract from the endometrial tumor cell line. Matched normal and tumors tissues were obtained from the same patient. See example 6.

FIG. 14 shows a western blot of endometrial cancer tissue with antibody against a Biomarker of the invention: DDR1. The samples tested include a normal tissue (N) and a tumor tissue (T). Matched normal and tumors tissue were obtained from the same patient. As a positive control: total protein extract from the endometrial tumor cell line Isikawa. See Example 6.

FIG. 15 shows a western blot of endometrial cancer tissue with antibody against a Biomarker of the invention: CGN. The samples tested include four normal tissues (N) and four tumor tissues (T) from four different patients. Matched normal and tumors tissues were obtained from the same patient. As a positive control: total protein extract from the endometrial tumor cell line Isikawa. See Example 6.

FIG. 16 shows a western blot of endometrial cancer tissue with antibody against a Biomarker of the invention: TJP3. The samples tested include a normal tissue (N) and a tumor tissue (T). Matched normal and tumors tissue were obtained from the same patient. As a positive control: total protein extract from the endometrial tumor cell line Isikawa. See Example 6.

FIG. 17 shows the calculated risk of cancer using 48 non-tumor samples and 33 tumor samples using the ACAA1, AP1M2, EPS8L2, IKBKE, P2RX4, P4HB, PPFIBP2, PPP1R16A, SIRT6, EFEMP2. See Example 5.

FIG. 18 shows the calculated risk of cancer using 48 non-tumor samples and 33 tumor samples using the FASTKD1, GMIP, P4HB, EFEMP2, SIRT6, and PHKG2. See Example 5.

FIG. 19 shows the calculated risk of cancer using 48 non-tumor samples and 33 tumor samples using the FASTKD1, GMIP, P4HB, EFEMP2, DDR1, and SIRT6. See Example 5.

### DETAILED DESCRIPTION OF THE INVENTION

The present invention is based on the finding of the association of alterations in the mRNA expression levels of the biomarkers listed in Table 1 in samples from patients having endometrial cancer as compared to control values (*e.g.*, normal tissue (non-affected) or value). These biomarkers therefore represent endometrial cancer biomarkers. Additionally, the inventors surprisingly found that samples obtained from uterine fluid of endometrial cancer patients display expression profiles for the biomarkers listed in Table 1 that were generally correlated to the expression profiles from the primary tumor. Furthermore, a number of the markers found by the inventors are expected to be found on cell surfaces and/or in blood as blood based markers (or in other body fluids like uterine fluid). As shown in Example 6, the upregulated biomarkers of Table 1 were shown to be overexpressed at the protein level in primary tissue as compared to normal non-affected tissue. For example, the protein level of P4HB by western blot analysis, revealed that this biomarker is overexpressed at a protein level as well. FIG. 11 through FIG. 16 show overexpression, at the protein level, of AP1M2, IKBKE, EPS8L2, DDR1, CGN, and TJP3. Furthermore, P4HB, PPP1R16A and EPS8L2 presented a specific cytoplasmatic expression within the tumoral cells in all carcinoma histological types and grades, and an absence or faint cytoplasmatic staining within the normal epithelial glands as determined by tissue microarray (TMA) immunohistochemistry (IHC).

These studies provide endometrial cancer diagnostic biomarkers with excellent predictive value, alone or in combinations, that may be detected using methods which are less invasive as compared to the current standard of care. Furthermore, the inventors have identified specific subsets of biomarkers that are capable of distinguishing, in endometrial aspirates samples, endometrial cancer affected patients from different sub-groups of non-affected patients.

Several of the studies used to identify (expression microarray) and validate (RT-PCR) the biomarkers of the invention are described briefly below and in more detail in the Example section.

More specifically, the inventors performed gene expression analysis on expression microarrays to detect genes that are differentially expressed in endometrial cancer as compared to normal tissues. The gene expression microarray studies disclosed herein revealed that a number of genes in endometrial cancer samples were overexpressed as compared to normal endometrial tissue. It was found that ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, and TJP3, were overexpressed in endometrial cancer samples and EFEMP2, SOCS2, and DCN were underexpressed, as compared to their respective levels in normal endometrial tissue using a microarray experimental strategy. These results are summarized in Table 1 which has the common abbreviation for the gene, the ENSEMBL accession numbers (corresponding to the gene, transcript(s), and protein related to the biomarkers of the invention), the fold change values and the p-values for statistical significance.

Table 1: Differential expression of endometrial cancer biomarkers in primary tumor as compared to control values (obtained from a pool of unaffected tissue, see Example 1).

| Name     | gene            | Transcrip                                                                                   | Protein                                                                                     | Array data  |         |
|----------|-----------------|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|-------------|---------|
|          |                 |                                                                                             |                                                                                             | Fold change | p-value |
| RASSF7   | ENSG00000099849 | ENST00000397583<br>ENST00000397582                                                          | ENSP00000380713<br>ENSP00000380712                                                          | 1.94        | 0.07    |
| CGN      | ENSG00000143375 | ENST00000271636                                                                             | ENSP00000271636                                                                             | 1.79        | 0.22    |
| AP1M2    | ENSG00000129354 | ENST00000250244                                                                             | ENSP00000250244                                                                             | 1.71        | 0.11    |
| PHKG2    | ENSG00000156873 | ENST00000328273                                                                             | ENSP00000329968                                                                             | 1.34        | 0.09    |
| PPP1R16A | ENSG00000160972 | ENST00000292539                                                                             | ENSP00000292539                                                                             | 1.44        | 0.10    |
| DDR1     | ENSG00000137332 | ENST00000259875<br>ENST00000400414<br>ENST00000400411<br>ENST00000383377<br>ENST00000400410 | ENSP00000259875<br>ENSP00000383265<br>ENSP00000383262<br>ENSP00000372868<br>ENSP00000383261 | 1.93        | 0.13    |
| P4HB     | ENSG00000185624 | ENST00000331483                                                                             | ENSP00000327801                                                                             | 1.90        | 0.13    |
| RNF183   | ENSG00000165188 | ENST00000297894                                                                             | ENSP00000297894                                                                             | 1.73        | 0.19    |
| IKBKE    | ENSG00000143466 | ENST00000367120                                                                             | ENSP00000356087                                                                             | 1.37        | 0.17    |
| EPS8L2   | ENSG00000177106 | ENST00000318562                                                                             | ENSP00000320828                                                                             | 1.34        | 0.20    |
| TJP3     | ENSG00000105289 | ENST00000262968<br>ENST00000382008                                                          | ENSP00000262968<br>ENSP00000371438                                                          | 1.57        | 0.17    |
| SIRT6    | ENSG00000077463 | ENST00000269860<br>ENST00000305232<br>ENST00000337491<br>ENST00000381935                    | ENSP00000269860<br>ENSP00000305310<br>ENSP00000337332<br>ENSP00000371360                    | 1.27        | 0.15    |
| GMIP     | ENSG00000089639 | ENST00000203556                                                                             | ENSP00000203556                                                                             | 1.42        | 0.05    |
| ACAA1    | ENSG00000060971 | ENST00000333167<br>ENST00000301810<br>ENST00000358122                                       | ENSP00000333664<br>ENSP00000301810<br>ENSP00000350838                                       | 1.26        | 0.11    |
| FASTKD1  | ENSG00000138399 | ENST00000260971<br>ENST00000361619<br>ENST00000361819                                       | ENSP00000260971<br>ENSP00000354598<br>ENSP00000354821                                       | 1.71        | 0.06    |
| DCN      | ENSG00000011465 | ENST00000052754<br>ENST00000228329<br>ENST00000303320<br>ENST00000350856                    | ENSP00000052754<br>ENSP00000228329<br>ENSP00000302031<br>ENSP00000308451                    | -2.55       | 0.06    |
| SOCS2    | ENSG00000120833 | ENST00000340600<br>ENST00000393123                                                          | ENSP00000339428<br>ENSP00000376831                                                          | -1.69       | 0.06    |
| EFEMP2   | ENSG00000172638 | ENST00000307998                                                                             | ENSP00000309953                                                                             | -1.22       | 0.08    |
| P2RX4    | ENSG00000135124 | ENST00000337233<br>ENST00000359949                                                          | ENSP00000336607<br>ENSP00000353032                                                          | 1.70        | 0.12    |
| PPFIBP2  | ENSG00000166387 | ENST00000299492                                                                             | ENSP00000299492                                                                             | 1.52        | 0.11    |

As shown in FIG. 1, it was found that the markers of Table 1 were also found to be differentially expressed in samples obtained from uterine fluid in patients having endometrial cancer. Markers which were not highly correlated fall off or further away from the correlation line in FIG. 1.

The overexpression of ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, and TJP3, and the underexpression of DCN, SOCS2, and EFEMP2 in endometrial cancer was validated by RT-PCR using an independent set of samples. The samples used in this study were obtained from uterine fluid of individuals having endometrial cancer and from patients not having endometrial cancer. These results are summarized in Table 2 and illustrated in FIG. 2A and FIG. 2B. These results demonstrate that these markers displayed statistically significant differential expression in endometrial cancer samples in samples from individuals having

endometrial cancer as compared to normal individuals and/or samples (*e.g.*, control value).

Table 2: Differential expression of biomarkers in aspirate samples from patients having endometrial cancer compared to aspirates from patients not having endometrial cancer.

|          | Mean RQ | SEM   | p value  |
|----------|---------|-------|----------|
| ACAA1    | 1.472   | 0.476 | < 0.0001 |
| AP1M2    | 1.688   | 0.422 | < 0.0001 |
| CGN      | 2.348   | 1.312 | < 0.0001 |
| DCN      | 0.246   | 0.196 | 0.002    |
| DDR1     | 1.515   | 0.534 | 0.0167   |
| EFEMP2   | 0.414   | 0.289 | < 0.0001 |
| EPS8L2   | 1.646   | 0.559 | 0.0016   |
| FASTKD1  | 1.693   | 0.662 | < 0.0001 |
| GMIP     | 1.338   | 0.491 | < 0.0001 |
| IKBKE    | 2.877   | 1.617 | < 0.0001 |
| P2RX4    | 1.544   | 0.504 | 0.0002   |
| P4HB     | 1.998   | 0.647 | < 0.0001 |
| PHKG2    | 1.557   | 0.378 | < 0.0001 |
| PPFIBP2  | 1.540   | 0.725 | 0.0094   |
| PPP1R16A | 1.915   | 0.789 | < 0.0001 |
| RASSF7   | 1.848   | 0.770 | 0.0001   |
| RNF183   | 3.648   | 2.368 | < 0.0001 |
| SIRT6    | 1.611   | 0.550 | < 0.0001 |
| SOCS2    | 0.265   | 0.177 | < 0.0001 |
| TJP3     | 2.088   | 0.928 | < 0.0001 |

The p-values were calculated using a non-parametric Mann-Whitney test. Mean RQ refers to relative quantity, and SEM refers to standard error of the mean.

The finding of the correlation of expression levels of these biomarkers in primary tissue and uterine fluid was surprising given the heterogeneity of uterine fluid and the findings in the initial microarrays studies. It is believed that this is the first time that the levels of biomarkers in primary endometrial cancer were shown to be correlated in a statistically significant manner to those found in uterine fluid and therefore this provides a less invasive and more standardized method of screening for endometrial cancer and/or an increased risk of endometrial cancer. The invention

therefore provides a method for diagnosing endometrial cancer and/or an increased likelihood of endometrial cancer by obtaining a uterine fluid sample and determining the level of biomarkers differentially expressed in endometrial cancer as compared to control value. In one aspect, the uterine fluid sample is obtained by aspiration. In one aspect, the uterine fluid sample is obtained gently washing and/or rinse the uterine cavity. In one aspect, the level of mRNA is determined. In one aspect, the level of protein is determined. In one aspect, the biomarkers are chosen from the 20 listed in Table 1.

Surprisingly, the p-values for the individual biomarkers in Table 1 as determined in the microarray studies with one sample set were significantly improved upon when the same biomarkers were analyzed by a different technique (quantitative RT-PCR) using a different set of samples, obtained from the patient by a different method. In general the p-values were over 100 fold improved compared to the microarray studies.

The inventors have found that individually each of the biomarkers of Table 1 have predictive value for the diagnosis of endometrial cancer. Furthermore, combinations of these biomarkers have additional predictive value for the diagnosis of endometrial cancer. For example, the inventors have surprisingly found that numerous subgroups of the biomarkers of Table 1 having from 2-20 biomarkers in various combinations give fingerprint patterns having excellent predictive value for diagnosis or detection of endometrial cancer. Additionally, the inventors have also contemplate that addition of other biomarkers besides those listed in Table 1, to the fingerprint pattern also can increase predictive value, and can be useful for classifying endometrial cancers, for differential diagnosis of diseases other than endometrial cancer, and for endometrial cancer prognosis.

In one embodiment, the present invention provides a method for characterizing a sample obtained from a patient for prognostic, diagnostic and/or pharmacogenomic uses. Characterization of the a sample obtained from a patient according to the levels one or more of the biomarkers of Table 1 can be used to provide information regarding disease progression, diagnosis of endometrial cancer type (and/or subtype), and selection of an appropriate therapeutic treatment. According to the method of

the invention, a sample is obtained from an individual. The individual can be a healthy person, an individual diagnosed with cancer, an individual suspected of having cancer, an individual displaying one or more symptoms of cancer and/or an individual desiring screening for cancer. The method comprises the step of determining the level of the biomarker(s) of Table 1 in a sample obtained for a patient. Alternative methods for determining the biomarkers (IHC, mRNA expression analysis, *etc*) can be used in these methods.

In one embodiment, the invention provides a method for diagnosing endometrial cancer and/or an increased likelihood of having endometrial cancer which comprises obtaining a sample from an individual and determining the level of from 1 to 20 biomarkers of Table 1 in the sample. If the level of from 1 to 17 of the upregulated biomarkers are increased relative to control value and/or the level of from 1 to 3 of the downregulated markers are decreased compared to control value, then the patient has an increased likelihood of having endometrial cancer.

In one embodiment, the invention provides a method for diagnosing endometrial cancer which comprises obtaining a sample from a patient having a symptom of endometrial cancer and determining the level of from 1 to 20 biomarkers of Table 1 in the sample. In one aspect of this embodiment, the symptom of endometrial cancer is chosen from vaginal bleeding and/or spotting in postmenopausal women, abnormal uterine bleeding, abnormal menstrual periods, bleeding between normal periods in premenopausal women in women older than 40, extremely long, heavy, or frequent episodes of bleeding, anemia caused by chronic loss of blood, lower abdominal pain or pelvic cramping, thin white or clear vaginal discharge in postmenopausal women, and suspect symptoms in peri-menopausal. Thus, in one aspect of this embodiment, the invention relates to a method for diagnosing endometrial cancer comprising obtaining or providing a sample from an individual having vaginal bleeding and/or spotting in postmenopausal women, abnormal uterine bleeding, abnormal menstrual periods, bleeding between normal periods in premenopausal women in women older than 40, extremely long, heavy, or frequent episodes of bleeding, anemia caused by chronic loss of blood, lower abdominal pain or pelvic cramping, thin white or clear vaginal discharge in postmenopausal women, or suspect symptoms in peri-menopausal and determining the level of from 1-17 biomarkers chosen from ACAA1,

AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, and/or from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. In a specific aspect of this embodiment, when the level of from 1 to 17 biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, are increased relative to a control value and/or the level from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN are decreased relative to control value then this indicates endometrial cancer or an increased chance of having endometrial cancer. According to one aspect of this embodiment, the levels of the one or more biomarkers for detecting endometrial cancer are normalized to one or more endogenous biomarkers or genes. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to another aspect of this embodiment, the level of protein corresponding to the biomarker is determined.

In one embodiment, the invention provides a method for diagnosing endometrial cancer which comprises obtaining a sample from a patient having a risk factor for endometrial cancer and determining the level of from 1 to 20 biomarkers of Table 1 in the sample. In one aspect of this embodiment, the risk factor for endometrial cancer is chosen from high levels of estrogen, endometrial hyperplasia, obesity, hypertension, polycystic ovary syndrome, nulliparity, infertility, early menarche, late menopause, endometrial polyps or other benign growths of the uterine lining, diabetes, tamoxifen exposure, hyperplasia, high intake of animal fat, pelvic radiation therapy, breast cancer, ovarian cancer, heavy daily alcohol consumption, family history of cancer, family history of HNPCC, and being an HNPCC mutation carrier. In one aspect of this embodiment, the biomarkers are selected for distinguishing patients having tumor from those in secretory phase of the menstrual cycle. Thus, in one aspect of this embodiment, the invention relates to a method for diagnosing endometrial cancer comprising obtaining or providing a sample from an individual



having a risk factor for cancer which is high levels of estrogen, endometrial hyperplasia, obesity, hypertension, polycystic ovary syndrome, nulliparity, infertility, early menarche, late menopause, endometrial polyps or other benign growths of the uterine lining, diabetes, tamoxifen exposure, hyperplasia, high intake of animal fat, pelvic radiation therapy, breast cancer, ovarian cancer, heavy daily alcohol consumption, family history of cancer, family history of HNPCC, or being an HNPCC mutation carrier which is and determining the level of from 1-17 biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, and/or from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. In a specific aspect of this embodiment, when the level of from 1 to 17 biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, are increased relative to a control value and/or the level from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN are decreased relative to control value then this indicates endometrial cancer or an increased chance of having endometrial cancer. According to one aspect of this embodiment, the levels of the one or more biomarkers for detecting endometrial cancer are normalized to one or more endogenous biomarkers or genes. According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to another aspect of this embodiment, the level of protein corresponding to the biomarker is determined. In a preferred aspect of this embodiment, the method involves determining the level of from 1-17 upregulated biomarkers of Table 1 and from 1-3 downregulated markers of Table 1 by quantitative PCR in a uterine fluid sample.

In one embodiment, the invention provides a method for diagnosing endometrial cancer which comprises obtaining a sample from a patient having an endometrium with an increased thickness. In one aspect of this embodiment, the thickness of the endometrium is measured by transvaginal ultrasound. "Increased thickness" refers a

thickness above a value common employed in the art to identify patients that warrant further work-up or investigation. The method of this embodiment involves determining the level of from 1 to 20 biomarkers of Table 1 in a sample obtained from a patient having an endometrium of increased thickness. According to an aspect of this embodiment, the sample is a uterine fluid sample. In another aspect of this embodiment, the level of from 1-20 mRNA biomarkers is determined. In another aspect of this embodiment, the level of from 1-20 protein biomarkers is determined. In one aspect of this embodiment, the biomarkers are chosen from those that are capable of distinguishing samples from endometrial cancer affected patients and from those patients having another condition that increases the thickness of the endometrium. Conditions that increases the thickness of the endometrium but are not necessarily present in endometrial cancer patients include, but are not limited to, tamoxifen exposure, exposure to hormones, phase of menstrual cycle (in general the endometrium thickness increase in going from proliferative to secretory phase). Some preferred biomarkers which performed well in separating samples from patients affected with endometrial cancer from non-endometrial cancer affected patients in the secretory phase are shown in Table 9 in the Examples. Thus, in one aspect of this embodiment, the invention relates to a method for diagnosing endometrial cancer comprising obtaining or providing a sample from an individual having increased endometrial thickness and determining the level of from 1-17 biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, and/or from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN wherein if said markers are differentially expressed compared to a control value, then the individual is diagnosed with endometrial cancer and/or an increased likelihood of endometrial cancer. In a specific aspect of this embodiment, when the level of from 1 to 17 biomarkers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, are increased relative to a control value and/or the level from 1 to 3 biomarkers chosen from EFEMP2, SOCS2, and DCN are decreased relative to control value then this indicates endometrial cancer or an increased chance of having endometrial cancer. According to one aspect of this embodiment, the levels of the one or more biomarkers for detecting endometrial cancer are normalized to one or more endogenous biomarkers or genes.

According to one aspect of this embodiment, the sample is chosen from a tissue sample and a fluid sample. In one aspect, the fluid sample is a uterine fluid sample or uterine aspirate. According to one aspect of this embodiment, the level of mRNA corresponding to the biomarker is determined. According to another aspect of this embodiment, the level of protein corresponding to the biomarker is determined. In a preferred aspect of this embodiment, the method involves determining the level of from 1-17 upregulated biomarkers of Table 1 and from 1-3 downregulated markers of Table 1 by quantitative PCR in a uterine fluid sample.

#### Profiles, fingerprint patterns, and combinations

The initial microarray studies disclosed herein demonstrated that each of the biomarkers of Table 1, as independent biomarkers, have predictive value for diagnosing endometrial cancer. Furthermore, it was found that combinations of markers (e.g., profiles or fingerprint patterns) have increased predictive value for endometrial cancer. Thus, in addition to using these markers as individual markers, they can be used in combinations of 2 to 20 biomarkers for diagnosing endometrial cancer. In some embodiments additional markers can be included in the profile or fingerprint pattern for differential diagnostic purposes (exclude or confirm a disease or conditions other than endometrial cancer (*e.g.*, endometrial hyperplasia, endometriosis, ovarian cancer, fibroids, *etc.*)), classification of type of endometrial cancer (*e.g.*, type I versus type II), classification of cell type of endometrial cancer, and prognosis.

In one embodiment, the invention provides for profiles and/or fingerprint patterns having 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, of the biomarkers of Table 1. In one aspect of this embodiment, the level of mRNA corresponding to the biomarkers in the profile is determined for use in diagnosis endometrial cancer and/or an increased likelihood of endometrial cancer. In one aspect of this embodiment, the level of protein corresponding to the biomarkers in the profile is determined for use in diagnosis endometrial cancer and/or an increased likelihood of endometrial cancer. In one aspect of this embodiment, the level of the biomarkers is determined in a sample obtained from uterine fluid. In one aspect of

this embodiment, the level of the biomarkers is determined in a sample obtained from serum, blood, or plasma.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of an ACAA1 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from AP1M2, CGN,

DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including ACAA1 are ACAA1 and AP1M2; ACAA1 and CGN; ACAA1 and DDR1; ACAA1 and EPS8L2; ACAA1 and FASTKD1; ACAA1 and GMIP; ACAA1 and IKBKE; ACAA1 and P2RX4; ACAA1 and P4HB; ACAA1 and PHKG2; ACAA1 and PPFIBP2; ACAA1 and PPP1R16A; ACAA1 and RASSF7; ACAA1 and RNF183; ACAA1 and SIRT6; ACAA1 and TJP3; ACAA1 and EFEMP2; ACAA1 and SOCS2; or ACAA1 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of an AP1M2 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers,

prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including AP1M2 are AP1M2 and ACAA1; AP1M2 and CGN; AP1M2 and DDR1; AP1M2 and EPS8L2; AP1M2 and FASTKD1; AP1M2 and GMIP; AP1M2 and IKBKE; AP1M2 and P2RX4; AP1M2 and P4HB; AP1M2 and PHKG2; AP1M2 and PPFIBP2; AP1M2 and PPP1R16A; AP1M2 and RASSF7; AP1M2 and RNF183; AP1M2 and SIRT6; AP1M2 and TJP3; AP1M2 and EFEMP2; AP1M2 and SOCS2; or AP1M2 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a CGN biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3,

EFEMP2, SOCS2, and DCN. Combinations or subcombinations including CGN are CGN and AP1M2; ACAA1 and CGN; CGN and DDR1; CGN and EPS8L2; CGN and FASTKD1; CGN and GMIP; CGN and IKBKE; CGN and P2RX4; CGN and P4HB; CGN and PHKG2; CGN and PPFIBP2; CGN and PPP1R16A; CGN and RASSF7; CGN and RNF183; CGN and SIRT6; CGN and TJP3; CGN and EFEMP2; CGN and SOCS2; or CGN and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a DDR1 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is DDR1 and P4HB; DDR1 and GMIP; DDR1 and IKBKE; DDR1 and EFEMP2; DDR1 and SOCS2; DDR1, P4HB, and GMIP; DDR1, P4HB, GMIP, and IKBKE; DDR1, P4HB, GMIP, IKBKE and EFEMP2; or DDR1, GMIP, IKBKE, P4HB, and SOCS2. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this

embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of an EPS8L2 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including EPS8L2 are EPS8L2 and AP1M2; EPS8L2 and CGN; EPS8L2 and DDR1; EPS8L2 and EPS8L2; EPS8L2 and FASTKD1; EPS8L2 and GMIP; EPS8L2 and IKBKE; EPS8L2 and P2RX4; EPS8L2 and P4HB; EPS8L2 and PHKG2; EPS8L2 and PPFIBP2; EPS8L2 and PPP1R16A; EPS8L2 and RASSF7; EPS8L2 and RNF183; EPS8L2 and SIRT6; EPS8L2 and TJP3; EPS8L2 and EFEMP2; EPS8L2 and SOCS2; EPS8L2 and ACAA1; or EPS8L2 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a FASTKD1 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment

the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is FASTD1 and P4HB; FASTKD1 and GMIP; FASTKD1 and IKBKE; FASTKD1 and EFEMP2; FASTKD1 and SOCS2; FASTD1 and DDR1; FASTKD1 and SIRT6; FASTKD1 and PHKG2; FASTKD1, P4HB, and GMIP; FASTKD1, P4HB and IKBKE; FASTKD1, P4HB, and EFEMP2; FASTKD1, P4HB, EFEMP2, IKBKE, and GMIP; FASTKD1, P4HB, EFEMP2, SIRT6, DDR1, and GMIP; or FASTKD1, P4HB, EFEMP2, SIRT6, PHKG2, and GMIP. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a GMIP biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of



this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is GMIP and P4HB; FASTKD1 and GMIP; GMIP and IKBKE; GMIP and EFEMP2; GMIP and SOCS2; GMIP and DDR1; GMIP and SIRT6; GMIP and PHKG2; GMIP, P4HB, and IKBKE; GMIP, SOCS2, and IKBKE; GMIP, SOCS2, and P4HB; GMIP, IKBKE, P4HB, and EFEMP2; GMIP, IKBKE, P4HB, and SOCS2; GMIP, P4HB, EFEMP2, IKBKE, and FASTKD1; GMIP, P4HB, EFEMP2, SIRT6, DDR1, and FASTKD1; or GMIP, P4HB, EFEMP2, SIRT6, PHKG2, and FASTKD1. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of an IKBKE biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is IKBKE and P4HB; IKBKE and GMIP; IKBKE and FASTKD1; IKBKE and EFEMP2; IKBKE and

SOCS2; IKBKE and DDR1; IKBKE and SIRT6; IKBKE and PHKG2 ; IKBKE, P4HB, and GMIP; IKBKE, P4HB, and EFEMP2; IKBKE, GMIP, and EFEMP2; IKBKE, P4HB, and SOCS2; IKBKE, GMIP, P4HB, and SOCS2; IKBKE, GMIP, P4HB, and EFEMP2; IKBKE, P4HB, EFEMP2, GMIP, and FASTKD1; or IKBKE, DDR1, GMIP, P4HB, PHKG2, SIRT6, and EFEMP2. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a P2RX4 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including P2RX4 are P2RX4and AP1M2; P2RX4 and CGN; P2RX4 and DDR1; P2RX4 and EPS8L2; P2RX4and FASTKD1; P2RX4 and GMIP; P2RX4 and IKBKE; P2RX4 and P4HB; P2RX4 and PHKG2; P2RX4 and PPFIBP2; P2RX4 and PPP1R16A; P2RX4 and RASSF7; P2RX4 and RNF183; P2RX4 and SIRT6; P2RX4 and TJP3; P2RX4 and EFEMP2; P2RX4 and SOCS2; P2RX4 and ACAA1; or P2RX4 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is

analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a P4HB biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is FASTD1 and P4HB; P4HB and GMIP; P4HB and IKBKE; P4HB and EFEMP2; P4HB and SOCS2; P4HB and DDR1; P4HB and SIRT6; P4HB and PHKG2; P4HB, GMIP, and IKBKE; P4HB, GMIP, and SOCS2; P4HB, GMIP, and EFEMP2; P4HB, IKBKE, GMIP, and SOCS2; P4HB, IKBKE, GMIP, and EFEMP2; P4HB, EFEMP2, IKBKE, GMIP, and FASTKD1; P4HB, EFEMP2, SIRT6, GMIP, DDR1, and FASTKD1; P4HB, EFEMP2, SIRT6, GMIP, PHKG2, and FASTKD1; or DDR1, FASTKD1, GMIP, IKBKE, P4HB, PHKG2, SIRT6, and EFEMP2. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a PHKG2 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is PHKG2 and P4HB; PHKG2 and GMIP; PHKG2 and IKBKE; PHKG2 and EFEMP2; PHKG2 and SOCS2; PHKG2 and DDR1; PHKG2 and SIRT6; FASTKD1 and PHKG2; PHKG2, P4HB, and EFEMP2; PHKG2, P4HB, GMIP; PHKG2, P4HB, IKBKE, and EFEMP2; PHKG2, P4HB, IKBKE, and SOCS2; P4HB, EFEMP2, SIRT6, GMIP, PHKG2, and FASTKD1; or DDR1, FASTKD1, GMIP, IKBKE, P4HB, PHKG2, SIRT6, and EFEMP2. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a PPFIBP2 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers

are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including PPFIBP2 are PPFIBP2 and AP1M2; PPFIBP2 and CGN; PPFIBP2 and DDR1; PPFIBP2 and EPS8L2; PPFIBP2 and FASTKD1; PPFIBP2 and GMIP; PPFIBP2 and IKBKE; PPFIBP2 and P2RX4; PPFIBP2 and P4HB; PPFIBP2 and PHKG2; PPFIBP2 and PPP1R16A; PPFIBP2 and RASSF7; PPFIBP2 and RNF183; PPFIBP2 and SIRT6; PPFIBP2 and TJP3; PPFIBP2 and EFEMP2; PPFIBP2 and SOCS2; PPFIBP2 and ACAA1; or PPFIBP2 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a PPP1R16A biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including PPP1R16A are PPP1R16A and AP1M2; PPP1R16A and CGN; PPP1R16A

and DDR1; PPP1R16A and EPS8L2; PPP1R16A and FASTKD1; PPP1R16A and GMIP; PPP1R16A and IKBKE; PPP1R16A and P2RX4; PPP1R16A and P4HB; PPP1R16A and PHKG2; PPFIBP2 and PPP1R16A; PPP1R16A and RASSF7; PPP1R16A and RNF183; PPP1R16A and SIRT6; PPP1R16A and TJP3; PPP1R16A and EFEMP2; PPP1R16A and SOCS2; PPP1R16A and ACAA1; or PPP1R16A and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a RASSF7 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including RASSF7 are RASSF7 and AP1M2; RASSF7 and CGN; RASSF7 and DDR1; RASSF7 and EPS8L2; RASSF7 and FASTKD1; RASSF7 and GMIP; RASSF7 and IKBKE; RASSF7 and P2RX4; RASSF7 and P4HB; RASSF7 and PHKG2; RASSF7 and PPP1R16A; RASSF7 and RNF183; RASSF7 and SIRT6; RASSF7 and TJP3; RASSF7 and EFEMP2; RASSF7 and SOCS2; RASSF7 and ACAA1; or RASSF7 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or

suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a RNF183 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including RNF183 are RNF183 and AP1M2; RNF183 and CGN; RNF183 and DDR1; RNF183 and EPS8L2; RNF183 and FASTKD1; RNF183 and GMIP; RNF183 and IKBKE; RNF183 and P2RX4; RNF183 and P4HB; RNF183 and PHKG2; RNF183 and PPP1R16A; RASSF7 and RNF183; RNF183 and SIRT6; RNF183 and TJP3; RNF183 and EFEMP2; RNF183 and SOCS2; RNF183 and ACAA1; or RNF183 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a SIRT6 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one

or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is SIRT6 and P4HB; SIRT6 and GMIP; SIRT6 and IKBKE; SIRT6 and EFEMP2; SIRT6 and SOCS2; SIRT6 and DDR1; FASTKD1 and SIRT6; SIRT6 and PHKG2; SIRT6, P4HB, and EFEMP2; SIRT6, P4HB, and IKBKE; SIRT6, IKBKE, and EFEMP2; SIRT6, P4HB, and SOCS2; SIRT6, P4HB, IKBKE, and GMIP; SIRT6, P4HB, EFEMP2, GMIP, DDR1, and FASTKD1; SIRT6, P4HB, EFEMP2, GMIP, PHKG2, and FASTKD1; or SIRT6, P4HB, EFEMP2, GMIP, IKBKE, PHKG2, DDR1, and FASTKD1. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a TJP3 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of



this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, EFEMP2, SOCS2, and DCN. Combinations or subcombinations including TJP3 are TJP3 and AP1M2; TJP3 and CGN; TJP3 and DDR1; TJP3 and EPS8L2; TJP3 and FASTKD1; TJP3 and GMIP; TJP3 and IKBKE; TJP3 and P2RX4; TJP3 and P4HB; TJP3 and PHKG2; TJP3 and PPP1R16A; TJP3 and RNF183; TJP3 and SIRT6; TJP3 and RASSF7; TJP3 and EFEMP2; TJP3 and SOCS2; TJP3 and ACAA1; or TJP3 and DCN. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of an EFEMP2 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, SOCS2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is EFEMP2 and P4HB; EFEMP2 and GMIP; EFEMP2 and IKBKE; FASTKD1 and EFEMP2; EFEMP2 and SOCS2; EFEMP2 and DDR1; EFEMP2 and SIRT6; EFEMP2 and PHKG2; EFEMP2, P4HB, and IKBKE; EFEMP2, IKBKE, and GMIP; EFEMP2, IKBKE, and FASTKD1; EFEMP2, GMIP, and DDR1;

EFEMP2, SIRT6, and FASTKD1; EFEMP2, IKBKE, GMIP, and P4HB; EFEMP2, P4HB, IKBKE, GMIP, and FASTKD1; EFEMP2, P4HB, SIRT6, DDR1, GMIP, and FASTKD1; EFEMP2, P4HB, SIRT6, PHKG2, GMIP, and FASTKD1; or EFEMP2, P4HB, IKBKE, GMIP, DDR1, PHKG2, SIRT6, and FASTKD1; In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a SOCS2 biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, and DCN. A preferred combination or subcombination useful for detecting endometrial cancer or an increased likelihood of endometrial cancer is SOCS2 and P4HB; SOCS2 and GMIP; SOCS2 and IKBKE; SOCS2 and EFEMP2; FASTKD1 and SOCS2; SOCS2 and DDR1; SOCS2 and SIRT6; SOCS2 and PHKG2; SOCS2, P4HB, and IKBKE; SOCS2, GMIP, and P4HB; SOCS2, P4HB, and IKBKE; GMIP, P4HB, IKBKE, and SOCS2; SOCS2, GMIP, IKBKE, P4HB, and DDR1; or SOCS2, DDR1, FASTKD1, GMIP, IKBKE, P4HB, PHKG2, SIRT6, and EFEMP2. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or

suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In one embodiment, the invention provides a method for diagnosing endometrial cancer comprising determining the level of a DCN biomarker in combination with the level of one or more biomarkers. In a specific aspect of this embodiment the one or more biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classify endometrial cancer and auxiliary biomarkers for detecting endometrial cancer. In one aspect of this embodiment, the one or more biomarkers are chosen from differential diagnosis biomarkers, biomarkers useful for detecting endometrial cancer, and biomarkers useful for classifying endometrial cancer. In one aspect of this embodiment, the one or more biomarkers useful for detecting endometrial cancer are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, and SOCS2. Combinations or subcombinations including DCN are DCN and AP1M2; DCN and CGN; DCN and DDR1; DCN and EPS8L2; DCN and FASTKD1; DCN and GMIP; DCN and IKBKE; DCN and P2RX4; DCN and P4HB; DCN and PHKG2; DCN and PPP1R16A; DCN and RNF183; DCN and SIRT6; DCN and RASSF7; DCN and EFEMP2; DCN and SOCS2; or DCN and ACAA1. In one aspect of this embodiment, the level(s) of gene expression of the biomarker is determined. In another aspect of this embodiment, the level(s) of protein expression is determined. In one aspect of this embodiment, a tumor or suspected sample is analyzed. In another aspect a fluid sample is analyzed. In another aspect of this embodiment, a sample obtained from uterine fluid is analyzed. In yet another aspect of this embodiment, a serum or blood samples is analyzed. In one aspect, the sample that is analyzed is obtained from a cell.

In a preferred aspect of the in vitro diagnostic method of the invention the levels of a combination of markers is detected where said combination comprises IKBKE and P4HB; IKBKE and SOCS2; P4HB and SOCS2; GMIP and IKBKE; GMIP and P4HB; GMIP and SOCS2; GMIP, SOCS2, and IKBKE; GMIP, SOCS2, and P4HB; GMIP,

IKBKE, and P4HB; IKBKE,P4HB, and SOCS2; GMIP, IKBKE, P4HB, and SOCS2; GMIP, SOCS2, IKBKE, and EPS8L2; GMIP, SOCS2, P4HB, and EPS8L2; GMIP, IKBKE, P4HB, and EPS8L2; IKBKE, P4HB, SOCS2, and EPS8L2; GMIP, IKBKE, P4HB, SOCS2, and DDR1; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, and PPP1R16A; GMIP, IKBKE, P4HB, SOCS2, PHKG2, and RASSF7; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, and DDR1; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, PPP1R16A, and DDR1; DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, RASSF7, SIRT6, TJP3, and SOCS2; or DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, RASSF7, SIRT6, TJP3, RNF183 and SOCS2.

In another preferred aspect of the in vitro diagnostic method of the invention a the levels of a combination of markers is detected where said combination comprises GMIP, IKBKE, P4HB, SOCS2 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2 and DDR1; GMIP, IKBKE, P4HB, SOCS2 and PHKG2; GMIP, IKBKE, P4HB, SOCS2 and SIRT6; GMIP, IKBKE, P4HB, SOCS2 and ACAA1; GMIP, IKBKE, P4HB, SOCS2 and EFEMP2; GMIP, IKBKE, P4HB, SOCS2 and EPS8L2; GMIP, IKBKE, P4HB, SOCS2 and P2RX4; GMIP, IKBKE, P4HB, SOCS2 and PPFIBP2; GMIP, IKBKE, P4HB, SOCS2 and PPP1R16A; GMIP, IKBKE, P4HB, SOCS2, ACAA1 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2, PHKG2 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2, SIRT6 and FASTKD1; ACAA1, AP1M2, EPS8L2, IKBKE, P2RX4, P4HB, PPFIBP2, PPP1R16A, SIRT6, and EFEMP2; GMIP, IKBKE, P4HB, and EFEMP2; DDR1, FASTKD1, PHKG2, SIRT6, SOCS2, GMIP, IKBKE, P4HB, and EFEMP2; DDR1, FASTKD1, PHKG2, SIRT6, GMIP, IKBKE, P4HB, and EFEMP2; or P4HB, EFEMP2, IKBKE, GMIP, and FASTKD1.

In yet another preferred aspect of the in vitro diagnostic method of the invention the levels of a combination of markers is detected where said combination comprises GMIP, IKBKE, P4HB, EFEMP2 and FASTKD1; GMIP, IKBKE, P4HB, EFEMP2 and DDR1; GMIP, IKBKE, P4HB, EFEMP2 and PHKG2; GMIP, IKBKE, P4HB, EFEMP2 and SIRT6; GMIP, IKBKE, P4HB, EFEMP2 and ACAA1; GMIP, IKBKE, P4HB, SOCS2 and EFEMP2; GMIP, IKBKE, P4HB, EFEMP2 and EPS8L2; GMIP, IKBKE, P4HB, EFEMP2 and P2RX4; GMIP, IKBKE, P4HB, EFEMP2 and PPFIBP2; GMIP, IKBKE, P4HB, EFEMP2 and PPP1R16A; GMIP, IKBKE, P4HB, EFEMP2,

ACAA1 and FASTKD1; GMIP, IKBKE, P4HB, EFEMP2, PHKG2 and FASTKD1; or GMIP, IKBKE, P4HB, EFEMP2, SIRT6 and FASTKD1.

#### Auxiliary Biomarkers

“Auxiliary biomarkers” refer to biomarkers that can be used in conjunction with the one or more biomarkers of Table 1. The auxiliary biomarkers can be used in the methods of the invention to provide further characterization of a disease or condition a patient may have.

Differential diagnosis biomarkers are useful for distinguishing between diseases that may present with similar clinical symptoms. For example, a patient may have symptoms of endometrial cancer (*e.g.*, vaginal bleeding and/or pelvic pain) but these symptoms can also be caused by different diseases (*e.g.*, ovarian cancer). Therefore, the differential diagnosis biomarkers provide information for characterization a disease. Examples of diseases that may present similar symptoms as endometrial cancer include uterine fibroids, endometriosis, endometrial hyperplasia, uterine sarcoma - another type of uterus cancer, uterine leiomyomas, endometrial polyp (type of polyp), cervical cancer, atrophic endometrium, adenomyosis, atrophic vaginitis, ovarian tumour, leiomyosarcoma, and endometrial proliferation.

According to the inventors' finding that the level of biomarkers in primary endometrial cancer tissue can be correlated to their levels in uterine fluid, it is contemplated that uterine fluid samples can be used for differential diagnosis of conditions other than endometrial cancer. Thus, in one aspect, the invention provides a method for the differential diagnosis of endometrial cancer by obtaining a uterine fluid sample from a patient and determining the level of one or more biomarkers that are capable of distinguishing endometrial cancer from non-endometrial cancer. Differential diagnosis biomarkers for endometriosis are useful for distinguishing endometriosis from endometrial cancer. Differential diagnosis biomarkers for ovarian cancer are useful for distinguishing ovarian cancer from endometrial cancer. Examples of biomarkers useful for distinguishing endometrial cancer from ovarian cancer include, but are not limited to, those described in Yurkovetsky *et al.* (*Gyn. Onc.* (2007) 107:58-65) where they reported a five-

biomarker panel of prolactin, GH, eotaxin, E-selectin, and TSH for discriminating endometrial cancer from ovarian and breast cancer.

A number of endometrial cancer biomarkers have been identified. CA 125 correlates with tumor size and stage and is an independent predictor of the extrauterine spread. Serum markers for the detection of uterine cancer have been reported in the literature.

Prognosis biomarkers: Elevated levels of CA 125, CA 15-3, and CA 19-9 are associated with shorter survival time. They found serum CA 125 CA 15-3 and CEA are higher in patients with Stage III disease as compared to stage I. Another group of prognostic markers include estrogen receptor, progesterone receptor, and HER2.

Biomarkers for classifying endometrial cancer include those for estimating stage of the cancer, cell-type, and/or type of endometrial cancer (*e.g.*, type I versus type II). Examples of biomarkers for classifying endometrial cancer include, but are not limited to, those described in Sugiyama *et al.* (2003) *Clin. Can. Res.* 9:5589-5600. Genes showing higher expression in type I as compared to type II include MMP11, RHOG, and platelet-derived growth factor B subunit precursor, STAT2, octamer-binding transcription factor 1, and GATA-6, growth factor VEGF-C precursor, caspase (caspase 1/IL-1  $\beta$  converting enzyme). Genes showing higher expression in type II as compared to type I included PIRIN, EGR1, STAT1, IFN regulatory factor 1, and KRAS. Konecny *et al.* ((2009) *British Journal of Cancer* 100, 89–95) report that the rate HER2 gene amplification as measured by fluorescence in situ hybridization was greater in type II cancers whereas EGFR expression as measured by IHC techniques was significantly lower in type II cancers. Deng *et al.* ((2005) *Clin. Can. Res.* vol. 11, no 23:8258-8264) report that EIG121 is a marker for type I estrogen associated cancers. Markers for classifying endometrial cancer can also be used to distinguish different histological types of endometrial cancer like serous and endometrioid cancers. Risinger *et al.* ((2003) *Canc. Res.* 63:6-11) identified biomarkers that could distinguish papillary serous cancers from endometrioid cancers. For example AGR2, TFF3, DUSP6, IGF2, FOLR1, and UCHL1 were found to be differentially expressed between papillary serous and endometrioid cancers as found by microarray and validated by RT-PCR. AGR2, TFF3, DUSP6 were found to

be upregulated in endometrioid type cancers whereas IGF2, FOLR1 and UCHL1 were found to be upregulated in papillary serous cancers.

According to the inventor's finding that the level of biomarkers in primary endometrial cancer tissue can be correlated to their levels in uterine fluid, it is contemplated that uterine fluid samples can be used to classify the type of endometrial cancer. Classifying the type of endometrial cancer can refer to distinguishing type I and type II cancers. Classifying the type of endometrial cancer can also refer to determining the histological type and/or sub-type of endometrial cancer. Thus, in one aspect, the invention provides a method for classifying an endometrial cancer by obtaining a uterine fluid sample from a patient and determining the level of one or more biomarkers that are capable of classifying an endometrial cancer.

"Auxiliary biomarkers for detecting endometrial cancer" refer to biomarkers that can be used in addition to the biomarkers of Table 1 for the diagnosis of endometrial cancer and/or an increased risk of having endometrial cancer: Yurkovetsky *et al.* (*Gyn. Onc.* (2007) 107:58-65) identified that prolactin is a serum biomarker with sensitivity and specificity for endometrial cancer. Yurkovetsky *et al.* found that prolactin, GH, eotaxin, E-selectin, and TSH were useful markers for diagnosing endometrial cancer.

In some aspects of these embodiments, one or more auxiliary biomarkers are examined for alterations in a sample from a patient suspected of having endometrial cancer. In a specific aspect, the auxiliary biomarkers are chosen from serum biomarkers. In a more specific aspect the serum biomarkers are one or more proteins chosen from CA 125, CA 15-3, CA 19-9, CEA, AFP, CA 72-4, VEGF, bFGF, IGFBPI, HGF, ErbB2, EGFR, TGF  $\alpha$ , Fas, FasL, Cyfra 21-1, MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13, tPAI, sICAM, sVCAM, sE-selectin, adiponectin, resistin, IL-6, IL-8, TNF  $\alpha$ , TNFR I, G-CSF, CD40L, IL-2R, IP-10, MCP-1, MIP-1 $\alpha$ , MIP-1 $\beta$ , MIF, eotaxin, RANTES, FSH, LH, TSH, ACTH, Prolactin, GH,  $\beta$ HCG, hK8, hK10, active PAI-1, ULBP-1, ULBP-2, ULBP-3, MICA, angiostatin, SCC, serum amyloid A, TTR, S100, mesothelin, and myeloperoxidase (MPO). In a more specific aspect, the serum biomarkers are chosen from prolactin, GH, eotaxin, e-selectin and FSH. In an even more specific aspect, the serum

biomarker is prolactin. In some aspects, the auxiliary biomarker(s) can be examined in uterine aspirates (e.g., mRNA level and/or protein levels).

### Samples

The invention, in some embodiments, relates to characterizing one or more biomarkers of Table 1, from a sample from a patient suspected of having endometrial cancer or desiring screening for cancer. Examples of such samples that can be used in the invention are fluid, tissue samples, and/or cells. Depending on the specific marker, the methods used for characterizing the biomarkers of the invention can include *e.g.*, examining the DNA copy number of the gene corresponding to the biomarker, detecting the protein related to the biomarker, determining the mRNA expression levels of the biomarker, *etc.* The invention is useful for a number of applications including diagnosis, prognosis, staging, predicting response to therapy. The inventors have found evidence of differential expression of the biomarkers of Table 1 in a number of different samples including mRNA in primary tumor, protein in primary tumor, and mRNA in aspirates, and protein in aspirates. The biomarkers of Table 1 include those that are overexpressed in samples from endometrial cancer patients as compared to normal levels. Additionally some of the biomarkers of Table 1 are underexpressed in samples from endometrial cancer patients as compared to normal levels

The invention, in some embodiments, relates to characterizing one or more of the biomarkers of Table 1, from a patient sample (*e.g.*, tumor, cancer cell, sample suspected of being cancer, body fluid (*e.g.*, uterine fluid), blood, serum, plasma, and vaginal blood/discharge) and/or from a "normal" cell, from an individual (or alternatively a control value can be used in lieu of the normal value from the cell).

In one aspect, the sample to be analyzed is obtained from a patient that has risk factors for endometrial cancer. Risk factors for endometrial cancer include, but are not limited to, having Lynch Syndrome, being genetically related to a person having Lynch Syndrome, obese, taking estrogen-alone hormone replacement therapy, and prior treatment with tamoxifen.



In one aspect of this embodiment, the sample is analyzed is a uterine fluid sample. In one aspect, the sample is that is used is obtained by using a soft, straw-like device (pipelle) to suction off a small sample of lining from the uterus. In one aspect, the sample is obtained by using a sharp-edged tool called a curette by scraping a small sample and collect it with a syringe or suction (*e.g.*, dilation and curettage). In one aspect, the sample is obtained by using an electronic suction device (*e.g.*, Vabra aspiration). In one aspect, the sample is obtained by using a spray of liquid (jet irrigation) to wash off some of the tissue that lines the uterus. In some aspects, a brush may be used to remove some of the lining before the washing is done.

In one embodiment, the sample for analyzing the biomarkers is obtained using a syringe or pipelle type device. In one embodiment, the device for collection of the uterine fluid sample from an internal cavity (*e.g.*, uterus) of a patient, comprises a barrel having an opening at one end thereof, a plunger operable axially within the barrel, the barrel and the plunger defining a fluid chamber having a volume which varies on axial movement of the plunger within the barrel, and a hollow, elongate tube extending from the fluid chamber through the opening in the barrel, the tube being in operative engagement with the plunger for axial movement to extend and retract the tube within respect to the barrel on axial movement of the plunger, and the tube being in fluid communication with the fluid chamber to provide a fluid flow path to and from the fluid chamber through the hollow tube. In one aspect of this embodiment, after the sample is obtained using the device, it is stored in an agent that preserves the integrity of the biomarkers of interest. For example, when the biomarker being analyzed is a nucleic acid like RNA, the sample can be stored in an agent that prevents degradation of RNA molecules in the sample, or if the biomarker is a protein the sample can be stored *e.g.*, in an agent that preserves protein. Example of agents that prevent degradation of RNA molecules in a sample are RNase inhibitors (*e.g.*, RNeasy from Qiagen, SUPERase•In™ from Ambion or ScriptGuard™ RNase Inhibitor from epicenter biotechnologies) or molecules that precipitate RNA out of biological solutions (*e.g.*, triphenylmethane dyes (*e.g.*, methyl green, crystal violet, and pararosaniline), cresyl violet, polyamines, and cobalt ions). Example of agents that prevent the degradation of protein is protease inhibitors (*e.g.*, PMSF (phenylmethanesulfonyl fluoride, Complete protease inhibitor cocktail from Roche, or Pepstatin) or agents that fix tissues (formalin).

Thus the invention provides in one embodiment, an in vitro diagnostic method for endometrial cancer comprising obtaining a uterine fluid aspirate sample from a patient having a symptom or risk factor for endometrial cancer and determining the level of from 1 to 100 biomarkers markers that are differentially expressed in endometrial cancer as compared to control values representative of individuals not affected by endometrial cancer, wherein (1) if the levels of 1-100 biomarkers are upregulated in the endometrial aspirate sample in the patient and in the control value then the patient has an increased likelihood of having endometrial cancer and wherein (2) if the level of the 1-100 biomarkers are downregulated in the aspirate sample and then the patient has an increased likelihood of having endometrial cancer. The biomarkers of this aspect can be any biomarkers that are differentially represented in endometrial cancer patient samples compared to samples from patients not affected with endometrial cancer and are useful for diagnosis of endometrial cancer or an increased likelihood of endometrial cancer. Preferred biomarkers are the 1-20 described herein in Table 1.

#### Methods of Detecting Biomarkers

The invention relates to the identification of biomarkers that are useful for diagnosing endometrial cancer. The invention provides methods for detecting one or more of the biomarkers of Table 1 for diagnosing endometrial cancer. The method of the invention can be used to detect one or more proteins corresponding to the biomarkers of Table 1 for diagnosing endometrial cancer. The method of the invention can be used to detect one or more mRNA corresponding to the biomarkers of Table 1 for diagnosing endometrial cancer. The biomarkers can be detected in a sample obtained from a patient *e.g.*, a sample obtained from uterine tissue, uterine fluid, or blood.

In some embodiments, the method of the invention involves obtaining a sample and determining the level of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, of the biomarkers of Table 1 in the sample. In a specific aspect, the method involves determining the level of 2 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 3 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 4

or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 5 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 6 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 7 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 8 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 9 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 10 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 11 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 12 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 13 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 14 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 15 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of from 2 to 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of from 3 to 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of from 3 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of from 4 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of from 5 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of from 10 to 17 of the biomarkers listed in Table 1. In one aspect of this embodiment, the method involves determining the level of less than 500 different biomarkers. In one aspect of this embodiment, the method involves determining the level of less than 250 different biomarkers. In one aspect of this embodiment, the method involves determining the level of less than 100 different biomarkers. In one aspect of this embodiment, the method involves determining the level of less than 50 different biomarkers. Increased levels of one or more biomarkers of Table 1 that are overexpressed and/or decreased levels of one or more biomarkers of Table 1 that are underexpressed indicate that there is an increased likelihood of endometrial cancer.

It is understood that in some aspects of this embodiment, the biomarkers analyzed include more than those listed in Table 1.

In some aspects of these embodiments, the method involves obtaining a sample and determining the level of mRNA of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, of the biomarkers of Table 1 in the sample. In a specific aspect, the method involves determining the level of mRNA of 2 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 3 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 4 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 5 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 6 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 7 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 8 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 9 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 10 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 11 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 12 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 13 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 14 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 15 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of from 2 to 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of from 3 to 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of from 3 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of from 4 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of from 5 to 17 of the biomarkers

listed in Table 1. In a specific aspect, the method involves determining the level of mRNA of from 10 to 20 of the biomarkers listed in Table 1. In one aspect of this embodiment, the method involves determining the level of mRNA of less than 500 different biomarkers. In one aspect of this embodiment, the method involves determining the level of mRNA of less than 250 different biomarkers. In one aspect of this embodiment, the method involves determining the level of mRNA of less than 100 different biomarkers. In one aspect of this embodiment, the method involves determining the level of mRNA of less than 50 different biomarkers. Increased levels of one or more mRNAs corresponding to the biomarkers of Table 1 that are overexpressed and/or decreased levels of one or more biomarkers of Table 1 that are underexpressed indicate that there is an increased likelihood of endometrial cancer. It is understood that in some aspects of this embodiment, the biomarkers analyzed include more than those listed in Table 1.

In some aspects of these embodiments, the method involves obtaining a sample and determining the protein level of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, of the biomarkers of Table 1 in the sample. In a specific aspect, the method involves determining the protein level of 2 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 3 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 4 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 5 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 6 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 7 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 8 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 9 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 10 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 11 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 12 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 13 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining

the protein level of 14 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 15 or more biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of from 2 to 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of from 3 to 20 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of from 3 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of from 4 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of from 5 to 17 of the biomarkers listed in Table 1. In a specific aspect, the method involves determining the protein level of from 10 to 17 of the biomarkers listed in Table 1. In one aspect of this embodiment, the method involves determining the protein level of less than 500 different biomarkers. In one aspect of this embodiment, the method involves determining the protein level of less than 250 different biomarkers. In one aspect of this embodiment, the method involves determining the protein level of less than 100 different biomarkers. In one aspect of this embodiment, the method involves determining the protein level of less than 50 different biomarkers. In one aspect of this embodiment, the method involves determining the protein level of from 1 to 10 different biomarkers. Increased levels of one or more proteins corresponding to the biomarkers of Table 1 indicate that there is an increased likelihood of endometrial cancer. It is understood that in some aspects of this embodiment, the biomarkers analyzed include more than those listed in Table 1.

In one embodiment, the invention provides a method for detecting one or more protein biomarkers in serum, blood, and/or plasma. In a specific aspect of this embodiment, the one or more biomarkers are chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN. In a more specific aspect, the one or more biomarkers are chosen from IKBKE, P4HB, SOCS2, GMIP, DDR1, EPS8L2, PPP1R16A, P2RX4, PHKG2, RASSF7, SIRT6, TJP3, AP1M2, RNF183, and DCN. In another specific aspect of this embodiment, the method comprises detecting the level of IKBKE. In another specific aspect of

this embodiment, the method comprises detecting the level of P4HB. In another specific aspect of this embodiment, the method comprises detecting the level of SOCS2. In another specific aspect of this embodiment, the method comprises detecting the level of GMIP. In another specific aspect of this embodiment, the method comprises detecting the level of AP1M2. In another specific aspect of this embodiment, the method comprises detecting the level of EPS8L2. In another specific aspect of this embodiment, the method comprises detecting the level of DDR1. In another specific aspect of this embodiment, the method comprises detecting the level of CGN. In another specific aspect of this embodiment, the method comprises detecting the level of TJP3.

In some aspects of these embodiments, the method involves determining the level of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, or 50 or more of biomarkers in addition to one or more of those listed in Table 1. These markers can be those whose expression levels are known to be altered in patients having endometrial cancer. Alternatively, the additional biomarkers can be used for differential diagnosis of other diseases (*e.g.*, endometriosis, ovarian cancer, and fibroids), for classifying the type of cancer, prognostic information and/or for providing information for selecting a therapy. In a specific aspect of this embodiment, the additional biomarkers are analyzed in uterine fluid samples.

In a specific aspect of the invention, the one or more biomarkers listed in Table 1 are detected on an array having different probes on the array which are oligonucleotides having from about 5 to 200 bases in length. In another specific aspect, each of the different probes on the array is an oligonucleotide having from about 15 to 200, 15 to 150, 15 to 100, 15 to 75, 15 to 60, or 20 to 55 bases in length. In one aspect, the array has probes to 2 or more biomarkers listed in Table 1. In one aspect, the array has probes to 3 or more biomarkers listed in Table 1. In one aspect, the array has probes to 4 or more biomarkers listed in Table 1. In one aspect, the array has probes to 5 or more biomarkers listed in Table 1. In one aspect, the array has probes to 6 or more biomarkers listed in Table 1. In one aspect, the array has probes to 7 or more biomarkers listed in Table 1. In one aspect, the array has probes to less than 1000

different genes. In one aspect, the array has probes to less than 500 different genes. In one aspect, the array has probes to less than 100 different genes.

In some aspects of these embodiments, the copy number of the one or more biomarkers listed in Table 1 is determined. In another aspect of this embodiment, the copy number profile of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the biomarkers of Table 1 (or loci corresponding to the biomarker) are determined for detecting endometrial cancer.

In one aspect, the invention provides primers that can hybridize to a nucleic acid corresponding to a biomarker listed in Table 1 and be used to amplify a nucleic acid or fragment thereof corresponding to said biomarker for diagnosing endometrial cancer according to the methods of the invention. In a more specific aspect, the primers are designed to amplify one or more exons of the biomarker. In another aspect, the primers are designed to amplify a fragment of one or more exons of the biomarker. In one aspect, the primers are suitable for RT-PCR analysis. In one aspect, the method of the invention involves the use of primers to amplify a nucleic acid corresponding to a biomarker of Table 1, and detecting the amplification product with a probe to the amplification product. In another aspect, the method of the invention involves the use of primers to amplify a nucleic acid corresponding to a biomarker of Table 1, and detecting the amplification product with a dye that allows for quantification of the amplification product.

In one aspect, the invention provides probes to the biomarkers of Table 1 for detecting a nucleic acid or fragment thereof corresponding to the biomarker. The probes can be used in the methods of the invention *e.g.*, for diagnosing endometrial cancer. In a specific aspect, the probe is for the biomarker mRNA or a nucleic acid, is obtained from the mRNA corresponding to the biomarker. In a specific aspect, the probe corresponds to two contiguous exons of the biomarker of Table 1, (or fragments of two or more contiguous exons). In a specific aspect, the probe corresponds to an exon of the biomarker or a fragment thereof. In a specific aspect, the probe corresponds to at least a portion of the promoter region of the biomarker and at least a portion of exon 1 of the biomarker.



In one aspect of the invention, a multiplex PCR assay is used to assess the levels of from 2 to 20 of the biomarkers of Table 1 to detect the presence or absence of endometrial cancer. In a more specific aspect, the levels of from 3 to 20 biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 4 to 20 biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 5 to 20 biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 6 to 20 biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 7 to 20 biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 8 to 20 or more biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 9 to 20 biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 10 to 20 or more biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 15 to 20 biomarkers of Table 1 are assessed by multiplex PCR. In a more specific aspect, the levels of from 20 of the biomarkers of Table 1 are assessed by multiplex PCR.

#### Quantitative

#### PCR

In some embodiments, the invention relies on quantitative PCR to determine the level of one or more biomarkers of Table 1. In a specific aspect the quantitative PCR method is quantitative RT-PCR. The methods can be semi-quantitative or fully quantitative.

The methods of the invention for detecting the biomarkers of the invention can comprise competitive quantitative PCR or real-time quantitative PCR which both estimate target gene concentration in a sample by comparison with standard curves constructed from amplifications of serial dilutions of standard DNA. Quantitative PCR or real-time quantitative PCR differ substantially in how the standard curves are generated. In competitive QPCR, an internal competitor DNA is added at a known concentration to both serially diluted standard samples and unknown (*e.g.*, obtained from a patient) samples. After coamplification, ratios of the internal competitor and target PCR products are calculated for both standard dilutions and unknown samples, and a standard curve is constructed that plots competitor-target PCR product ratios against the initial target DNA concentration of the standard dilutions. Given equal

amplification efficiency of competitor and target DNA, the concentration of the latter in patient samples can be extrapolated from this standard curve.

In real-time QPCR, the accumulation of amplification product is measured continuously in both standard dilutions of target DNA and samples containing unknown amounts of target DNA. A standard curve is constructed by correlating initial template concentration in the standard samples with the number of PCR cycles ( $C_t$ ) necessary to produce a specific threshold concentration of product. In the test samples, target PCR product accumulation is measured after the same  $C_t$ , which allows interpolation of target DNA concentration from the standard curve. Although real-time QPCR permits more rapid and facile measurement of target DNA during routine analyses, competitive QPCR remains an important alternative for target quantification in environmental samples. The coamplification of a known amount of competitor DNA with target DNA is an intuitive way to correct for sample-to-sample variation of amplification efficiency due to the presence of inhibitory substrates and large amounts of background DNA that are obviously absent from the standard dilutions.

Another type of QPCR is applied quantitatively PCR. Often termed "relative quantitative PCR," this method determines the relative concentrations of specific nucleic acids. In the context of the present invention, RT-PCR is performed on mRNA species isolated from patients. By determining that the concentration of a specific mRNA species, it can be determined if the gene encoding the specific mRNA species is differentially expressed.

In one embodiment, the invention provides a method comprising, obtaining a test sample from cells, tissue, or fluid of a patient; detecting the level of one or more of the biomarkers of Table 1 and comparing the level of the biomarker(s) in the sample to the level expected for a normal sample (or control value).

In one embodiment, the invention provides a method comprising, obtaining a suspected tumor sample from a patient; detecting the level of one or more biomarkers listed in Table 1 and comparing the level of biomarker(s) in the sample to the level expected for a normal unaffected sample (or control value).

In one embodiment, the invention provides a method comprising, obtaining a sample from a patient comprising a cell; detecting the level of one or more of the biomarkers of Table 1 in said cell and comparing the level of the biomarker(s) in the cell to the level expected for a normal unaffected cell (or control value).

In one embodiment, the invention provides a method comprising, obtaining a test sample from a fluid of a patient; detecting the level of one or more of the biomarkers of Table 1 and comparing the level of the biomarker(s) in the sample to the level expected for a normal unaffected sample. In one aspect of this embodiment, the fluid is uterine fluid obtained by aspiration. In one aspect of this embodiment, the fluid is uterine fluid obtained by aspiration with a cornier pipelle. In one aspect of this embodiment, the fluid is uterine fluid. In another aspect of this embodiment, the fluid is vaginal discharge. In one embodiment, the invention provides a method comprising, obtaining a test sample from a blood or serum sample from a patient; and detecting the level of one or more of the biomarkers of Table 1 and comparing the level of the biomarker(s) in the sample to the level expected for a normal unaffected sample.

In one embodiment, the invention provides a method comprising, obtaining a test sample from the urine of a patient; detecting the level of one or more of the biomarkers of Table 1 and comparing the level of the biomarkers in the urine to the level expected for a control value.

In one embodiment, the invention provides a method comprising, obtaining a test sample from the uterus of a patient using a brush; and detecting the level of one or more of the biomarkers of Table 1 and comparing the level of the biomarkers in the sample to the level expected for a normal sample.

The presence of increased levels of one or more of the biomarkers of Table 1 can indicate endometrial cancer or a precancerous condition in the tissue *e.g.*, endometrial hyperplasia. In one aspect of this embodiment, the method involves identifying a patient in need of analysis of one or more biomarkers of Table 1.

In another aspect of this embodiment, the present invention provides methods for diagnosing or predicting a endometrial cancer. The method of this aspect can comprise (1) obtaining a test sample from cells, tissue, and/or fluid (2) obtaining a control sample from cells, tissue, or fluid that is normal, or obtaining a normal control value, and (3) detecting or measuring in both the test sample and the control sample the level of one or more mRNA transcripts corresponding to one or more of the biomarkers of Table 1. If the level of the one or more transcripts is higher in the test sample than that in the control sample, this indicates endometrial cancer (and/or and increased risk of having endometrial cancer) or a precancerous condition in the test sample cells or tissue. In another aspect the control sample may be obtained from a different individual or be a normalized value based on baseline data obtained from a population. In one aspect of this embodiment, the method involves identifying a patient in need of analysis of one or more of the biomarkers of Table 1. In one aspect, the patient in need of analysis of one or more of the biomarkers of Table 1 is one that is at risk of having endometrial cancer, is suspected of having endometrial cancer, or and/or is undergoing screening.

In yet another aspect of this embodiment, the method comprises, obtaining a test sample from cells, tissue, or fluid; detecting the number of DNA copies of one or more of the biomarkers of Table 1 (*e.g.*, per cell) in the sample; and comparing the number of DNA copies detected (for example, quantitatively and/or qualitatively) in the sample to a control sample or a known value (or a control value), thereby determining whether the copy number of the biomarker(s) is amplified in the test sample. In one aspect of this embodiment, the method involves identifying a patient in need of analysis of one or more of the biomarkers of Table 1. In one aspect, the patient in need of analysis of one or more of the biomarkers of Table 1 is one that is at risk of having endometrial cancer, is suspected of having endometrial cancer, or and/or is undergoing screening.

In yet another aspect of this embodiment, the method comprises (1) obtaining a test sample from cells, tissue, or fluid; contacting the sample with an antibody to a protein or fragment thereof corresponding to one or more of the biomarkers of Table 1, and detecting in the test sample, the level of the biomarker(s), wherein an increased level the biomarker(s), as compared to a control value indicates the patient

may have a precancerous or a cancerous condition. In another aspect, the control value may be obtained from a different individual or be a normalized value based on baseline data obtained from a population. Alternatively, a given level of a biomarker, representative of the endometrial cancer-free population, that has been previously established based on measurements from normal, endometrial cancer-free patients, can be used as a control value. A control data point from a reference database, based on data obtained from control samples representative of an endometrial cancer-free population, also can be used as a control value. In one aspect of this embodiment, the method involves identifying a patient in need of analysis of one or more of the biomarkers of Table 1. In one aspect, the patient in need of analysis of the biomarker(s) is one that is at risk of having endometrial cancer, is suspected of having endometrial cancer, or and/or is undergoing screening.

In some embodiments, the method of the invention involves comparing the expression of a biomarker of the invention to an endogenous biomarker. For example, the expression level of one or more of the biomarkers listed in Table 1 are normalized to the level of expression of an endogenous biomarker. Thus, in one specific aspect, the endogenous biomarker is chosen from POLR2A, B2M, PFN1, HMBS, G6PD, and PABPN1. The ENSMBL reference numbers are given below for these endogenous biomarkers.

| Name          | Gene            | Transcript      | Protein         |
|---------------|-----------------|-----------------|-----------------|
| <b>POLR2A</b> | ENSG00000181222 | ENST00000322644 | ENSP00000314949 |
| <b>B2M</b>    | ENSG00000166710 | ENST00000349264 | ENSP00000340858 |
| <b>PFN1</b>   | ENSG00000108518 | ENST00000225655 | ENSP00000225655 |
| <b>HMBS</b>   | ENSG00000149397 | ENST00000278715 | ENSP00000278715 |
| <b>G6PD</b>   | ENSG00000160211 | ENST00000393562 | ENSP00000377192 |
| <b>PABPN1</b> | ENSG00000100836 | ENST00000216727 | ENSP00000216727 |

#### Diagnostic and Prognostic Reagents

The invention provides reagents for detecting the biomarkers of the invention (*e.g.*, those in Table 1). The reagents are useful for detecting protein and nucleic acid levels of the biomarkers of Table 1 for detecting and/or diagnosing endometrial cancer. The reagents below can be used for detecting combinations of the biomarkers to diagnose endometrial cancer. Specific examples of nucleic acids,

probes, primers, etc. related to each of the individual biomarkers are given in the Examples.

In one embodiment, the invention provides an ACAA1 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying an ACAA1 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to an ACAA1 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to an ACAA1 protein for detecting endometrial cancer. In a related aspect the invention provides an ACAA1 polypeptide for generating an antibody. In yet another related aspect, the invention provides an ACAA1 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides an AP1M2 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying an AP1M2 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to an AP1M2 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to an AP1M2 protein for detecting endometrial cancer. In a related aspect the invention provides an AP1M2 polypeptide for generating an antibody. In yet another related aspect, the invention provides an AP1M2 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a CGN nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a CGN nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a CGN nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a CGN protein for detecting endometrial cancer. In a related aspect the invention provides a CGN polypeptide for generating an antibody. In yet another related aspect, the invention provides a CGN polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a DDR1 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a DDR1 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a DDR1 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a DDR1 protein for detecting endometrial cancer. In a related aspect the invention provides a DDR1 polypeptide for generating an antibody. In yet another related aspect, the invention provides a DDR1 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides an EPS8L2 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying an EPS8L2 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to an EPS8L2 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to an EPS8L2 protein for detecting endometrial cancer. In a related aspect the invention provides an EPS8L2 polypeptide for generating an antibody. In yet another related aspect, the invention provides an EPS8L2 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a FASTKD1 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a FASTKD1 nucleic acid for detecting endometrial cancer. In another

related aspect the invention provides a probe that can hybridize to a FASTKD1 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a FASTKD1 protein for detecting endometrial cancer. In a related aspect the invention provides a FASTKD1 polypeptide for generating an antibody. In yet another related aspect, the invention provides a FASTKD1 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a GMIP nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a GMIP nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a GMIP nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a GMIP protein for detecting endometrial cancer. In a related aspect the invention provides a GMIP polypeptide for generating an antibody. In yet another related aspect, the invention provides a GMIP polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides an IKBKE nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying an IKBKE nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to an IKBKE nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to an IKBKE protein for detecting endometrial cancer. In a related aspect the invention provides an IKBKE polypeptide for generating an antibody. In yet another related aspect, the invention provides an IKBKE polypeptide for generating an immune response against the marker.



In one embodiment, the invention provides a P2RX4 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a P2RX4 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a P2RX4 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a P2RX4 protein for detecting endometrial cancer. In a related aspect the invention provides a P2RX4 polypeptide for generating an antibody. In yet another related aspect, the invention provides a P2RX4 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a P4HB nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a P4HB nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a P4HB nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a P4HB protein for detecting endometrial cancer. In a related aspect the invention provides a P4HB polypeptide for generating an antibody. In yet another related aspect, the invention provides a P4HB polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a PHKG2 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a PHKG2 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a PHKG2 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a PHKG2 protein for detecting endometrial cancer. In a related aspect the invention provides a PHKG2 polypeptide for generating an antibody. In

yet another related aspect, the invention provides a PHKG2 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a PPFIBP2 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a PPFIBP2 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a PPFIBP2 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a PPFIBP2 protein for detecting endometrial cancer. In a related aspect the invention provides a PPFIBP2 polypeptide for generating an antibody. In yet another related aspect, the invention provides a PPFIBP2 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a PPP1R16A nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a PPP1R16A nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a PPP1R16A nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a PPP1R16A protein for detecting endometrial cancer. In a related aspect the invention provides a PPP1R16A polypeptide for generating an antibody. In yet another related aspect, the invention provides a PPP1R16A polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a RASSF7 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a RASSF7 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a RASSF7 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a RASSF7 protein for detecting endometrial cancer. In a related aspect the invention provides a RASSF7 polypeptide for generating an antibody. In yet another related aspect, the invention provides a RASSF7 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a RNF183 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a RNF183 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a RNF183 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a RNF183 protein for detecting endometrial cancer. In a related aspect the invention provides a RNF183 polypeptide for generating an antibody. In yet another related aspect, the invention provides a RNF183 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a SIRT6 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a SIRT6 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a SIRT6 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a SIRT6 protein for detecting endometrial cancer. In a related aspect the invention provides a SIRT6 polypeptide for generating an antibody. In yet another related aspect, the invention provides a SIRT6 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a TJP3 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a TJP3 nucleic acid for detecting endometrial cancer. In another related

aspect the invention provides a probe that can hybridize to a TJP3 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a TJP3 protein for detecting endometrial cancer. In a related aspect the invention provides a TJP3 polypeptide for generating an antibody. In yet another related aspect, the invention provides a TJP3 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides an EFEMP2 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying an EFEMP2 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to an EFEMP2 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to an EFEMP2 protein for detecting endometrial cancer. In a related aspect the invention provides an EFEMP2 polypeptide for generating an antibody. In yet another related aspect, the invention provides an EFEMP2 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a SOCS2 nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a SOCS2 nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a SOCS2 nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a SOCS2 protein for detecting endometrial cancer. In a related aspect the invention provides a SOCS2 polypeptide for generating an antibody. In yet another related aspect, the invention provides a SOCS2 polypeptide for generating an immune response against the marker.

In one embodiment, the invention provides a DCN nucleic acid for detecting endometrial cancer. In a related aspect, the invention provides primers for amplifying a DCN nucleic acid for detecting endometrial cancer. In another related aspect the invention provides a probe that can hybridize to a DCN nucleic acid for detecting endometrial cancer.

In another related aspect, the invention provides an antibody that binds immunologically to a DCN protein for detecting endometrial cancer. In a related aspect the invention provides a DCN polypeptide for generating an antibody. In yet another related aspect, the invention provides a DCN polypeptide for generating an immune response against the marker.

### Kits

The invention also provides kits for detecting one or more of the biomarkers of Table 1. In one embodiment, the kit is useful for detecting and/or diagnosing a gynecological cancer. In another embodiment, the kit is useful for detecting and/or diagnosing endometrial cancer. In one aspect, the kit contains reagents for detecting CGN. In one aspect, the kit contains means for detecting CGN. In one aspect, the kit contains reagents for detecting AP1M2. In one aspect, the kit contains means for detecting AP1M2. In one aspect, the kit contains reagents for detecting EPS8L2. In one aspect, the kit contains means for detecting EPS8L2. In one aspect, the kit contains reagents for detecting IKBKE. In one aspect, the kit contains means for detecting IKBKE. In one aspect, the kit contains reagents for detecting PPP1R16A. In one aspect, the kit contains means for detecting PPP1R16A. In one aspect, the kit contains reagents for detecting RASSF7. In one aspect, the kit contains means for detecting RASSF7. In one aspect, the kit contains reagents for detecting TJP3. In one aspect, the kit contains means for detecting TJP3. In one aspect, the kit contains reagents for detecting P2RX4. In one aspect, the kit contains means for detecting P2RX4. In one aspect, the kit contains reagents for detecting RNF183. In one aspect, the kit contains means for detecting RNF183. In one aspect, the kit contains reagents for detecting GMIP. In one aspect, the kit contains means for detecting GMIP. In one aspect, the kit contains reagents for detecting PHKG2. In one aspect, the kit contains means for detecting PHKG2. In one aspect, the kit contains reagents for detecting P4HB. In one aspect, the kit contains means for detecting P4HB. In

one aspect, the kit contains reagents for detecting PPFIBP2. In one aspect, the kit contains means for detecting PPFIBP2. In one aspect, the kit contains reagents for detecting FASTKD1. In one aspect, the kit contains means for detecting FASTKD1. In one aspect, the kit contains reagents for detecting DDR1. In one aspect, the kit contains means for detecting DDR1. In one aspect, the kit contains reagents for detecting SIRT6. In one aspect, the kit contains means for detecting SIRT6. In one aspect, the kit contains reagents for detecting ACAA1. In one aspect, the kit contains means for detecting ACAA1. In one aspect, the kit contains reagents for detecting DCN. In one aspect, the kit contains means for detecting DCN. In one aspect, the kit contains reagents for detecting SOCS2. In one aspect, the kit contains means for detecting SOCS2. In one aspect, the kit contains reagents for detecting EFEMP2. In one aspect, the kit contains means for detecting EFEMP2.

In one aspect, the kit contains reagents for detecting from 2 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 2 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 3 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 3 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 4 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 4 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 5 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 5 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 6 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 6 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 7 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 7 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 8 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 8 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 9 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 9 to 20 of the biomarkers of Table 1. In one aspect, the kit contains reagents for detecting from 10 to 20 of the biomarkers of Table 1. In one aspect, the kit contains means for detecting from 10 to 20 of the biomarkers of Table 1. In one aspect, the kit contains

means for detecting from 15 to 20 of the biomarkers of Table 1. In one aspect, the kit comprises reagents for the RT-PCR evaluation of from 1 to 20 of the biomarkers of Table 1. In one aspect, the kit comprises means for the RT-PCR evaluation of from 1 to 20 of the biomarkers of Table 1. In one aspect, the kit comprises reagents for microarray evaluation of from 1 to 20 of the biomarkers of Table 1. In one aspect, the kit comprises means for microarray evaluation of from 1 to 20 of the biomarkers of Table 1. In one aspect, the kit comprises reagents for antibody-based evaluation of from 1 to 20 of the biomarkers of Table 1. In one aspect, the kit comprises means for antibody-based evaluation of from 1 to 20 of the biomarkers of Table 1. In one aspect, the kit has reagents for detecting different biomarkers in addition to one or more of those listed in Table 1. In one aspect, the kit has means for detecting different biomarkers in addition to the 1 to 20 of those listed in Table 1. In one aspect, the kit has reagents for multiplex PCR of from 2 to 20 markers of Table 1. In one aspect, the kit has means for multiplex PCR of from 2 to 20 markers of Table 1.

In some aspects, the kit has a device for obtaining a sample for analysis. In one aspect the device is a pipette. In another aspect, the device is as described in US patent no. 7,207,951, Issued Apr 24, 2007, which is incorporated by herein reference in its entirety. In another aspect, the device is curettage. In another aspect, the device is a brush. One example of a brush device is the tao brush

In some aspects, the kit has an agent to stabilizing the samples obtained from the patient. For example, in a specific aspect, the agent is a buffer for stabilizing the sample obtained from the patient comprises an RNA preserving solution. In another aspect, the agent is useful for stabilizing blood or serum samples.

#### Diagnostic Antibodies to the Biomarkers of Table 1

Diagnostic antibodies to one or more of the biomarkers of Table 1 (also referred to as a target protein) for diagnostic uses can be obtained in any number of ways. Furthermore, antibodies to some of the biomarkers of Table 1 are commercially available or described in the literature. These known antibodies can be used in the methods of the invention and/or as the basis of engineering new antibodies. Phage display techniques can be used to generate antibodies to one or more of the

biomarkers of Table 1. Standard hybridoma technologies can be used to generate antibodies to one or more of the biomarkers of Table 1. Antibodies to some of the biomarkers of Table 1 are known in the art see the examples. In some aspects, the antibody to one or more of the biomarkers of Table 1 is derived from an animal source (*e.g.*, mouse, rat, or rabbit).

#### Polyclonal Antibodies

The target protein antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the target protein polypeptide (or fragment thereof) or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and M PL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

#### Monoclonal Antibodies

The target protein antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein (1975) *Nature* 256:495. In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

The immunizing agent will typically include the target protein polypeptide (or fragment thereof) or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or



lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, *Monoclonal Antibodies: Principles and Practice*, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, Calif. and the American Type Culture Collection, Manassas, Va. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor (1984) *J. Immunol.* 133:3001; Brodeur *et al.*, *Monoclonal Antibody Production Techniques and Applications*, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against target protein. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard (1980) *Anal. Biochem.* 107:220.

After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Pat. No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (*e.g.*, by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Pat. No. 4,816,567; Morrison *et al.*, *supra*] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy

chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

In vitro methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

### Phage Display

Antibodies to the biomarkers of the invention can also be made by using combinatorial libraries to screen for synthetic antibody clones with the desired activity or activities. In principle, synthetic antibody clones are selected by screening phage libraries containing phage that display various fragments of antibody variable region (Fv) fused to phage coat protein. Such phage libraries are panned by affinity chromatography against the desired antigen. Clones expressing Fv fragments capable of binding to the desired antigen are adsorbed to the antigen and thus separated from the non-binding clones in the library. The binding clones are then eluted from the antigen, and can be further enriched by additional cycles of antigen adsorption/elution. Antibodies to the biomarkers of the invention can be obtained by designing a suitable antigen screening procedure to select for the phage clone of interest followed by construction of a full length antibody clone using the Fv sequences from the phage clone of interest and suitable constant region (Fc) sequences described in Kabat *et al.*, Sequences of Proteins of Immunological Interest, Fifth Edition, NIH Publication 91-3242, Bethesda MD (1991), vols. 1-3.

### Antibody Conjugates

The antibodies (and fragments thereof) of the invention can be conjugated to molecules for diagnostic purposes. For example, an antibody to a biomarker of Table 1 can be conjugated to a detectable label (*e.g.*, for imaging purposes) for diagnosing or detecting endometrial cancer. Suitable detectable markers include, but are not limited to, a radioisotope, a nanoparticle, a fluorescent compound, a bioluminescent compound, chemiluminescent compound, a metal chelator or an enzyme. Techniques for conjugating diagnostic agents to antibodies are well known (Holmes *et al.* (2001) Curr Protoc Cytom. May; Chapter 4:Unit 4.2; Kumar *et al*

(2008) ACS Nano. Mar;2(3):449-56; Rosenthal *et al.* (2006) *Laryngoscope* Sep;116(9):1636-41). Additionally kits for conjugating agents to diagnostic antibodies are commercially available.

#### Data and Information

In one aspect of the invention, the present invention relates to methods for comparing and compiling data wherein the data is stored in electronic or paper format. Electronic format can be selected from the group consisting of electronic mail, disk, compact disk (CD), digital versatile disk (DVD), memory card, memory chip, ROM or RAM, magnetic optical disk, tape, video, video clip, microfilm, internet, shared network, shared server and the like; wherein data is displayed, transmitted or analyzed via electronic transmission, video display, telecommunication, or by using any of the above stored formats; wherein data is compared and compiled at the site of sampling specimens or at a location where the data is transported following a process as described above. The data of this embodiment is information regarding the results of the analysis of the biomarkers of Table 1.

The biomarkers, reagents, targets, assays, tests, inquiries and methodologies described herein can be employed in a variety of contexts, including diagnostic discovery, diagnostic development, safety and efficacy monitoring, comparative studies, marketing and the like. The information provided by the invention can be communicated to regulators, physicians and other healthcare providers, manufacturers, owners, investors, patients, and/or the general public. This information and the like can be used in exploratory research, pre-clinical and clinical settings, labeling, production, advertising, and sales, for example.

#### Definitions

As used herein an "ACAA1 biomarker" refers to an "ACAA1 nucleic acid" or an "ACAA1 protein" that can be specifically detected. An ACAA1 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human ACAA1 gene or a fragment thereof. For example, an ACAA1 nucleic acid can be a cDNA, or fragment thereof, corresponding to an ACAA1 mRNA molecule. An ACAA1 protein refers to a protein (or fragment thereof) encoded or expressed by the

ACAA1 gene. Examples of ACAA1 biomarkers are given in the examples as well as some reagents useful for detecting ACAA1 biomarkers, nucleic acids, and proteins.

As used herein an "AP1M2 biomarker" refers to an "AP1M2 nucleic acid" or an "AP1M2 protein" that can be specifically detected. An AP1M2 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human AP1M2 gene or a fragment thereof. For example, an AP1M2 nucleic acid can be a cDNA, or fragment thereof, corresponding to an AP1M2 mRNA molecule. An AP1M2 protein refers to a protein (or fragment thereof) encoded or expressed by the AP1M2 gene. Examples of AP1M2 biomarkers are given in the examples as well as some reagents useful for detecting AP1M2 biomarkers, nucleic acids, and proteins.

As used herein a "CGN biomarker" refers to a "CGN nucleic acid" or a "CGN protein" that can be specifically detected. A CGN nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human CGN gene or a fragment thereof. For example, a CGN nucleic acid can be a cDNA, or fragment thereof, corresponding to a CGN mRNA molecule. A CGN protein refers to a protein (or fragment thereof) encoded or expressed by the CGN gene. Examples of CGN biomarkers are given in the examples as well as some reagents useful for detecting CGN biomarkers, nucleic acids, and proteins.

As used herein a "DDR1 biomarker" refers to a "DDR1 nucleic acid" or a "DDR1 protein" that can be specifically detected. A DDR1 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human DDR1 gene or a fragment thereof. For example, a DDR1 nucleic acid can be a cDNA, or fragment thereof, corresponding to a DDR1 mRNA molecule. A DDR1 protein refers to a protein (or fragment thereof) encoded or expressed by the DDR1 gene. Examples of DDR1 biomarkers are given in the examples as well as some reagents useful for detecting DDR1 biomarkers, nucleic acids, and proteins.

As used herein an "EPS8L2 biomarker" refers to an "EPS8L2 nucleic acid" or an "EPS8L2 protein" that can be specifically detected. An EPS8L2 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human EPS8L2 gene or a fragment thereof. For example, an EPS8L2 nucleic acid can be a

cDNA, or fragment thereof, corresponding to an EPS8L2 mRNA molecule. An EPS8L2 protein refers to a protein (or fragment thereof) encoded or expressed by the EPS8L2 gene. Examples of EPS8L2 biomarkers are given in the examples as well as some reagents useful for detecting EPS8L2 biomarkers, nucleic acids, and proteins.

As used herein a "FASTKD1 biomarker" refers to a "FASTKD1 nucleic acid" or an "FASTKD1 protein" that can be specifically detected. A FASTKD1 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human FASTKD1 gene or a fragment thereof. For example, a FASTKD1 nucleic acid can be a cDNA, or fragment thereof, corresponding to an FASTKD1 mRNA molecule. A FASTKD1 protein refers to a protein (or fragment thereof) encoded or expressed by the FASTKD1 gene. Examples of FASTKD1 biomarkers are given in the examples as well as some reagents useful for detecting FASTKD1 biomarkers, nucleic acids, and proteins.

As used herein a "GMIP biomarker" refers to an "GMIP nucleic acid" or an "GMIP protein" that can be specifically detected. An GMIP nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human GMIP gene or a fragment thereof. For example, a GMIP nucleic acid can be a cDNA, or fragment thereof, corresponding to a GMIP mRNA molecule. A GMIP protein refers to a protein (or fragment thereof) encoded or expressed by the GMIP gene. Examples of GMIP biomarkers are given in the examples as well as some reagents useful for detecting GMIP biomarkers, nucleic acids, and proteins.

As used herein an "IKBKE biomarker" refers to an "IKBKE nucleic acid" or an "IKBKE protein" that can be specifically detected. An IKBKE nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human IKBKE gene or a fragment thereof. For example, an IKBKE nucleic acid can be a cDNA, or fragment thereof, corresponding to an IKBKE mRNA molecule. An IKBKE protein refers to a protein (or fragment thereof) encoded or expressed by the IKBKE gene. Examples of IKBKE biomarkers are given in the examples as well as some reagents useful for detecting IKBKE biomarkers, nucleic acids, and proteins.

As used herein a “P2RX4 biomarker” refers to a “P2RX4 nucleic acid” or an “P2RX4 protein” that can be specifically detected. A P2RX4 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human P2RX4 gene or a fragment thereof. For example, a P2RX4 nucleic acid can be a cDNA, or fragment thereof, corresponding to a P2RX4 mRNA molecule. A P2RX4 protein refers to a protein (or fragment thereof) encoded or expressed by the P2RX4 gene. Examples of P2RX4 biomarkers are given in the examples as well as some reagents useful for detecting P2RX4 biomarkers, nucleic acids, and proteins.

As used herein a “P4HB biomarker” refers to a “P4HB nucleic acid” or a “P4HB protein” that can be specifically detected. A P4HB nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human P4HB gene or a fragment thereof. For example, a P4HB nucleic acid can be a cDNA, or fragment thereof, corresponding to a P4HB mRNA molecule. A P4HB protein refers to a protein (or fragment thereof) encoded or expressed by the P4HB gene. Examples of P4HB biomarkers are given in the examples as well as some reagents useful for detecting P4HB biomarkers, nucleic acids, and proteins.

As used herein a “PHKG2 biomarker” refers to a “PHKG2 nucleic acid” or an “PHKG2 protein” that can be specifically detected. A PHKG2 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human AP1M2 gene or a fragment thereof. For example, a PHKG2 nucleic acid can be a cDNA, or fragment thereof, corresponding to a PHKG2 mRNA molecule. A PHKG2 protein refers to a protein (or fragment thereof) encoded or expressed by the PHKG2 gene. Examples of PHKG2 biomarkers are given in the examples as well as some reagents useful for detecting PHKG2 biomarkers, nucleic acids, and proteins.

As used herein a “PPFIBP2 biomarker” refers to a “PPFIBP2 biomarker nucleic acid” or a “PPFIBP2 biomarker protein” that can be specifically detected. A PPFIBP2 biomarker nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human PPFIBP2 biomarker gene or a fragment thereof. For example, a PPFIBP2 biomarker nucleic acid can be a cDNA, or fragment thereof, corresponding to an PPFIBP2 biomarker mRNA molecule. A PPFIBP2 biomarker protein refers to a protein (or fragment thereof) encoded or expressed by the

PPFIBP2 biomarker gene. Examples of PPFIBP2 biomarker biomarkers are given in the examples as well as some reagents useful for detecting PPFIBP2 biomarker biomarkers, nucleic acids, and proteins.

As used herein a “PPP1R16A biomarker” refers to a “PPP1R16A nucleic acid” or a “PPP1R16A protein” that can be specifically detected. A PPP1R16A nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human PPP1R16A gene or a fragment thereof. For example, a PPP1R16A nucleic acid can be a cDNA, or fragment thereof, corresponding to a PPP1R16A mRNA molecule. A PPP1R16A protein refers to a protein (or fragment thereof) encoded or expressed by the PPP1R16A gene. Examples of PPP1R16A biomarkers are given in the examples as well as some reagents useful for detecting PPP1R16A biomarkers, nucleic acids, and proteins.

As used herein a “TJP3 biomarker” refers to a “TJP3 nucleic acid” or a “TJP3 protein” that can be specifically detected. A TJP3 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human TJP3 gene or a fragment thereof. For example, a TJP3 nucleic acid can be a cDNA, or fragment thereof, corresponding to a TJP3 mRNA molecule. A TJP3 protein refers to a protein (or fragment thereof) encoded or expressed by the TJP3 gene. Examples of TJP3 biomarkers are given in the examples as well as some reagents useful for detecting TJP3 biomarkers, nucleic acids, and proteins.

As used herein an “RASSF7 biomarker” refers to an “RASSF7 nucleic acid” or an “RASSF7 protein” that can be specifically detected. An RASSF7 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human RASSF7 gene or a fragment thereof. For example, an RASSF7 nucleic acid can be a cDNA, or fragment thereof, corresponding to an RASSF7 mRNA molecule. An RASSF7 protein refers to a protein (or fragment thereof) encoded or expressed by the RASSF7 gene. Examples of RASSF7 biomarkers are given in the examples as well as some reagents useful for detecting RASSF7 biomarkers, nucleic acids, and proteins.



As used herein a “RNF183 biomarker” refers to a “RNF183 nucleic acid” or a “RNF183 protein” that can be specifically detected. A RNF183 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human RNF183 gene or a fragment thereof. For example, a RNF183 nucleic acid can be a cDNA, or fragment thereof, corresponding to a RNF183 mRNA molecule. A RNF183 protein refers to a protein (or fragment thereof) encoded or expressed by the RNF183 gene. Examples of RNF183 biomarkers are given in the examples as well as some reagents useful for detecting RNF183 biomarkers, nucleic acids, and proteins.

As used herein a “SIRT6 biomarker” refers to a “SIRT6 nucleic acid” or a “SIRT6 protein” that can be specifically detected. A SIRT6 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human SIRT6 gene or a fragment thereof. For example, a SIRT6 nucleic acid can be a cDNA, or fragment thereof, corresponding to a SIRT6 mRNA molecule. A SIRT6 protein refers to a protein (or fragment thereof) encoded or expressed by the SIRT6 gene. Examples of SIRT6 biomarkers are given in the examples as well as some reagents useful for detecting SIRT6 biomarkers, nucleic acids, and proteins.

As used herein a “DCN biomarker” refers to a “DCN nucleic acid” or a “DCN protein” that can be specifically detected. A DCN nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human DCN gene or a fragment thereof. For example, a DCN nucleic acid can be a cDNA, or fragment thereof, corresponding to a DCN mRNA molecule. A DCN protein refers to a protein (or fragment thereof) encoded or expressed by the DCN gene. Examples of LSR biomarkers are given in the examples as well as some reagents useful for detecting DCN biomarkers, nucleic acids, and proteins.

As used herein a “SOCS2 biomarker” refers to a “SOCS2 nucleic acid” or a “SOCS2 protein” that can be specifically detected. A SOCS2 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human SOCS2 gene or a fragment thereof. For example, a SOCS2 nucleic acid can be a cDNA, or fragment thereof, corresponding to a SOCS2 mRNA molecule. A SOCS2 protein refers to a protein (or fragment thereof) encoded or expressed by the SOCS2

gene. Examples of SOCS2 biomarkers are given in the examples as well as some reagents useful for detecting SOCS2 biomarkers, nucleic acids, and proteins.

As used herein an "EFEMP2 biomarker" refers to an "EFEMP2 nucleic acid" or an "EFEMP2 protein" that can be specifically detected. An EFEMP2 nucleic acid can be a RNA molecule, DNA molecule, or other nucleic acid that corresponds to the human EFEMP2 gene or a fragment thereof. For example, an EFEMP2 nucleic acid can be a cDNA, or fragment thereof, corresponding to an EFEMP2 mRNA molecule. An EFEMP2 protein refers to a protein (or fragment thereof) encoded or expressed by the EFEMP2 gene. Examples of EFEMP2 biomarkers are given in the examples as well as some reagents useful for detecting EFEMP2 biomarkers, nucleic acids, and proteins.

As used herein, the term "sensitivity" refers to the proportion of reference test positive (diseased) subjects who test positive with the screening test.

As used herein, the term "specificity" refers to the proportion of reference test negative (healthy) subjects who test negative with the screening test.

As used herein, the term "secretory phase" refers to a phase of the menstrual cycle that is distinguishable from the other phases of the menstrual cycle using standard procedures in the art, *e.g.*, pathological examination of tissue obtained from endometrium or uterus. Secretory phase is associated with bleeding (menstruation).

As used herein, the term "ROC" or "receiver operator characteristic" refers to a graphical plot of sensitivity vs. (1-specificity) or in other words a plot of true positive rate versus fraction of false positives. The area under the ROC, or AUROC, curve can range from 0 to 1. An area under the ROC curve of 1 is a perfect test or separation of groups while an area under the ROC of 0.5 indicates that the classifier is essentially unable to separate the groups and is therefore not useful.

A "cancer" in an animal refers to the presence of cells possessing characteristics typical of cancer-causing cells, for example, uncontrolled proliferation, loss of specialized functions, immortality, significant metastatic potential, significant

increase in anti-apoptotic activity, rapid growth and proliferation rate, and certain characteristic morphology and cellular markers.

The phrase "detecting a cancer" or "diagnosing a cancer" refers to determining the presence or absence of cancer or a precancerous condition in an animal. "Detecting a cancer" also can refer to obtaining evidence regarding the likelihood of the presence of precancerous or cancerous cells in the animal or assessing the predisposition of a patient to the development of a cancer. Detecting a cancer can be accomplished using the methods of this invention alone, in combination with other methods, or in light of other information regarding the state of health of the animal.

A "tumor," as used herein, refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all precancerous and cancerous cells and tissues.

The term "precancerous" refers to cells or tissues having characteristics relating to changes that may lead to malignancy or cancer.

In general, a "gene" is a region on the genome that is capable of being transcribed to an RNA that either has a regulatory function, a catalytic function, and/or encodes a protein. An eukaryotic gene typically has introns and exons, which may organize to produce different RNA splice variants that encode alternative versions of a mature protein. The skilled artisan will appreciate that the present invention encompasses all encoding transcripts that may be found, including splice variants, allelic variants and transcripts that occur because of alternative promoter sites or alternative polyadenylation sites of the biomarkers as listed in Table 1. A "full-length" gene or RNA therefore encompasses any naturally occurring splice variants, allelic variants, other alternative transcripts, splice variants generated by recombinant technologies which bear the same function as the naturally occurring variants, and the resulting RNA molecules. A "fragment" of a gene, including an oncogene, can be any portion from the gene, which may or may not represent a functional domain, for example, a catalytic domain, a DNA binding domain, *etc.* A fragment may preferably include nucleotide sequences that encode for at least 25 contiguous amino acids, and preferably at least about 30, 40, 50, 60, 65, 70, 75 or more contiguous amino acids or any integer thereabout or therebetween. In some aspects of the invention, the skilled

artisan recognizes that the term gene is used interchangeably with the term "locus", which refers more generically to a region of genomic DNA regardless if it codes for RNA, protein, or a regulatory element.

A "differentially expressed gene transcript", as used herein, refers to a gene, transcript that is found at a different level in different cell or tissue types of an organism having a tumor or cancer, compared to the level or state of the gene transcript found in the cells of the same tissue in a healthy organism, or in the cells of the same tissue in the same organism. Multiple copies of gene transcripts may be found in an organism having the tumor or cancer, while fewer copies of the same gene transcript are found in a healthy organism or healthy cells of the same tissue in the same organism, or vice-versa for underexpressed genes. In general, differentially expressed transcripts are those which when measured in an affected sample or sample from an affected patient have a detectably different level of expression as compared to a control value which is representative of a non-affected sample or sample from a non-affected patient. Examples of differential expression include a change of 10% or more, 20% or more 30% or more, 40% or more, or 50% or more in affected as compared to non-affected.

As used herein the term "polypeptide" means a sequence of amino acids joined together by peptide bonds. The amino acid sequence of the polypeptide can be determined by the sequence of the DNA bases which encode the amino acids of the polypeptide chain. The polypeptides described herein include, but are not limited to, complete proteins, fragments of complete proteins, epitopes of proteins etc. As used herein the term polypeptide, peptide, and protein refer to molecule having two or more amino acid residues (natural or unnatural) joined together by one or more peptide bonds.

A "differentially expressed gene," can be a target, fingerprint, or pathway gene. For example, a "fingerprint gene", as used herein, refers to a differentially expressed gene whose expression pattern can be used as a prognostic or diagnostic marker for the evaluation of tumors and cancers, or which can be used to identify compounds useful for the treatment of tumors and cancers, for example, endometrial cancer.

Fingerprint genes can be one or more genes (or corresponding biomarkers *e.g.*, protein) corresponding to the biomarkers of Table 1.

A "fingerprint pattern", as used herein, refers to a pattern generated when the expression pattern of a series (which can range from two up to all the fingerprint genes that exist for a given state) of fingerprint genes is determined. A fingerprint pattern also may be referred to as a "profile". A fingerprint pattern or expression profile having from 1 to 20 of the biomarkers of Table 1 can be used in the same diagnostic, prognostic, and methods of the invention.

"Pathway genes", as used herein, are genes that encode proteins or polypeptides that interact with other gene products involved in tumors and cancers. Pathway genes also can exhibit target gene and/or fingerprint gene characteristics.

A "detectable" RNA expression level, as used herein, means a level that is detectable by standard techniques currently known in the art or those that become standard at some future time, and include for example, differential display, RT (reverse transcriptase)-coupled polymerase chain reaction (PCR), Northern Blot, and/or RNase protection analyses.

The nucleic acid molecules of the invention, for example, those corresponding to one or more biomarkers of Table 1, and its subsequences/alternative transcripts, can be inserted into a vector, as described below, which will facilitate expression of the insert. The nucleic acid molecules and the polypeptides they encode can be used directly as diagnostic agents, or can be used (directly in the case of the polypeptide or indirectly in the case of a nucleic acid molecule) to generate antibodies that, in turn, are clinically useful as a diagnostic agent. Accordingly, vectors containing the nucleic acids of the invention, cells transfected with these vectors, the polypeptides expressed, and antibodies generated against either the entire polypeptide or an antigenic fragment thereof, are among the aspects of the invention.

An "isolated DNA molecule" is a fragment of DNA that has been separated from the chromosomal or genomic DNA of an organism. Isolation also is defined to connote a degree of separation from original source or surroundings.

"Complementary DNA" (cDNA), often referred to as "copy DNA", is a single-stranded DNA molecule that is formed from an mRNA template by the enzyme reverse transcriptase. Those skilled in the art also use the term "cDNA" to refer to a double-stranded DNA molecule that comprises such a single-stranded DNA molecule and its complement DNA strand.

The term "expression" refers to the biosynthesis of a gene product.

A "cloning vector" is a nucleic acid molecule, for example, a plasmid, cosmid or bacteriophage that has the capability of replicating autonomously in a host cell. Cloning vectors typically contain (i) one or a small number of restriction endonuclease recognition sites at which foreign DNA sequences can be inserted in a determinable fashion without loss of an essential biological function of the vector, and (ii) a marker gene that is suitable for use in the identification and selection of cells transformed or transfected with the cloning vector. Marker genes include, but are not limited to, genes that provide tetracycline resistance or ampicillin resistance..

An "expression vector" is a nucleic acid construct, generated recombinantly or synthetically, bearing a series of specified nucleic acid elements that enable transcription of a particular gene in a host cell. Typically, gene expression is placed under the control of certain regulatory elements, including constitutive or inducible promoters, tissue-preferred regulatory elements, and enhancers.

A "recombinant host" may be any prokaryotic or eukaryotic cell that contains either a cloning vector or expression vector. This term also includes those prokaryotic or eukaryotic cells that have been genetically engineered to contain the cloned gene(s) in the chromosome or genome of the host cell.

The term "operably linked" is used to describe the connection between regulatory elements and a gene or its coding region. That is, gene expression is typically placed under the control of certain regulatory elements, including constitutive or inducible promoters, tissue-specific regulatory elements, and enhancers. Such a gene or coding region is said to be "operably linked to" or "operatively linked to" or

"operably associated with" the regulatory elements, meaning that the gene or coding region is controlled or influenced by the regulatory element.

"Sequence homology" is used to describe the sequence relationships between two or more nucleic acids, polynucleotides, proteins, or polypeptides, and is understood in the context of and in conjunction with the terms including: (a) reference sequence, (b) comparison window, (c) sequence identity, (d) percentage of sequence identity, and (e) substantial identity or "homologous."

A "reference sequence" is a defined sequence used as a basis for sequence comparison. A reference sequence may be a subset of or the entirety of a specified sequence; for example, a segment of a full-length cDNA or gene sequence, or the complete cDNA or gene sequence. For polypeptides, the length of the reference polypeptide sequence can be chosen from at least about 16 amino acids, at least about 20 amino acids, at least about 25 amino acids, and about 35 amino acids, about 50 amino acids, or about 100 amino acids. For nucleic acids, the length of the reference nucleic acid sequence can be chosen from at least about 50 nucleotides, at least about 60 nucleotides, at least about 75 nucleotides, and about 100 nucleotides or about 300 nucleotides or any integer thereabout or there between.

A "comparison window" includes reference to a contiguous and specified segment of a polynucleotide sequence, wherein the polynucleotide sequence may be compared to a reference sequence and wherein the portion of the polynucleotide sequence in the comparison window may comprise additions, substitutions, or deletions (*i.e.*, gaps) compared to the reference sequence (which does not comprise additions, substitutions, or deletions) for optimal alignment of the two sequences. Generally, the comparison window is at least 20 contiguous nucleotides in length, and optionally can be 30, 40, 50, 100, or longer. Those of skill in the art understand that to avoid a misleadingly high similarity to a reference sequence due to inclusion of gaps in the polynucleotide sequence a gap penalty is typically introduced and is subtracted from the number of matches.

Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison may be conducted by the local

homology algorithm of Smith and Waterman (1981) *Adv. Appl. Math.*, 2: 482;; by the homology alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.*, 48: 443 ; by the search for similarity method of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA*, 8: 2444; by computerized implementations of these algorithms, including, but not limited to: CLUSTAL in the PC/Gene program by Intelligenetics, Mountain View, Calif., GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 7 Science Dr., Madison, Wisc., USA; the CLUSTAL program is well described by Higgins and Sharp (1988) *Gene* 73: 237-244; Corpet *et al.* (1988) *Nucleic Acids Research*, 16:881-90; Huang, *et al.*, Computer Applications in the Biosciences, 8:1-6, 1992; and Pearson, *et al.* (1994) *Methods in Molecular Biology*, 24:7-331. The BLAST family of programs which can be used for database similarity searches includes: BLASTN for nucleotide query sequences against nucleotide database sequences; BLASTX for nucleotide query sequences against protein database sequences; BLASTP for protein query sequences against protein database sequences; TBLASTN for protein query sequences against nucleotide database sequences; and TBLASTX for nucleotide query sequences against nucleotide database sequences. See, Current Protocols in Molecular Biology, Chapter 19, Ausubel, *et al.*, Eds., Greene Publishing and Wiley-Interscience, New York, 1995. New versions of the above programs or new programs altogether will undoubtedly become available in the future, and can be used with the present invention.

Unless otherwise stated, sequence identity/similarity values provided herein refer to the value obtained using the BLAST 2.0 suite of programs, or their successors, using default parameters. Altschul *et al.* (1997) *Nucleic Acids Res*, 2:3389-3402. It is to be understood that default settings of these parameters can be readily changed as needed in the future.

As those ordinary skilled in the art will understand, BLAST searches assume that proteins can be modeled as random sequences. However, many real proteins comprise regions of nonrandom sequences which may be homopolymeric tracts, short-period repeats, or regions enriched in one or more amino acids. Such low-complexity regions may be aligned between unrelated proteins even though other regions of the protein are entirely dissimilar. A number of low-complexity filter



programs can be employed to reduce such low-complexity alignments. For example, the SEG (Wooten and Federhen, (1993) *Comput. Chem.* 17:149-163) and XNU (Claverie and States (1993) *Comput. Chem.*, 17:191-1) low-complexity filters can be employed alone or in combination.

"Sequence identity" or "identity" in the context of two nucleic acid or polypeptide sequences includes reference to the residues in the two sequences which are the same when aligned for maximum correspondence over a specified comparison window, and can take into consideration additions, deletions and substitutions. When percentage of sequence identity is used in reference to proteins it is recognized that residue positions which are not identical often differ by conservative amino acid substitutions, where amino acid residues are substituted for other amino acid residues with similar chemical properties (for example, charge or hydrophobicity) and therefore do not deleteriously change the functional properties of the molecule. Where sequences differ in conservative substitutions, the percent sequence identity may be adjusted upwards to correct for the conservative nature of the substitution. Sequences which differ by such conservative substitutions are said to have sequence similarity. Approaches for making this adjustment are well-known to those of skill in the art. Typically this involves scoring a conservative substitution as a partial rather than a full mismatch, thereby increasing the percentage sequence identity. Thus, for example, where an identical amino acid is given a score of 1 and a non-conservative substitution is given a score of zero, a conservative substitution is given a score between zero and 1. The scoring of conservative substitutions is calculated, for example, according to the algorithm of Meyers and Miller (1988) *Computer Applic. Biol. Sci.*, 4: 11-17 for example, as implemented in the program PC/GENE (Intelligenetics, Mountain View, Calif., USA).

"Percentage of sequence identity" means the value determined by comparing two optimally aligned sequences over a comparison window, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions, substitutions, or deletions (*i.e.*, gaps) as compared to the reference sequence (which does not comprise additions, substitutions, or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both

sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity.

The term "substantial identity" or "homologous" in their various grammatical forms in the context of polynucleotides means that a polynucleotide comprises a sequence that has a desired identity, for example, at least 60% identity, preferably at least 70% sequence identity, more preferably at least 80%, still more preferably at least 90% and even more preferably at least 95%, compared to a reference sequence using one of the alignment programs described using standard parameters. One of skill will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like. Substantial identity of amino acid sequences for these purposes normally means sequence identity of at least 60%, more preferably at least 70%, 80%, 90%, and even more preferably at least 95%.

Another indication that nucleotide sequences are substantially identical is if two molecules hybridize to each other under stringent conditions. However, nucleic acids which do not hybridize to each other under stringent conditions are still substantially identical if the polypeptides which they encode are substantially identical. This may occur, for example, when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. One indication that two nucleic acid sequences are substantially identical is that the polypeptide which the first nucleic acid encodes is immunologically cross reactive with the polypeptide encoded by the second nucleic acid, although such cross-reactivity is not required for two polypeptides to be deemed substantially identical.

The term "substantial identity" or "homologous" in their various grammatical forms in the context of peptides indicates that a peptide comprises a sequence that has a desired identity, for example, at least 60% identity, preferably at least 70% sequence identity to a reference sequence, more preferably 80%, still more preferably 85%, even more preferably at least 90% or 95% sequence identity to the reference sequence over a specified comparison window. Preferably, optimal alignment is

conducted using the homology alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.*, 48:443. An indication that two peptide sequences are substantially identical is that one peptide is immunologically reactive with antibodies raised against the second peptide, although such cross-reactivity is not required for two polypeptides to be deemed substantially identical. Thus, a peptide is substantially identical to a second peptide, for example, where the two peptides differ only by a conservative substitution. Peptides which are "substantially similar" share sequences as noted above except that residue positions which are not identical may differ by conservative amino acid changes. Conservative substitutions typically include, but are not limited to, substitutions within the following groups: glycine and alanine; valine, isoleucine, and leucine; aspartic acid and glutamic acid; asparagine and glutamine; serine and threonine; lysine and arginine; and phenylalanine and tyrosine, and others as known to the skilled person.

"Biological subject" as used herein refers to a target biological object obtained, reached, or collected *in vivo*, *ex-vivo*, or *in situ*, that contains or is suspected of containing nucleic acids or polypeptides corresponding to a biomarker of Table 1.

"Biological sample" as used herein refers to a sample obtained from a biological subject, including sample of biological tissue or fluid origin, obtained, reached, or collected *in vivo*, *ex-vivo*, or *in situ*, that contains or is suspected of containing nucleic acids or polypeptides corresponding to a biomarker of Table 1. A biological sample also includes samples from a region of a biological subject containing precancerous or cancer cells or tissues. Such samples can be, but are not limited to, organs, tissues, fractions and cells isolated from mammals including, humans such as a patient. Biological samples also may include sections of the biological sample including tissues, for example, frozen sections taken for histologic purposes. A biological sample, as described herein, can be: a "control" or a "control sample" or a "test sample". A biological sample can be obtained from the uterus using commonly employed clinical practices (*e.g.*, aspiration, brush, curettage, or hysteroscopy).

A "control" or "control value" refers to a representative of healthy, endometrial cancer-free biological subject or information obtained from a different individual or a normalized value, which can be based on baseline data obtained from a population

or other acceptable sources. A control also can refer to a given level of a biomarker of Table 1, representative of the endometrial cancer-free population, that has been previously established based on measurements from normal, endometrial cancer-free individuals. A control also can be a reference data point in a database based on data obtained from control samples representative of a cancer-free population. Further, a control can be established by a specific age, sex, ethnicity or other demographic parameters. In some contexts, the control is implicit in the particular measurement. A control value or control can also refer to a "control score". Control scores can be values obtained from the determination of the expression level of one or more biomarkers of the invention. For example, different programs and algorithms are commercially available for generating formulas that yield a score value based on the measurement of the levels of one or more biomarkers, that can indicate whether an individual is likely to have a condition or not. In another example, a score over or below a certain threshold that may indicate an increased (or decreased) likelihood of having the disease. A control score value can be based on a single marker or a combination of markers.

A "control sample" refers to a sample of biological material representative of healthy, cancer-free animals or a normal biological subject obtained from a cancer-free population. The level of a biomarker of Table 1, in a control sample is desirably typical of the general population of normal, cancer-free animals of the same species. This sample either can be collected from an animal for the purpose of being used in the methods described in the present invention or it can be any biological material representative of normal, cancer-free animals suitable for use in the methods of this invention. A control sample also can be obtained from normal tissue from the animal that has cancer or is suspected of having cancer.

A "test sample" as used herein refers to a biological sample, including sample of biological tissue or fluid origin, obtained, reached, or collected *in vivo*, *ex-vivo*, or *in situ*, that contains or is suspected of containing nucleic acids or polypeptides corresponding to a biomarker of Table 1. A test sample also includes biological samples containing precancerous or cancer cells or tissues. A test sample also may include sections of the biological sample including tissues, for example, frozen sections taken for histologic purposes.

"Providing a biological subject, a biological sample, or a test sample" means to obtain a biological subject *in vivo*, *ex-vivo*, or *in situ*, including tissue or cell sample for use in the methods described in the present invention. Most often, this will be done by removing a sample of cells from an animal, but also can be accomplished *in vivo*, *ex-vivo*, or *in situ*, or by using previously isolated cells (for example, isolated from another person, at another time, and/or for another purpose). The sample can also be obtained from sources such as blood, serum, and uterine fluid.

"Data" includes, but is not limited to, information obtained that relates to "biological sample", "test sample", "control sample", and/or "control", as described above, wherein the information is applied in generating a test level for diagnostics, prevention, monitoring or therapeutic use. The present invention relates to methods for comparing and compiling data wherein the data is stored in electronic or paper formats. Electronic format can be selected from the group consisting of electronic mail, disk, compact disk (CD), digital versatile disk (DVD), memory card, memory chip, ROM or RAM, magnetic optical disk; tape, video, video clip, microfilm, internet, shared network, shared server and the like; wherein data is displayed, transmitted or analyzed via electronic transmission, video display, telecommunication, or by using any of the above stored formats; wherein data is compared and compiled at the site of sampling specimens or at a location where the data is transported following a process as: described above.

"Overexpression" of a gene or an "increased," or "elevated," level of a ribonucleotide or protein refers to a level of the gene, ribonucleotide or polypeptide that, in comparison with a control level/value of gene, ribonucleotides or polypeptide, is detectably higher. Comparison may be carried out by statistical analyses on numeric measurements of the expression; or, it may be done through visual examination of experimental results by qualified researchers. Examples of overexpression include a change of 10% or more, 20% or more 30% or more, 40% or more, or 50% or more in affected as compared to non-affected.

"Underexpression" of a gene or a "decreased," or "lower," level of a ribonucleotide or protein refers to a level of the gene, ribonucleotide or polypeptide that, in comparison with a control level of gene, ribonucleotides or polypeptide, is detectably lower. Comparison may be carried out by statistical analyses on numeric measurements of the expression; or, it may be done through visual examination of experimental results by qualified researchers. Examples of underexpression include a change of 10% or more, 20% or more 30% or more, 40% or more, or 50% or more in affected as compared to non-affected.

A level of ribonucleotide or polypeptide, that is "expected" in a control sample refers to a level that represents a typical, cancer-free sample, and from which an elevated, or diagnostic, presence of the polypeptide or polynucleotide, can be distinguished. Preferably, an "expected" level will be controlled for such factors as the age, sex, medical history, *etc.* of the mammal, as well as for the particular biological subject being tested.

The terms "isolated," "purified," or "biologically pure" refer to material that is free to varying degrees from components which normally accompany it as found in its native state. "Isolate" denotes a degree of separation from original source or surroundings. "Purify" denotes a degree of separation that is higher than isolation. A "purified" or "biologically pure" protein is sufficiently free of other materials such that any impurities do not materially affect the biological properties of the protein or cause other adverse consequences. That is, a nucleic acid or peptide of this invention is purified if it is substantially free of cellular material, viral material, or culture medium when produced by recombinant DNA techniques, or chemical precursors or other chemicals when chemically synthesized. Purity and homogeneity are typically determined using analytical chemistry techniques, for example, polyacrylamide gel electrophoresis or high performance liquid chromatography. The term "purified" can denote that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. For a protein that can be subjected to modifications, for example, phosphorylation or glycosylation, different modifications may give rise to different isolated proteins, which can be separately purified. Various levels of purity may be applied as needed according to this invention in the different methodologies

set forth herein; the customary purity standards known in the art may be used if no standard is otherwise specified.

An "isolated nucleic acid molecule" can refer to a nucleic acid molecule, depending upon the circumstance, that is separated from the 5' and 3' coding sequences of genes or gene fragments contiguous in the naturally occurring genome of an organism. The term "isolated nucleic acid molecule" also includes nucleic acid molecules which are not naturally occurring, for example, nucleic acid molecules created-by recombinant DNA techniques.

"Nucleic acid" refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. The term encompasses nucleic acids containing known nucleotide analogs or modified backbone residues or linkages, which are synthetic, naturally occurring, and non-naturally occurring, which have similar binding properties as the reference nucleic acid, and which are metabolized in a manner similar to the reference nucleotides. Examples of such analogs include, without limitation, phosphorothioates, phosphoramidates, methyl phosphonates, chiral methyl phosphonates, 2-O-methyl ribonucleotides, and peptide-nucleic acids (PNAs).

Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively, modified variants thereof (for example, degenerate codon substitutions) and complementary sequences, as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with suitable mixed base and/or deoxyinosine residues (Batzner *et al.* (1991) *Nucleic Acid Res.*, 19:081; Ohtsuka *et al.* (1985) *J. Biol. Chem.*, 260:2600-2608; Rossolini *et al.* (1994) *Mol. Cell Probes*, 8:91-98). The term nucleic acid can be used interchangeably with gene, cDNA, mRNA, oligonucleotide, and polynucleotide.

A "label" or a "detectable moiety" is a composition that when linked with the nucleic acid or protein molecule of interest renders the latter detectable, via spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example,

useful labels include radioactive isotopes, magnetic beads, metallic beads, colloidal particles, fluorescent dyes, electron-dense reagents, enzymes (for example, as commonly used in an ELISA), biotin, digoxigenin, or haptens. A "labeled nucleic acid or oligonucleotide probe" is one that is bound, either covalently, through a linker or a chemical bond, or noncovalently, through ionic bonds, van der Waals forces, electrostatic attractions, hydrophobic interactions, or hydrogen bonds, to a label such that the presence of the nucleic acid or probe may be detected by detecting the presence of the label bound to the nucleic acid or probe.

As used herein a "nucleic acid or oligonucleotide probe" is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (*i.e.*, A, G, C, or T) or modified bases (7-deazaguanosine, inosine, *etc.*). In addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not unduly interfere with hybridization. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence depending upon the stringency of the hybridization conditions. The probes are preferably directly labeled with isotopes, for example, chromophores, lumiphores, chromogens, or indirectly labeled with biotin to which a streptavidin complex may later bind. By assaying for the presence or absence of the probe, one can detect the presence or absence of a target gene of interest.

The phrase "selectively (or specifically) hybridizes to" refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (for example, total cellular or library DNA or RNA).

The phrase "stringent hybridization conditions" refers to conditions under which a probe will hybridize to its target complementary sequence, typically in a complex mixture of nucleic acids, but to no other sequences. Stringent conditions are sequence-dependent and circumstance-dependent; for example, longer sequences can hybridize with specificity at higher temperatures. An extensive guide to the



hybridization of nucleic acids is found in Tijssen (1993) Techniques in Biochemistry and Molecular Biology-Hybridization with Nucleic Probes, "Overview of principles of hybridization and the strategy of nucleic acid assays". In the context of the present invention, as used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other. Preferably, the conditions are such that sequences at least about 65%, more preferably at least about 70%, and even more preferably at least about 75% or more homologous to each other typically remain hybridized to each other.

Generally, stringent conditions are selected to be about 5 to 10 C lower than the thermal melting point ( $T_m$ ) for the specific sequence at a defined ionic strength pH. The  $T_m$  is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at  $T_m$ , 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30 C for short probes (for example, 10 to 50 nucleotides) and at least about 60 C for long probes (for example, greater than 50 nucleotides). Stringent conditions also may be achieved with the addition of destabilizing agents, for example, formamide. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization.

Exemplary stringent hybridization conditions can be as following, for example: 50% formamide, 5xSSC and 1% SDS, incubating at 42 C, or 5xSSC and 1% SDS, incubating at 65 C., with wash in 0.2xSSC and 0.1% SDS at 65 C. Alternative conditions include, for example, conditions at least as stringent as hybridization at 68 C for 20 hours, followed by washing in 2xSSC, 0.1% SDS, twice for 30 minutes at 55 C and three times for 15 minutes at 60 C. Another alternative set of conditions is hybridization in 6xSSC at about 45 C, followed by one or more washes in 0.2xSSC, 0.1% SDS at 50-65 C. For PCR, a temperature of about 36 C is typical for low

stringency amplification, although annealing temperatures may vary between about 32 C and 48 C depending on primer length. For high stringency PCR amplification, a temperature of about 62 C is typical, although high stringency annealing temperatures can range from about 50 C to about 65 C, depending on the primer length and specificity. Typical cycle conditions for both high and low stringency amplifications include a denaturation phase of 90 C to 95 C for 30 sec. to 2 min., an annealing phase lasting 30 sec. to 2 min., and an extension phase of about 72 C for 1 to 2 min.

Nucleic acids that do not hybridize to each other under stringent conditions can still be substantially identical if the polypeptides which they encode are substantially identical. This occurs, for example, when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary "moderately stringent hybridization conditions" include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37 C, and a wash in 1xSSC at 45 C. A positive hybridization is at least twice background. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency.

The term "target gene" or "target biomarker" or "target nucleic acid" or "target protein" can refer to a target nucleic acid (DNA and RNA) or protein (or polypeptide), (*e.g.*, corresponding to the biomarkers in Table 1) and can include their polymorphic variants, alleles, mutants, and interspecies homologs that have (i) substantial nucleotide sequence homology (for example, at least 60% identity, preferably at least 70% sequence identity, more preferably at least 80%, still more preferably at least 90% and even more preferably at least 95%) with the nucleotide sequence indicated in Ensembl database for the indicated ID number; or (ii) at least 65% sequence homology with the amino acid sequence as indicated in the Ensembl record; or (iii) substantial nucleotide sequence homology (for example, at least 60% identity, preferably at least 70% sequence identity, more preferably at least 80%, still more preferably at least 90% and even more preferably at least 95%) with the nucleotide sequence as set forth in the Ensembl record with substantial sequence homology with the encoded amino acid sequence. As used in herein, and unless

otherwise specified, these terms refer the entire gene sequence, mRNA sequence, and/or protein sequence as well as fragments of these sequences. In a more specific definition, these terms refer to the minimal amount of nucleic acid or amino acid sequence that can be used to identify biomarker in a specific manner. The skilled artisan recognizes that the target genes/biomarker can have numerous splice forms and variants. When referring to a specific target gene or locus by a reference number (*e.g.*, Entrez gene ID or Ensembl), all splices forms and variant which are included in the various embodiments of the invention. The target gene/biomarker can also comprise a regulatory element. These sequences are representative of one particular individual in the population of humans. Humans vary from one to another in their gene sequences. These variations are very minimal, sometimes occurring at a frequency of about 1 to 10 nucleotides per gene. Different forms of any particular gene exist within the human population. These different forms are called allelic variants. Allelic variants often do not change the amino acid sequence of the encoded protein; such variants are termed synonymous. Even if they do change the encoded amino acid (non-synonymous), the function of the protein is not typically affected. Such changes are evolutionarily or functionally neutral. When a gene ID (*e.g.*, genbank or Ensembl) is referred to in the present application all allelic variants are intended to be encompassed by the term. The gene ID sequences given for a biomarker are provided merely as representative examples of a wild-type human sequence. The invention is not limited to a single allelic form of the amplified genes or regions (and proteins they encode).

### Examples

The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques used by the inventor to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention.

### Example 1: Identification of Endometrial Cancer Biomarkers

In order to identify biomarkers for predicting and/or diagnosing endometrial cancer, gene expression levels from fifty-six endometrial primary tumors in several differentiation stages were compared with 10 normal (*i.e.*, not having endometrial cancer) endometrial tissues by DNA microarray technique. This technique allows us to check the expression of the whole genome in a particular type of cell, tissue, organ, or in this case, check the differential gene expression between endometrial cancer and healthy endometrial tissue. A microarray chip contains small DNA sequences arranged in a regular pattern with specific addresses for probes for typically thousands of genes.

The amount of specific mRNAs in a sample can be estimated by its hybridization signal on the array.

#### Sample Description

Tumor samples were obtained from patients who underwent surgery and control tissue was obtained from non affected regions of endometrial tissue from the same patients. During preparation of the specimens, care was taken to macroscopically dissect the cancer away from any adjacent myometrium.

Ten control samples (nine of them were paired with their corresponding tumor samples and the tenth was an atrophic endometrium) were used and the basic characteristics of the other test samples are summarized in Table 3 below.

Table 3. Affected Samples used in Microarray studies

| Samples | Sample Diagnosis      | Tumor Grade | FIGO stage |
|---------|-----------------------|-------------|------------|
| 1       | Endometroid carcinoma | G1          | Ia         |
| 2       | Endometroid carcinoma | G1          | Ib         |
| 3       | Endometroid carcinoma | G1          | Ib         |
| 4       | Endometroid carcinoma | G1          | Ib         |
| 5       | Endometroid carcinoma | G1          | Ia         |
| 6       | Endometroid carcinoma | G1          | Ia         |
| 7       | Endometroid carcinoma | G1          | Ia         |
| 8       | Endometroid carcinoma | G2          | Ib         |
| 9       | Endometroid carcinoma | G2          | IIb        |
| 10      | Endometroid carcinoma | G2          | IIla       |
| 11      | Endometroid carcinoma | G2          | Ib         |
| 12      | Endometroid carcinoma | G2          | Ic         |
| 13      | Endometroid carcinoma | G2          | Ia         |
| 14      | Endometroid carcinoma | G2          | Ic         |
| 15      | Endometroid carcinoma | G2          | Ic         |
| 16      | Endometroid carcinoma | G2          | Ib         |
| 17      | Endometroid carcinoma | G2          | IIb        |
| 18      | Endometroid carcinoma | G2          | IIb        |
| 19      | Endometroid carcinoma | G2          | Ib         |
| 20      | Endometroid carcinoma | G2          | Ic         |
| 21      | Endometroid carcinoma | G2          | IVb        |
| 22      | Endometroid carcinoma | G2          | IIb        |
| 23      | Endometroid carcinoma | G2          | Ic         |
| 24      | Endometroid carcinoma | G2          | IIb        |
| 25      | Endometroid carcinoma | G2          | Ib         |
| 26      | Endometroid carcinoma | G2          | Ic         |
| 27      | Endometroid carcinoma | G2          | Ib         |
| 28      | Endometroid carcinoma | G2          | Ib         |
| 29      | Endometroid carcinoma | G2          | IIb        |
| 30      | Endometroid carcinoma | G2          | Ib         |
| 31      | Endometroid carcinoma | G3          | Ic         |
| 32      | Endometroid carcinoma | G3          | IIla       |
| 33      | Endometroid carcinoma | G3          | IIb        |
| 34      | Endometroid carcinoma | G3          | IIb        |
| 35      | Endometroid carcinoma | G3          | Ib         |
| 36      | Endometroid carcinoma | G3          | IIa        |
| 37      | Endometroid carcinoma | G3          | IIa        |
| 38      | Endometroid carcinoma | G3          | Ic         |
| 40      | ATIPIC HIPERPLASIA    |             |            |
| 41      | ATIPIC HIPERPLASIA    |             |            |
| 42      | ATIPIC HIPERPLASIA    |             |            |
| 43      | Serous carcinoma      | G3          | IIlc       |
| 44      | Serous carcinoma      | G3          | IIlc       |
| 45      | Serous carcinoma      | G3          | Ib         |
| 46      | Serous carcinoma      | G3          | Ib         |
| 47      | Serous carcinoma      | G3          | IIla       |
| 48      | Clara cell type       | G3          | IIlc       |
| 49      | Undifferentiated      | G3          | IIb        |
| 50      | Undifferentiated      | G3          | IIla       |
| 51      | Villoglandular        | G3          | Ib         |
| 52      | Villoglandular        | G2          | Ib         |
| 53      | Adeno-squamous        | G2          | Ib         |
| 54      | Adeno-squamous        | G2          | IIb        |
| 55      | Adeno-squamous        | G3          | Ic         |
| 56      | Mucinous type         | G3          | IIla       |

Total RNA was extracted with the RNeasy mini kit (Qiagen, Hilden, Germany), following the instructions provided by the manufacturer. Quantity and quality of the obtained RNA was measured with a Nanodrop (Nandrop ND-1000, Agilent 2100

Bioanalyzer) and low quality RNA was discarded from the array hybridization process.

#### Microarray Design

Microarrays for Gene Expression were designed by the Tethys algorithm using the ENSEMBL database. For sequences where we did not find high quality probes, we complemented the design with Oryzon Optimized Agilent probes. DNA microarray synthesis was outsourced to Agilent.

The Whole Genome Gene Expression Array contains:

- 20148 Oryzon High Quality probes from ENSEMBL Database.
- 5698 Oryzon Tm optimized Agilent probes.

The total number of probes was 25846.

#### aRNA labeling

Cy3 and Cy5 labeled aRNA was produced using the MessageAmplification kit by Ambion (Ref: 1819 for 96x kit or Ref: 1751 for 20x kit). These kits are used with some modifications introduced by Oryzon genomics. RNA labeling was performed essentially using the Eberwine protocol (Van Gelder, 1992) commercialized by Ambion with the MessageAmplification Kit (Ambion/Applied Biosystems) with minor modifications. 500 ng of total RNA was reverse transcribed in presence of oligo(dT)<sub>24</sub>, second-strand synthesis was generated and transcription of this dsDNA was prepared using CTP\_Cy3 or CTP\_Cy5 (PerkinElmer). Amplified cRNA was quantified by Nanodrop ND-1000 and cRNA quality was controlled with the Agilent RNA Bionalyzer 2100.

#### Microarray hybridization

Microarray hybridization was performed at 60°C and 17 hours hybridization time according to Agilent indications, using Agilent gaskets (G2534-60002), Agilent hybridization chambers (G2534A) and in an Agilent DNA Hybridization Oven (G2545A). Oryzon hybridization controls are also used in hybridization process. Controls for the hybridization process corresponding to 3 cDNA clones of maize (Xet, Zm42, Exp) were included in all analysis. Exp is used as the negative spike control and was not amplified nor labeled. For Xet and Zm42 PCR fragments were

generated by PCR amplification from the vector with universal primers and cRNA was generated using in vitro transcription systems (T7 or T3 Megascript kit; Ambion) with CTP\_Cy3 or CTP\_Cy5 (PerkinElmer). Both of the positive spike controls Xet and Zm42 were with both the Cy5 and Cy3 fluorophore.

#### Data Acquisition

Initial Raw Data were obtained using an Agilent DNA Microarray Scanner (G2505B) and Agilent acquisition software (Feature Extraction Software). The extraction protocol performed does not use background subtraction, computation of dye biases and ratio correction.

#### Data analysis

A large number of controls were included in the microarray designs to monitor scanner and array performance and to control spatial homogeneity and correct deviations. This way, the overall error on the microarray data measurements can be estimated by the spreading analysis of the data from the controls.

The mean fold change or M values can be ranked based on their probability of being different from 0, according to the absolute value of the regularized t-statistic (Baldi and Long, 2001) which uses a Bayesian framework to derive a modified and improved t-student statistics. To make Fold Change based selection, the mean M distribution was used. This distribution is adjusted to a normal distribution and an iterative process is used to define the mean M numbers that are outside the distribution. The cut-off is chosen as n times the Standard deviations ( $\sigma$ ) from the mean. This method generates a robust mean and standard deviation and allows to dynamically adjusting the cut-off value to the noise distribution of the data. Typically, values with mean  $FC > 3\sigma$  or mean  $FC < -3\sigma$  of the sample data distribution were selected.

An indirect analysis comparison where the expression levels of particular biomarkers in tumor samples were compared to a reference RNA pool obtained from a group of over 20 cell lines (melanoma, lung cancer, ovarian cancer, colon cancer, and several non-cancer cell lines). The expression level of particular genes in the normal samples (controls) were compared to the same reference pool and final expression

fold changes between tumor and normal endometrial tissue were generated *in silico* eliminating the reference pool.

Candidate genes were selected as biomarkers for endometrial cancer based on fold overexpression, p-value, and other factors. Table 1 in the Detailed Description of the Invention shows 17 overexpressed genes and 3 genes underexpressed identified using these procedures. The overexpression of these genes was validated by RT-PCR as described in the next examples.

The results from the microarray studies are summarized in Table 1 in the Detailed Description of the Invention, which shows the common abbreviation used for the gene, the ENSEMBL gene, transcript and protein accession numbers along with the fold overexpression and calculated p-values.

#### Example 2: Uterine Fluid Sample Preparation

Endometrial aspirates were collected with the help of a Cornier pipelle, after complete informed consent was obtained from all patients. The aspirate (uterine fluid) was immediately transferred to an eppendorf tube containing 500 microliters of a RNA preserving solution (RNA later, Ambion). The sample was centrifuged and the pellet containing a representative population of cells from the uterine cavity was further processed for RNA extraction (Qiagen). Quality tests (Bioanalyzer) were performed before the analysis of gene expression by Taqman technology for the selected markers of endometrial carcinoma.

#### Example 3: Correlation of Biomarkers in Primary Tumor and in Uterine Fluid

The levels of biomarkers from primary tumor sample and uterine fluid sample obtained by the procedure of Example 2 were compared as by RT-PCR following the general RT-PCR protocol as described in Example 4. The biomarkers in this study included ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN whose expression level was found to be surprisingly correlated between the primary tumor and endometrial aspirates (uterine fluid). See Figure 1. As can be seen in Figure 1, the expression level of a number of biomarkers of endometrial cancer are correlated in uterine fluid and primary tumor. In



particular, it was found that there was a high level of correlation of expression of biomarkers corresponding to ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN in tumor sample and in samples obtained from uterine fluid. Thus, the inventors have surprisingly finding of a group of genes that can be used to diagnosis or predict an increased likelihood of endometrial cancer based on their expression levels in samples obtained from uterine fluid. Furthermore, the inventors have shown that uterine fluid can be used to assess biomarkers for endometrial cancer. For example, prognostic biomarkers for endometrial cancer, biomarkers for staging endometrial cancer, biomarkers for determining the type of endometrial cancer (*e.g.*, Type 1 vs. Type II) or type (endometrioid, clear cell, serrous, *etc.*), auxiliary diagnostic biomarkers, differential diagnosis biomarkers, can be assayed in uterine fluid to characterize the cancer.

Example 4: Confirmation of Overexpression of Biomarkers by quantitative RT-PCR

Once array data were obtained, a group of upregulated and downregulated genes in tumor samples compared with normal tissue were selected in-part based on their p-values and standard deviations. These candidates were selected to determine their expression levels by an independent technique using a different set of tumor samples.

Microfluidic Cards (MFC) from Applied Biosystems were used to perform RT-PCR with RNA isolated from tumor and normal endometrial tissue samples. In this case both types of tissues, healthy and carcinogenic were obtained from the same patient by microdissection procedures. These studies confirmed the microarray results for most of the markers of Table 1. Another set of RT-PCT studies were performed using aspirates obtained from endometrial cancer patients (confirmed) and aspirates from non-affected individuals. These studies using aspirates samples are described in more detail below.

Aspirate samples were obtained following a procedure similar to that described in Example 2. The description of patient characteristics for the affected and non-affected samples are given in Table 4 and Table 5 below.

Briefly, wells of the Microfluidic Card contain Applied Biosystems fluorogenic 5' nuclease assays that detect the real-time amplification of the array selected targets. Relative levels of gene expression are determined from the fluorescence data generated during PCR using the ABI PRISM® 7900HT Sequence Detection System (7900HT SDS) Relative Quantification software.

Data analysis was made using the comparative  $\Delta\Delta C_t$  method of relative quantification. Differentially expressed genes were confirmed by thorough statistical analysis using a modified T- test.

The samples used for the study described in this Example included:

Samples from 30 patients having endometrial cancer: 25 endometroid adenocarcinomas with 9 in G3, 9 in G2 and 7 in G1. And 5 tumor samples from different type II carcinomas (4 in G3 and 1 in G2)

Samples from 24 patients not having endometrial cancer ("controls" or "normals"). These were a heterogeneous mix of samples some of them from patients with other non-tumoral pathologies liked polyps: 4 samples from patients with atrophic endometriod, 4 normal samples, two from patients having polyps from post-menopausical women and 11 samples from pre-menopausical women (7 of them in secretory phase and 4 in proliferative phase of the cycle). See Tables below for a summary of samples.

Table 4: Affected Samples for RT-PCR Studies

| Aspirates from women with a tumor | Sample Diagnosis      | Tumor Grade | FIGO stage |
|-----------------------------------|-----------------------|-------------|------------|
| 1                                 | Endometroid carcinoma | G1          | Ib         |
| 2                                 | Endometroid carcinoma | G1          | Ia         |
| 3                                 | Endometroid carcinoma | G1          | Ib         |
| 4                                 | Endometroid carcinoma | G1          | Ib         |
| 5                                 | Endometroid carcinoma | G1          | Ia         |
| 6                                 | Endometroid carcinoma | G1          | Ia         |
| 7                                 | Endometroid carcinoma | G1          | Ib         |
| 8                                 | Endometroid carcinoma | G2          | Ib         |
| 9                                 | Endometroid carcinoma | G2          | Ib         |
| 10                                | Endometroid carcinoma | G2          | Ib         |
| 11                                | Endometroid carcinoma | G2          | Ib         |
| 12                                | Endometroid carcinoma | G2          | Ib         |
| 13                                | Endometroid carcinoma | G2          | Ia         |
| 14                                | Endometroid carcinoma | G2          | Ia         |
| 15                                | Endometroid carcinoma | G2          | Ib         |
| 16                                | Endometroid carcinoma | G2          | Ib         |
| 17                                | Endometroid carcinoma | G3          | Ib         |
| 18                                | Endometroid carcinoma | G3          | Ic         |
| 19                                | Endometroid carcinoma | G3          | Ic         |
| 20                                | Endometroid carcinoma | G3          | Ib         |
| 21                                | Endometroid carcinoma | G3          | Ic         |
| 22                                | Endometroid carcinoma | G3          | Ib         |
| 23                                | Endometroid carcinoma | G3          | Ib         |
| 24                                | Endometroid carcinoma | G3          | Ib         |
| 25                                | Endometroid carcinoma | G3          | Ic         |
| 26                                | Clara Cell type       | G3          | Ib         |
| 27                                | Clara Cell type       | G3          | IIIc       |
| 28                                | Adeno-squamous        | G3          | IIIa       |
| 29                                | Undifferentiated      | G3          | IIIc       |
| 30                                | squamo-transitional   | G2          | Ib         |

Table 5: Non-Affected Samples for RT-PCR Studies

| Control aspirates                       |
|-----------------------------------------|
| 7 pre-menopausal in secretory phase     |
| 6 pre-menopausal in proliferative phase |
| 11 aspirates from postmenopausal women  |

### Experimental procedures

RNA samples were isolated from aspirate samples following the procedure above described and a quality control was performed previously to final sample selection. Aspirate samples were collected as described in Example 2.

RT-PCR was performed following Applied Biosystem standard protocol for the 7900HT system. The protocol consisted in a two-step method where the first step is

the generation of cDNA from the RNA samples using a High Capacity cDNA Kit and the second step is the amplification of cDNA, once loaded in the MFC, by the ABI PRISM® 7900 HT system.

RT-PCR data were collected for a set of 20 genes identified in Example 1 and quantified relative to POLR2A levels. The RQ values for the aspirates corresponding to the 30 tumor samples and the 24 samples that were not endometrial cancer (normals) are illustrated in a box and whiskers plot, see Figure 2A and 2B. Table 2 in the Detailed Description of the Invention gives a summary of the mean RQ values, standard error of the mean and p-values calculated for these markers in this sample set. As can be seen, the p-values obtained using the control sample set in the microarray studies (Table 1) were significantly improved in a different sample set using different techniques (microarray versus RT-PCR) and different sources of sample (aspirates versus primary tumor). In most cases the p-value improved over 100-fold for the biomarkers. This is related in part to the robust nature of the microarray experimental design and robust selection of markers based on the Inventors' criteria.

The next table shows the sensitivity and specificity for each individual gene on the patent application and the area under de ROC (AUROC) curve for each gene when comparing the RQ values from the 30 tumour samples and the 24 control samples. A support vector machine (SVM) program was used to calculate the data. As can be seen in the table below, the markers identified in these studies have excellent sensitivity and/or specificity for predicting an increased likelihood and/or diagnosis of endometrial cancer. Furthermore, the AUROC values for these biomarkers indicate that these markers are very useful for diagnosis of endometrial cancer.

Table 6: Sensitivity, Specificity and AUROC values for the biomarkers of the invention determined from aspirates samples in affected (endometrial cancer) and non-affected individuals.

| GENE     | sensitivity | specificity | AUROC |
|----------|-------------|-------------|-------|
| ACAA1    | 66.67%      | 90.00%      | 0.81  |
| AP1M2    | 58.33%      | 86.67%      | 0.83  |
| CGN      | 79.17%      | 76.67%      | 0.81  |
| DDR1     | 79.17%      | 90.00%      | 0.89  |
| EPS8L2   | 70.83%      | 86.67%      | 0.81  |
| FASTKD1  | 70.83%      | 76.67%      | 0.84  |
| GMIP     | 75.00%      | 83.33%      | 0.88  |
| IKBKE    | 83.33%      | 73.33%      | 0.90  |
| P2RX4    | 62.50%      | 96.67%      | 0.82  |
| P4HB     | 91.67%      | 96.67%      | 0.97  |
| PHKG2    | 70.83%      | 93.33%      | 0.84  |
| PPFIBP2  | 58.33%      | 96.67%      | 0.78  |
| PPP1R16A | 75.00%      | 80.00%      | 0.85  |
| RASSF7   | 100.00%     | 60.00%      | 0.89  |
| RNF183   | 95.83%      | 73.33%      | 0.88  |
| SIRT6    | 79.17%      | 73.33%      | 0.84  |
| TJP3     | 79.17%      | 76.67%      | 0.82  |
| EFEMP2   | 66.67%      | 83.33%      | 0.88  |
| SOCS2    | 79.17%      | 93.33%      | 0.93  |
| DCN      | 66.67%      | 90.00%      | 0.85  |

Control samples were a heterogeneous group with pre and post-menopausal women. At the same time, aspirates from pre-menopausal women could be divided in two categories depending of the uterine endometrial cycle phase they were when the sample was taken: proliferative or secretory. The characterization of secretory versus proliferative phase patients was accomplished by a pathologist using standard techniques.

Some of the genes tested could give a false positive result for endometrial cancer if the aspirate was taken from pre-menopausal women in secretory phase. In order to check which genes could give false positives depending of the cycle phase or which others could distinguish between tumour samples and secretory phase, we performed a statistical analysis comparing tumours with different control groups.

- tumors versus control samples (all the control samples: 24 samples)
- tumors versus control samples minus the ones in secretory phase: 17 samples
- tumors samples versus control samples in secretory phase: 7 samples

- tumors samples versus control samples from postmenopausal women: 11 samples

The area ROC for each comparison was calculated using the GraphPad Prism program and anova test was applied to see if the differences among these groups were significant.

In the Tables below the following abbreviations are used for p-values:

\*\*\*  $p < 0.0001$

\*\*  $p < 0.001$

\*  $p < 0.01$

ns ( not significant).

As it is shown on the tables there are genes, like P4HB or SOCS2, which separate the tumour samples from the control independently of the nature of the control samples (post-menopausal, pre-menopausal in secretory or in proliferative). Other genes like P2RX4 or PPFIBP2, could distinguish between a tumour sample (affected) and a sample in secretory phase better as compared to controls from postmenopausal women.

This observation opens the possibility of using different algorithms and/or different set of genes depending if the test is interrogating pre-menopausal or post-menopausal women. Furthermore, a primary modality for screening for endometrial problems is the trans-vaginal ultrasound which is used to estimate endometrial thickness where patients having a thicker endometrium (over a certain threshold) are likely to have endometrial cancer or another disease or condition. Endometrium thickness also varies as a function of the phase of the menstrual with individuals in secretory phase having a thicker endometrium as compared to individuals in proliferative phase. Thus, these finding indicate that the methods and biomarkers of the invention can be used to aid and improve the ability of transvaginal ultrasound to identify endometrial cancer.

Table 7: Summary of Data for RT-PCR Studies comparing the expression levels of biomarkers in aspirates (30) from patients affected with endometrial cancer and aspirates obtained from individuals all patients non affected with endometrial cancer (24).

| Comparison por 30T/ 24Ctrl | ROC 30Tvs24Ctrl | Anova |
|----------------------------|-----------------|-------|
| P4HB                       | 0.974           | ***   |
| SOCS2                      | 0.955           | ***   |
| IKBKE                      | 0.897           | ***   |
| RNF183                     | 0.883           | ***   |
| EFEMP2                     | 0.881           | ***   |
| PHKG2                      | 0.875           | ***   |
| DCN                        | 0.854           | ***   |
| PPP1R16A                   | 0.846           | ***   |
| AP1M2                      | 0.843           | ***   |
| FASTKD1                    | 0.838           | ***   |
| SIRT6                      | 0.836           | ***   |
| CGN                        | 0.829           | ***   |
| GMIP                       | 0.824           | ***   |
| TJP3                       | 0.824           | ***   |
| RASSF7                     | 0.817           | ***   |
| ACAA1                      | 0.817           | ***   |
| EPS8L2                     | 0.813           | ***   |
| P2RX4                      | 0.807           | ***   |
| DDR1                       | 0.769           | **    |
| PPFIBP2                    | 0.745           | *     |

Table 7 shows that the 20 biomarkers capable of distinguishing aspirates from endometrial cancer affected patients from aspirate from all control non-affected patients with high ROC values and/or excellent statistical significance.

Table 8: Summary of Data for RT-PCR Studies comparing the expression levels of biomarkers in aspirates (30) from patients affected with endometrial cancer and aspirates obtained from individuals patients non-affected with endometrial cancer and that were not in secretory phase (17)

| <b>comparison 30T/ 17 Ctrl</b> | <b>ROC 30T vs 17Ctrl</b> | <b>Anova</b> |
|--------------------------------|--------------------------|--------------|
| <b>P4HB</b>                    | <b>0.963</b>             | <b>***</b>   |
| <b>SOCS2</b>                   | <b>0.936</b>             | <b>***</b>   |
| <b>RNF183</b>                  | <b>0.904</b>             | <b>***</b>   |
| <b>EFEMP2</b>                  | <b>0.900</b>             | <b>***</b>   |
| <b>FASTKD1</b>                 | <b>0.863</b>             | <b>***</b>   |
| <b>AP1M2</b>                   | <b>0.859</b>             | <b>***</b>   |
| <b>IKBKE</b>                   | <b>0.858</b>             | <b>***</b>   |
| <b>PHKG2</b>                   | <b>0.845</b>             | <b>***</b>   |
| <b>CGN</b>                     | <b>0.832</b>             | <b>***</b>   |
| <b>SIRT6</b>                   | <b>0.828</b>             | <b>**</b>    |
| <b>PPP1R16A</b>                | <b>0.817</b>             | <b>**</b>    |
| <b>DCN</b>                     | <b>0.801</b>             | <b>**</b>    |
| <b>TJP3</b>                    | <b>0.8</b>               | <b>**</b>    |
| <b>GMIP</b>                    | <b>0.798</b>             | <b>***</b>   |
| <b>RASSF7</b>                  | <b>0.798</b>             | <b>**</b>    |
| <b>ACAA1</b>                   | <b>0.784</b>             | <b>**</b>    |
| <b>EPS8L2</b>                  | <b>0.767</b>             | <b>**</b>    |
| <b>P2RX4</b>                   | <b>0.728</b>             | <b>*</b>     |
| <b>DDR1</b>                    | <b>0.680</b>             | <b>ns</b>    |
| <b>PPFIBP2</b>                 | <b>0.644</b>             | <b>ns</b>    |

Table 8 shows the rankings of 20 biomarkers of the invention capable of distinguishing aspirates from endometrial cancer affected patients from aspirates from all control non-affected patients excluding patients in the secretory phase. Table 7 shows the biomarkers of the invention have high ROC values and/or excellent statistical significance for separating these populations.



Table 9: Summary of Data for RT-PCR studies comparing the expression levels of biomarkers in aspirates (30) from patients affected with endometrial cancer and aspirates obtained from individuals patients non affected with endometrial cancer and that were in secretory phase (7)

| <b>comparison 30T/ 7 Sec</b> | <b>ROC 30T vs 7 Sec</b> | <b>Anova</b> |
|------------------------------|-------------------------|--------------|
| <b>P4HB</b>                  | <b>1</b>                | <b>**</b>    |
| <b>SOCS2</b>                 | <b>1.000</b>            | <b>***</b>   |
| <b>P2RX4</b>                 | <b>1</b>                | <b>***</b>   |
| <b>IKBKE</b>                 | <b>0.991</b>            | <b>***</b>   |
| <b>PPFIBP2</b>               | <b>0.991</b>            | <b>**</b>    |
| <b>DDR1</b>                  | <b>0.986</b>            | <b>**</b>    |
| <b>DCN</b>                   | <b>0.981</b>            | <b>**</b>    |
| <b>PHKG2</b>                 | <b>0.948</b>            | <b>**</b>    |
| <b>EPS8L2</b>                | <b>0.924</b>            | <b>*</b>     |
| <b>PPP1R16A</b>              | <b>0.917</b>            | <b>**</b>    |
| <b>GMIP</b>                  | <b>0.9</b>              | <b>*</b>     |
| <b>ACAA1</b>                 | <b>0.895</b>            | <b>*</b>     |
| <b>TJP3</b>                  | <b>0.881</b>            | <b>*</b>     |
| <b>RASSF7</b>                | <b>0.864</b>            | <b>*</b>     |
| <b>SIRT6</b>                 | <b>0.857</b>            | <b>*</b>     |
| <b>EFEMP2</b>                | <b>0.833</b>            | <b>ns</b>    |
| <b>RNF183</b>                | <b>0.831</b>            | <b>ns</b>    |
| <b>CGN</b>                   | <b>0.82</b>             | <b>ns</b>    |
| <b>AP1M2</b>                 | <b>0.805</b>            | <b>ns</b>    |
| <b>FASTKD1</b>               | <b>0.779</b>            | <b>ns</b>    |

As can be seen in the Table 9 preferred markers capable of distinguishing aspirates from endometrial cancer affected patients from aspirates from non-endometrial cancer affected patients in secretory phase include P4HB, SOCS2 P2RX4, IKBKE, PPFIB2, DDR1 and DCN which have high ROC values and/or excellent statistical significance.

As seen from the data in Tables 7 & 9 above examples of genes capable of differentiating between aspirates from patients having tumor and aspirates from all non-affected patients (including secretory phase) and/or between aspirates from patients having tumor and aspirates from non-affected patients in secretory phase include P4HB, SOCS2, and IKBKE which have high statistical significance and ROC values.

Table 10: Summary of Data for RT-PCR Studies comparing the expression levels of biomarkers in aspirates (30) from patients affected with endometrial cancer and aspirates obtained from post-menopausal patients non affected with endometrial cancer (11).

| Ranking por 30T/ 11N | ROC 30Tvs11ctrl postm | Anova |
|----------------------|-----------------------|-------|
| PHKG2                | 0.9476                | *     |
| P4HB                 | 0.9424                | ***   |
| EFEMP2               | 0.903                 | ***   |
| RNF183               | 0.8909                | ***   |
| SOCS2                | 0.8667                | *     |
| FASTKD1              | 0.8439                | **    |
| GMIP                 | 0.8394                | **    |
| SIRT6                | 0.8364                | **    |
| AP1M2                | 0.8182                | *     |
| IKBKE                | 0.7955                | ns    |
| CGN                  | 0.7864                | *     |
| PPP1R16A             | 0.7652                | ns    |
| TJP3                 | 0.7515                | ns    |
| RASSF7               | 0.7515                | ns    |
| ACAA1                | 0.7242                | ns    |
| DCN                  | 0.7167                | ns    |
| EPS8L2               | 0.697                 | ns    |
| P2RX4                | 0.6303                | ns    |
| DDR1                 | 0.5879                | ns    |
| PPFIBP2              | 0.5318                | ns    |

As can be seen in the Table 10 preferred markers capable of distinguishing aspirates from endometrial cancer affected patients from aspirate from post menopausal non endometrial cancer affected patients include PHKG2, P4HB, EFEMP2, RNF183, and SOCS2 which have high ROC values and/or excellent statistical significance.

In reference to Figure 2A and 2B (box and whisker plot), RQ: relative quantity, it is the relative amount of RNA for a specific gene present on the tumours samples referred to the amount present on the control sample for the same gene.

To calculate the RQ the Ct values of each gene were normalise respect to the Ct of the endogenous gene to get the delta Ct. The formula  $2^{-(\text{delta Ct})}$  was used to calculate de RQ.

A number of endogenous genes can be used as a control for normalization as well as other controls for normalization. In one example a preferred endogenous gene has the following characteristics: it is a gene constitutively expressed in the same tissue under different circumstances like for example cancer development. So it could be used to normalize differences in the amount of cDNA when loading the samples or variations due to experimental reasons for the qRT-PCR.

We have tested four different housekeeping genes as possible endogenous genes for normalization purposes: 18S, B2M, PFN-1 and POLR2A. Finally, POLR2A was the most stable gene from all of them and all the calculations and statistics were done using it as endogenous. Its expression level is similar to the genes questioned in our test and different as compared to 18 S whose expression is quite high compared to the genes selected for the test. It is contemplated that endogenous biomarkers such as POLR2A, B2M, PFN1, HMBS, G6PD, or PABPN1 or another stable gene can be used for normalization purposes in the methods of the invention if they so require.

#### Example 5: Profiles for Diagnosing Endometrial Cancer

A support vector machine based algorithm was used to identify combinations of markers of Table 1 that are useful for predicting endometrial cancer and/or an increased likelihood of having endometrial cancer. In particular, the publically available program DTREG program was used to analyze the data (see the www at DTREG.COM).

Support vector machine algorithm can be used for many applications including identifying gene expression profiles for separating populations having different phenotypic characteristics. The idea behind the algorithm is a multidimensional representation of the data, *e.g.*, each marker is plotted on a different dimension and a plane is sought through this multidimensional representation of the data that can separate the phenotypes. The plane through the “middle” is referred to as the separating hyperplane and represents a solution: answers (*e.g.*, expression level over a given threshold value) that fall on one side of the line fall into one category (*e.g.*, cancer) and answers (*e.g.*, expression level over a given threshold value) that follow on the other side of the line correspond to the other category (*e.g.*, no cancer). A

number of separating hyper plane can be possible for each dataset. The question becomes which is the best separating hyperplane. In support vector machine theory, the best solution is referred to as the maximum margin hyperplane. This maximum margin hyperplane is the one that separates the two groups and adopts the maximal distance from any one of the given expression profiles.

Although individual genes show a high sensitivity and specificity, these parameters are even higher when combined several genes. Some examples of the sensitivity, specificity and AUROC genes combined two to two, three to three, four to four, five to five, six to six, seven to seven and all of them together. See the Table below for a summary of the data.

Table 11: Data Summarizing Predictive Values for Combinations

| combinations                                                                    | sensitivity | specificity | AUROC |
|---------------------------------------------------------------------------------|-------------|-------------|-------|
| IKBKE+P4HB                                                                      | 91.67%      | 100.00%     | 0.978 |
| IKBKE+SOCS2                                                                     | 79.17%      | 96.67%      | 0.951 |
| P4HB+SOCS2                                                                      | 91.67%      | 100.00%     | 1     |
| GMIP+IKBKE                                                                      | 79.17%      | 90.00%      | 0.915 |
| GMIP+P4HB                                                                       | 95.83%      | 96.67%      | 0.982 |
| GMIP+SOCS2                                                                      | 100.00%     | 86.67%      | 0.999 |
| GMIP+SOCS2+IKBKE                                                                | 95.83%      | 100.00%     | 1     |
| GMIP+SOCS2+P4HB                                                                 | 91.67%      | 100.00%     | 0.983 |
| GMIP+IKBKE+P4HB                                                                 | 91.67%      | 100.00%     | 0.978 |
| IKBKE+P4HB+SOCS2                                                                | 91.67%      | 100.00%     | 0.981 |
| GMIP+IKBKE+P4HB+SOCS2                                                           | 100.00%     | 100.00%     | 1     |
| GMIP+SOCS2+IKBKE+EPS8L2                                                         | 91.67%      | 100.00%     | 0.993 |
| GMIP+SOCS2+P4HB+EPS8L2                                                          | 91.67%      | 100.00%     | 0.976 |
| GMIP+IKBKE+P4HB+EPS8L2                                                          | 91.67%      | 100.00%     | 0.976 |
| IKBKE+P4HB+SOCS2+EPS8L2                                                         | 87.50%      | 100.00%     | 0.981 |
| GMIP+IKBKE+P4HB+SOCS2+DDR1                                                      | 91.67%      | 100.00%     | 1     |
| GMIP+IKBKE+P4HB+SOCS2+EPS8L2+PPP1R16A                                           | 91.67%      | 100.00%     | 0.999 |
| GMIP+IKBKE+P4HB+SOCS2+PHKG2+RASSF7                                              | 95.83%      | 100.00%     | 1     |
| GMIP+IKBKE+P4HB+SOCS2+DDR1+EPS8L2                                               | 95.83%      | 100.00%     | 1     |
| GMIP+IKBKE+P4HB+SOCS2+EPS8L2+PPP1R16A+DDR1                                      | 95.83%      | 100.00%     | 1     |
| DDR1+EPS8L2+GMIP+IKBKE+P2RX4+P4HB+PHKG2+PPP1R16A+RASSF7+SIRT6+TJP3+SOCS2        | 100.00%     | 100.00%     | 1     |
| DDR1+EPS8L2+GMIP+IKBKE+P2RX4+P4HB+PHKG2+PPP1R16A+RASSF7+SIRT6+TJP3+SOCS2+RNF183 | 100.00%     | 100.00%     | 1     |
| ALL TOGETHER: 20 GENES                                                          | 100.00%     | 100.00%     | 1     |

As can be seen in the Table above very high sensitivity and specificities were obtained for combinations of the biomarkers of the invention and the AUROC values are very high. Thus, these results show that combinations of 2 or more markers chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS2, and DCN give unexpectedly good sensitivity and specificity for predicting an increased likelihood and/or diagnosing endometrial cancer. These results were obtained from samples from uterine fluid and indicate that combinations of biomarkers detected in uterine fluid can be useful for diagnosing and/or characterizing endometrial cancer. Furthermore, these results were obtained in samples from pre and post menopausal women and therefore represents a set of

markers that can be examined across these types of patients. It is noted that different programs and algorithms can be used to generate profiles or fingerprint patterns. The invention is intended to encompass profiles and/or fingerprint patterns using programs and algorithms other than DTREG as used herein. The profiles identified in Table 11 are non-limiting examples used to illustrate that combinations of the biomarkers of Table 1 have excellent sensitivity and specificity for endometrial cancer.

#### Additional combinations

The values of sensitivity and specificity although fully define the validity of a diagnostic test have the disadvantage of not providing relevant information when making a clinical decision to a particular test result. However, they have the advantage of being intrinsic properties to the test and define its validity irrespective of the prevalence of the disease in the population to which it applies.

#### Sensitivity

It is the probability of classifying correctly an individual patient or the probability that a individual with cancer obtains a positive result when applying the diagnostic test

#### Specificity

It is the probability of classifying correctly a healthy individual or the probability that a healthy individual obtaining a negative result when applying the diagnostic test. Sensitivity and specificity can, therefore, to assess the validity of a diagnostic test. However, these concepts are not much help in clinical practice. When a patient undergoes a diagnostic test, the doctor has no a priori information about their diagnosis so the question arises to the next one: given a positive (or negative) on the test? What is the probability that the individual tested has the disease (or not)? These probabilities are known as positive predictive value and negative predictive value of a particular test. Positive predictive value is the probability of having the disease if the individual has a positive result when applying the diagnostic test. Negative predictive value is the probability that an individual who has obtained a negative result on the test, is actually healthy.

Clinicians prefer diagnostic tests with high negative predictive value as they can not allow people with cancer get a wrong diagnosis. For this reason we have prioritized these combinations which give us the highest negative predictive values.

The follow values in Table 12 were calculated using the indicated markers as determined by RT-PCR in uterine fluid samples.

Table 12

| combinations                                                      | DTREG-SVM   |             |       |         |         |
|-------------------------------------------------------------------|-------------|-------------|-------|---------|---------|
|                                                                   | sensitivity | specificity | AUROC | NPV     | PPV     |
| P4HB+SOCS2                                                        | 91.67%      | 100.00%     | 1     | 93.75%  | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2                                             | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+FASTKD1                                     | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+DDR1                                        | 95.83%      | 100.00%     | 1     | 96.77%  | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+PHKG2                                       | 91.67%      | 100.00%     | 1     | 93.75%  | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+SIRT6                                       | 91.67%      | 100.00%     | 1     | 93.75%  | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+ACAA1                                       | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+AP1M2                                       | 91.67%      | 96.67%      | 0.979 | 93.65%  | 95.65%  |
| GMIP+IKBKE+P4HB+SOCS2+EFEMP2                                      | 91.67%      | 100.00%     | 1     | 93.75%  | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+EPS8L2                                      | 91.67%      | 100.00%     | 1     | 93.75%  | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+P2RX4                                       | 83.33%      | 96.67%      | 0.964 | 87.88%  | 95.24%  |
| GMIP+IKBKE+P4HB+SOCS2+PPFIBP2                                     | 91.67%      | 96.67%      | 0.979 | 93.65%  | 95.65%  |
| GMIP+IKBKE+P4HB+SOCS2+PPP1R16A                                    | 95.83%      | 100.00%     | 1     | 96.77%  | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+ACAA1+FASTKD1                               | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+FASTKD1+PHKG2                               | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| GMIP+IKBKE+P4HB+SOCS2+FASTKD1+SIRT6                               | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| ACAA1+AP1M2+EPS8L2+IKBKE+P2RX4+P4HB+PPFIBP2+PPP1R16A+SIRT6+EFEMP2 | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| GMIP+IKBKE+P4HB+EFEMP2                                            | 100.00%     | 93.33%      | 0.999 | 100.00% | 92.31%  |
| DDR1+FASTKD1+GMIP+IKBKE+P4HB+PHKG2+SIRT6+EFEMP2+SOCS2             | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| DDR1+FASTKD1+GMIP+IKBKE+P4HB+PHKG2+SIRT6+EFEMP2                   | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |
| P4HB+EFEMP2+IKBKE+GMIP+FASTKD1                                    | 100.00%     | 100.00%     | 1     | 100.00% | 100.00% |

The combinations shown in FIG. 18 (P4HB, EFEMP2, SIRT6, DDR1, GMIP, and FASTKD1) and FIG. 19 (P4HB, EFEMP2, SIRT6, PHKG2, GMIP, and FASTKD1), and the combination of all 20 markers have sensitivities, specificities, NPVs, and PPVs of 100% and AUROCs of 1.

Maximizing Negative Predictive Value: New samples: three new cancer samples and 24 no tumor samples giving a total amount of samples in the following analysis (33T and 48 non tumor) with the additional sample having the following characteristics:

| Aspirates from women with a tumor | Sample Diagnosis                | Tumor Grade | FIGO stage |
|-----------------------------------|---------------------------------|-------------|------------|
| 31                                | Endometroid carcinoma           | G1          | IA         |
| 32                                | Endometroid carcinoma           | G2          | IB         |
| 33                                | Endometroid/squamo-transitional | G3          | IA         |

| <b>Control aspirates</b>                |
|-----------------------------------------|
| 4 pre-menopausal in secretory phase     |
| 5 pre-menopausal in proliferative phase |
| 4 pre-menopausal ( unknown cycle phase) |
| 11 aspirates from postmenopausal women  |

The calculated the risk of cancer for 48 non tumor and 33 tumor samples using the following combination of genes ACAA1, AP1M2, EPS8L2, IKBKE, P2RX4, P4HB, PPFIBP2, PPP1R16A, SIRT6, and EFEMP2 the result is shown in FIG. 17.

FIG. 18 shows the calculated risk of cancer for the 48 non-tumor and 33 tumor samples using FASTKD1, GMIP, P4HB, EFEMP2, DDR1, and SIRT6.

FIG. 19 shows the calculated risk of cancer for the 48 non-tumor and 33 tumor samples using FASTKD1, GMIP, P4HB, EFEMP2, PHKG2, and SIRT6.

As shown on FIG. 17, the first combination is able to classify all the samples correctly but the percentage of some healthy samples of having cancer are very close to 50%: some cancer samples are too close to be misclassified when using this combination. In summary, the risk of misclassifying cancer patients with a false diagnosis. Although the combinations in FIG. 18 and FIG. 19 misclassify one and two healthy patients samples respectively, both of them classify correctly all the cancer patients and they do it with a higher percentage of risk of cancer than the previous combination. For that reason these combinations are valuable from a clinical point of view. Example 6: Detection of Protein Corresponding to the Biomarkers of Table 1

Detection of protein corresponding to the Biomarkers of Table 1 can be accomplished by any number of means available to the skill artisan. According to this method samples from controls (or a control value is established) and affected individuals are obtained (*e.g.*, serum, tissue, and uterine fluid) and probe for with antibodies selective or specific to the particular biomarker. One method for detecting the proteins is by western blot analysis and is exemplified as in the case of P4HB.

Western blot analysis from human samples from normal endometrial tissue and tumour endometrial cancer tissues in order to test the protein level of P4HB (approx. 60 kDa) in these samples.

Gels were loaded with 40 µg of total protein extracts from each sample. As can be seen in Figure 10, tumor samples stained much more strongly for P4HB as compared to normal tissue.

The samples tested include four normal tissues (N) and four tumour tissues (T). Normal and tumour tissues were obtained from the same patient. As a positive control: total protein extract from the endometrial tumour cell line Isikawa. The Antibody used: LS-C38385 from LifeSpan.

The results confirm to protein level the results obtained in the array and the TaqMan experiments.

Western blot analysis was performed for AP1M2, IKBKE, EPS8L2, DDR1, CGN, and TJP3. See FIG.1 through FIG.5. These results confirm at the protein level the results obtained in the array and the TaqMan experiments for these biomarkers.

For immunohistochemistry validation, tissue microarrays were constructed. In order to cover the complete range from normal tissue to different types and grades of endometrial carcinomas, representative areas from 70 paraffin-embedded carcinomas (56 endometrioid, 6 serous papillary, 1 mucinous, 4 clear cell carcinomas, 3 carcinosarcomas), and 11 non-neoplastic endometria (4 atrophic, 3 proliferative, 1 secretory endometrial and 3 hyperplasias), were carefully selected and marked on individual paraffin blocks. Two tissue cores of 1mm in diameter were obtained from each paraffin block and were precisely arrayed in a new paraffin block. Sections of 5µm were obtained from all tissue microarray paraffin blocks. The protocol was approved by the Institutional Review Board at Hospital Vall D'Hebron, and informed consent was obtained from all of the patients. P4HB, PPP1R16A and EPS8L2 were detected by the indirect immunoperoxidase assay with citrate buffer pH 7.3 for antigen retrieval. Sections were incubated with a primary antibodies against P4HB (LS-C38385) and PPP1R16A (H00084988-M06) for 1 h at room temperature using a



dilution 1:500 and 1:100, respectively, and EPS8L2 (H00064787-B01) overnight at 1:100 dilution. Thereafter sections were incubated with peroxidase conjugated goat anti-mouse immunoglobulin (EnVision Dual System, DAKO, Glostrup, Denmark). Endogenous peroxidase activity was quenched with 3% H<sub>2</sub>O<sub>2</sub>. Sections were washed, and reactions were developed with diaminobenzidine, followed by counterstaining with haematoxylin. Semiquantitative evaluation of the proteins was performed by three independent investigators, scoring the intensity of the stained and the percentage of positive cells.

TMA immunohistochemistry confirmed the differential expression of the three proteins at the tumoral glands when compared to the normal endometrial glands. P4HB, PPP1R16A and EPS8L2 presented a specific cytoplasmatic expression within the tumoral cells in all carcinoma histological types and grades, and an absence or faint cytoplasmatic stain within the normal epithelial glands. These results confirm at the protein level the results obtained for these proteins in the microarray and quantitative PCR experiments described herein. Example 7: ACAA1

ACAA1 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that ACAA1 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that ACAA1 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the methods described in Examples 2-4. Example 5 shows that ACAA1 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to ACAA1 is given in ENSEMBL accession no. ENST00000333167 and has a sequence as in SEQ ID NO:1

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1 ATGTGGTTCTGCGCGTGTGCGGACGGCTGTCTGTAACTCCGCGGTGAGTTCCCGGACTG
61 GTGGCTGGTCTGCAGGGTTGACCTGCGCAATGCAGAGGCTGCAGGTAGTGCTGGGGCCACC
121 TGAGGGGTCCGGCCGATTCCGGCTGGATGCCGCAGGCCGCGCCTTGCTGAGCGGTGCC
181 CGCAGGCCTCGGCCGCGGACGTGGTGGTGGTGCACGGGCGGCGCACGGCCATCTGCCGGG
241 CGGGCCGCGGCGGCTTCAAGGACACCACCCCGACGAGCTTCTCTCGGCAGTCATGACCG
301 CGGTTCTCAAGGACGTGAATCTGAGGCCGGAACAGCTGGGGGACATCTGTGTGCGAAATG
361 TGCTGCAGCCTGGGGCCGGGCAATCATGGCCCGAATCGCCAGTTTCTGAGTGACATCC
421 CGGAGACTGTGCCTTTGTCCACTGTCAATAGACAGTGTTCGTCGGGGCTACAGGCAGTGG

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481 CCAGCATAGCAGGTGGCATCAGAAATGGGTCTTATGACATTGGCATGGCCTGTGGGGTGG  
 541 AGTCCATGTCCCTGGCTGACAGAGGGAACCCTGGAAATATTACTTCGCGCTTGATGGAGA  
 601 AGGAGAAGGCCAGAGATTGCCTGATTCCTATGGGGATAACCTCTGAGAATGTGGCTGAGC  
 661 GGTTCGGCATTTACGGGAGAAGCAGGATACCTTTGCCCTGGCTTCCCAGCAGAAGGCAG  
 721 CAAGAGCCCAGAGCAAGGGCTGTTTCCAAGCTGAGATTGTGCCTGTGACCACCACGGTCC  
 781 ATGATGACAAGGGCACCAAGAGGAGCATCACTGTGACCCAGGATGAGGGTATCCGCCCCA  
 841 GCACCACCATGGAGGGCCTGGCCAAACTGAAGCCTGCCTTCAAGAAAGATGGTTCTACCA  
 901 CAGCTGGAAACTCTAGCCAGGTGAGTGATGGGGCAGCTGCCATCCTGCTGGCCCGGAGGT  
 961 CCAAGGCAGAAGAGTTGGGCCTTCCCATCCTTGGGGTCCTGAGGTCTTATGCAGTGGTTG  
 1021 GGGTCCACCTGACATCATGGGCATTGGACCTGCCTATGCCATCCCAGTAGCTTTGCAAA  
 1081 AAGCAGGGCTGACAGTGAGTGACGTGGACATCTTCGAGATCAATGAGGCCTTTGCAAGCC  
 1141 AGGCTGCCTACTGTGTGGAGAAGCTACGACTCCCCCTGAGAAGGTGAACCCCTGGGGG  
 1201 GTGCAGTGGCCTTAGGGCACCCACTGGGCTGCACTGGGGCACGACAGGTCATCACGCTGC  
 1261 TCAATGAGCTGAAGCGCCGTGGGAAGAGGGGCATACGGAGTGGTGTCCATGTGCATCGGGA  
 1321 CTGGAATGGGAGCCGCTGCCGTCTTTGAATACCCTGGGAACTGAGTGAGGTCCCAGGCTG  
 1381 GAGGCGCTACGCAGACAGTCTGTCTTAGCAGCAAGGCAGTAACACCACAAAAGCAA  
 1441 AACCACATGGGAAAACCTCAGCACTGGTGCTGGTGGCAGTGGACAGATCAAGGCACTTCAA  
 1501 CTCATTTGGAAAATGTGAACACTGATGACATGGTATAGGAGTGGGTGGGGTGTGAGCCA  
 1561 CCCATCAGACCCTCTTTAGCTGTGCAAGATAAAAGCAGCCTGGGTACCCAGGCCACAAG  
 1621 GCCATGGTTAATTCTTAAGGCAAGGCAAATCCATGGATGAGAAGTGCAATGGGCATAGTA  
 1681 AAAGTGCATGAATTT

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000333664 and has a sequence as in SEQ ID NO:2

1 MQRLQVVLGHLRGPADSGWMPQAAPCLSGAPQASAADV VVHGRRTAICRAGRGGFKD TT  
 61 PDELLSAVMTAVLKDVNLRPEQLGDICVGNVLQPGAGAIMARIAQFLSDIPETVPLSTVN  
 121 RQSSSLQAVASIAGGIRNGSYDIGMACGVESMSLADRGNPGNITSRLMEKEKARDCLIP  
 181 MGITSENV AERFGISREKQDTFALASQQAARAQSKGCFQAEIVPVT TTVHDDKGTKRSI  
 241 TVTQDEGIRPSTTMEGLAKLP AFKKDGSTTAGNSSQVSDGAAAILLARRSKAEELGLPI  
 301 LGVLSYAVVGVPPDIMGIGPAYAIPVALQKAGLTVSDVDIFEINEAFASQAAYCVEKLR  
 361 LPPEKVNPLGGAVALGHPLGCTGARQVITLLNELKRRGKRAYGVVSMCIGTGMGAAAVFE  
 421 YPGN

Primers for amplifying the sequence ACAA1 can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying ACAA1 include those in

Forward SEQ ID NO:3 GAGCTTCTCTCGGCAGTCAT  
 Reverse SEQ ID NO:4 CTCAGAAACTGGGCGATTC

Forward SEQ ID NO:5 GCAATCATGGCCCGAATC  
 Reverse SEQ ID NO:6 CCCCAGCAACACTGTCTAT

Forward SEQ ID NO:7 GTGCCTTTGTCCACTGTCAA  
 Reverse SEQ ID NO:8 ACAGGCCATGCCAATGTC

Forward SEQ ID NO:9 TCACGGGAGAAGCAGGATAC  
 Reverse SEQ ID NO:10 CTCTTGGTGGCCTTGTCATC

Forward SEQ ID NO:11 GGCTGACAGTGAGTGACGTG

Reverse SEQ ID NO:12 AGGGGGTTCACCTTCTCAG

Forward SEQ ID NO:13 GTGGCATCAGAAATGGGTCT

Reverse SEQ ID NO:14 CTCTGGCCTTCTCCTTCTCC

Forward SEQ ID NO:15 ATTACTTCGCGCTTGATGGA

Reverse SEQ ID NO:16 AGGGCAAAGGTATCCTGCTT

Forward SEQ ID NO:17 GCCTGCCTTCAAGAAAGATG

Reverse SEQ ID NO:18 TAAGACCTCAGGACCCCAAG

Forward SEQ ID NO:19 TGGGGTCCTGAGGTCTTATG

Reverse SEQ ID NO:20 TCTCGAAGATGTCCACGTCA

Forward SEQ ID NO:21 GTGGCATCAGAAATGGGTCT

Reverse SEQ ID NO:22 AGGGCAAAGGTATCCTGCTT

Forward SEQ ID NO:23 TGACCCAGGATGAGGGTATC

Reverse SEQ ID NO:24 TCTCGAAGATGTCCACGTCA

Forward SEQ ID NO:25 GGAGACTGTGCCTTTGTCCA

Reverse SEQ ID NO:26 CTCTGTCAGCCAGGGACAT

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting ACAA1 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include

SEQID NO:27 CGGTTCTCAAGGACGTGAAT

SEQ ID NO:28 AGTGACATCCCGGAGACTGT

SEQ ID NO:29 GTGGCATCAGAAATGGGTCT

SEQ ID NO:30 AGCTGAGATTGTGCCTGTGA

SEQ ID NO:31 ATCAATGAGGCCTTTGCAAG

SEQ ID NO:32 ACAGAGGGAACCCTGGAAAT

SEQ ID NO:33 GATTGCCTGATTCCTATGGG

SEQ ID NO:34 GTCCAAGGCAGAAGAGTTGG

SEQ ID NO:35 ATGCCATCCCAGTAGCTTTG

SEQ ID NO:36 GCCTGTGGGATAACCTCTGA

SEQ ID NO:37 AAAGTGAAGCCTGCCTTCAA

SEQ ID NO:38 ATAGACAGTGTTTCGTCGGGG

A probe for detecting a ACAA1 nucleic acid that was used on the microarray has a sequence as in SEQ ID NO:39

GCTACGCAGACAGTCCTGCTGCTCTAGCAGCAAGGCAGTAACACCACAAAA  
GCAAAACCA

Other probes to ACAA1 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against ACAA1 include, but are not limited to, Rabbit polyclonal anti-ACAA1 Cat# HPA006764 from atlas antibodies (just recognizes the first transcript); and Mouse polyclonal antibody raised against a full-length human ACAA1 protein. Catalog # : H00000030-B01 from abnova (MaxPab).

#### Example 8: AP1M2

AP1M2 (adaptor-related protein complex 1, mu 2 subunit) also known as D9Erd818e, HSMU1B, MU-1B, MU1B ) was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that AP1M2 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that AP1M2 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Examples 2-4. Example 5 shows that AP1M2 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

AP1M2 is a subunit of the heterotetrameric clathrin adaptor-related protein complex 1 (AP-1), that play pivotal roles in many vesicle trafficking pathways within the cell. This protein is capable of interacting with tyrosine-based sorting signals. AP1 is expressed exclusively in epithelial cells. All AP complexes comprise two large subunits of 100–130 kDa ( $\alpha$  and  $\beta$ 1 in AP1), a medium subunit of 50 kDa ( $\mu$ 1 in AP1), and a small subunit of 17–20 kDa ( $\sigma$ 1 in AP1). PMID: 10338135

In clathrin-coated vesicles, AP-2 is located between the lipid bilayer and clathrin lattice, and presumably is anchoring clathrin to membrane. AP1M2 is member of the adaptor medium chain family termed Mu1B, which is specifically expressed in polarized epithelial cells and some exocrine cells. Mu1B is most closely related to

the ubiquitously-expressed MulA subunit of AP-1 (79% identity at the amino acid level).

The sequence of an mRNA corresponding to AP1M2 is given in ENSEMBL accession number ENST00000250244 and has a sequence as in SEQ ID NO:40

```
GGCGCTTCCGCAGGAAGAAGGAAGCGGGCGCGCCATCGCCTCCCGGCGCTCCCTCCCGACTCCTAAGTC
CTTCGGCCGCCACCATGTCCGCTCGGCTGTCTTCATTCTGGACGTTAAGGGCAAGCCATTGATCAGCCG
CAACTACAAGGGCGATGTGGCCATGAGCAAGATTGAGCACTTCATGCCTTTGCTGGTACAGCGGGAGGAG
GAAGGCGCCCTGGCCCCGCTGCTGAGCCACGGCCAGGTCCACTTCCTATGGATCAAACACAGCAACCTCT
ACTTGGTGGCCACCACATCGAAGAATGCCAATGCCTCCCTGGTGTACTCCTTCCTGTATAAGACAATAGA
GGTATTCTGCGAATACTTCAAGGAGCTGGAGGAGGAGAGCATCCGGGACAACCTTTGTCATCGTCTACGAG
TTGCTGGACGAGCTCATGGACTTTGGCTTCCCGCAGACCACCGACAGCAAGATCCTGCAGGAGTACATCA
CTCAGCAGAGCAACAAGCTGGAGACGGGCAAGTCACGGGTGCCACCCACTGTCACCAACGCTGTGTCTTG
GCGCTCCGAGGGTATCAAGTATAAGAAGAACGAGGTCTTCATTGATGTCATAGAGTCTGTCAACCTGCTG
GTCAATGCCAACGGCAGCGTCCTTCTGAGCGAAATCGTCGGTACCATCAAGCTCAAGGTGTTTCTGTGAG
GAATGCCAGAGCTGCGGCTGGGCCTCAATGACCGCGTGCTCTTCGAGCTCACTGGCCGAGCAAGAACAA
ATCAGTAGAGCTGGAGGATGTAAATTCACACAGTGCGTGCGGCTCTCTCGCTTTGACAACGACCGCACC
ATCTCCTTCATCCCGCTGATGGTGACTTTGAGCTCATGTATACCGCCTCAGCACCAGGTCAAGCCAC
TGATCTGGATTGAGTCTGTCTATTGAGAAGTTCTCCACAGCCGCGTGGAGATCATGGTCAAGGCCAAGGG
GCAGTTTAAAGAAACAGTCAGTGGCCAACGGTGTGGAGATATCTGTGCCTGTACCCAGCGATGCCGACTCC
CCCAGATTCAAGACCAGTGTGGGCAGCGCCAAGTATGTGCCGGAGAGAAACGTCGTGATTTGGAGTATTA
AGTCTTTCCCGGGGGGCAAGGAGTACTTGATGCGAGCCCACTTTGGCCTCCCCAGTGTGGAAAAGGAAGA
GGTGGAGGGCGCGCCCCCATCGGGTCAAGTTTGAATCCCTACTTCACCGTCTCTGGGATCCAGGTC
CGATACATGAAGATCATTGAGAAAAGTGGTTACCAGGCCCTGCCCTGGGTTGCTACATCACCAGAGTG
GCGATTACCAACTTCGTACCAGCTAGAAGGGAGAGAGATGGGGGCTTGAACACGGGGCTTCCTTACAGC
CCCGGATGCAGATTTTAGAGGGAGGGCAGGTGCGGGCTGTGTGTGTCTGTGTGAGGGCAGGTCCTGGACT
TGGCAGTTTCTTGCTCCAGCACCCGCCCTTCTCACCTCTTCCTTATTCATAGGCTGGGAGAGAAAC
TCTCTGCTTCCCTCGCCCTTGGAGCTTTCCCCATCCCCCTGATTTTATATGAAGAAATAGAAGAGGGGCT
TGAAGTCCCCCTCGCGAGTGCCTTCTTGCAATTACCTGCCTTAGCGGGTGTGCGGGTCCCTCCTTACA
GCCGCTGAGCCCAGAGGTCCCGCTGGCCCTCCTCTGAATTTTAGGATGTCATTAAAAAGATGAATCTA
```

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000250244 and has a sequence as in SEQ ID NO:41

```
MSASAVFILDVKGKPLISRNYKGDVAMSKIEHFMPLLVQREEEGALAPLLSHGQVHFLWIKHSNLYLVATTSKNA
NASLVYSFLYKTIEVFCEYFKELEES
IRDNFVIVYELLDLMDFGFPQTDSKILQEYITQOSNKLETGKSRVPPTVTNAVSWR
SEGIKYKKNEVFIDVIESVNLLVNANGSVLLSEIVGTIKLKVFLSGMPELRLGLNDRV
LFELTGRSKNKSVELEDVKFHQCVRLSRFDNDRTISFIPPDGDFELMSYRLSTQVKPL
IWIESVIEKFHSRVEIMVKAKGQFKQSVANGVEISVPVPSDADSPRFKTSVGS AKY
VPERNVVIWSIKSFPGGKEYLMRAHFGLP SVEKEEVEGRPPIGVKFEIPYFTVSGIQV
RYMKIIEKSGYQALPWVRYITQSGDYQLRTS
```

Primers for amplifying the sequence ENST00000250244 can be designed using primer design software such as Oligo Calc.

Examples of primer pairs for amplifying AP1M2 include:

Forward SEQ ID NO:42 CGCCACCATGTCCGCTCGGCTG  
Reverse SEQ ID NO:43 GCTCAATCTTGCTCATGGCCAC (Ex2)

Forward SEQ ID NO:44 CAGGTCCACTTCCTATGGATC (ex 2)  
Reverse SEQ ID NO:45 CAAAGTTGTCCCGGATGCTC (Ex4)

Forward SEQ ID NO:46 CGCTCCGAGGGTATCAAG (EX5)  
Reverse SEQ ID NO:47 CTTGCTGCGGCCAGTGAGC (ex6-7)

Forward SEQ ID NO:48 GACTTTGAGCTCATGTCATACC (Ex7)  
Reverse SEQ ID NO:49 CTTAATACTCCAAATCACGACG (Ex9)

Forward SEQ ID NO:50 GTTTGAGATCCCCTACTTC (Ex10)  
Reverse SEQ ID NO:51 GCCTGGTAACCACTTTTCTCAATG (Ex11)

Forward SEQ ID NO:52 CTGGGTTCGCTACATCACC (Ex11)  
Reverse SEQ ID NO:53 GCCCCGTGTTCAAGC (Ex12)

Forward SEQ ID NO:54 CATGCCTTTGCTGGTACAG (Ex2)  
Reverse SEQ ID NO:55 GAGTACACCAGGGAGGCATTG (Ex3)

Forward SEQ ID NO:56 CTCCCTGGTGTACTCCTTC (Ex3)  
Reverse SEQ ID NO:57 GCTGTCGGTGGTCTGCGGGAA G (Ex4)

Forward SEQ ID NO:58 CAGCAAGATCCTGCAGGAG (Ex4-5)  
Reverse SEQ ID NO:59 CAGGTTGACAGACTCTATG (Ex5)

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting AP1M2 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Examples of probes include:

SEQ ID NO:60  
ATGAAGAAATAGAAGAGGGGCTTGAAGTCCTCCTCGCGAGTGCCTTCTTGCA  
ATTACCTG

SEQ ID NO:61  
CCAGGTCCACTTCCTATGGATCAAACACAGCAACCTCTACTTGGTGGCCACC  
ACATCG

SEQ ID NO:62  
GACAATAGAGGTATTCTGCGAATACTTCAAGGAGCTGGAGGAG

SEQ ID NO:63  
CAATGACCGCGTGCTCTTCGAGCTCACTGGCCGCAGCAAGAACAAATCAGT  
AGA

SEQ ID NO:64

TTTCCCGGGGGGCAAGGAGTACTTGATGCGAGCCCACTTTGGCCTCCCCAGT  
GTGG

Other probes to AP1M2 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against AP1M2 include, but are not limited to, Proteintech Group, Inc. Cat# 10618-1-AP which is an affinity purified rabbit polyclonal antibody with an antigen which was a recombinant AP1M2 protein that included the amino acids 1-320 of the protein and from Abnova Cat# H00010053-B01, which is a mouse polyclonal antibody against the full length protein.

#### Example 9: CGN

CGN (also known as DKFZp779N1112, FLJ39281, and KIAA1319) was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that CGN was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that CGN was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Examples 2-4. Example 5 shows that CGN can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to CGN is given in ENSEMBL accession number ENST00000271636 and has a sequence as in SEQ ID NO:65

ENSG00000143375: gene, just one transcript

ENST00000271636

GAGGGAGCTCCGAGGACGAGGGGGAGGGCCGGAGCTGCGCGTGCTGCTTTGCCCGAGCCCGAGCCCGAGC  
CCGAGCCCGAGCCCGAGCCCGAGCCCGAACGCAAGCCTGGGAGCGCGAGCCCGGCTAGGGACTCCTCCT  
ATTTATGGAGCAGGCACCCAACATGGCTGAGCCCCGGGGCCCGTAGACCATGGAGTCCAGATTGCTTC  
ATCACAGAGCCAGTGAGTGGTGCAGAGATGGGCACTCTACGTCGAGGTGGACGACGCCAGCTAAGGATG  
CAAGAGCCAGTACCTACGGGTTGCTGTGCGTGTGCAGGGAATCGCTGGGCAGCCCTTTGTGGTGCTCAA  
CAGTGGGGAGAAAGGCGGTGACTCCTTTGGGGTCCAAATCAAGGGGGCCAATGACCAAGGGGCCTCAGGA  
GCTCTGAGCTCAGATTTGGAACCTCCTGAGAACCCCTACTCTCAGGTCAAGGGATTCTCTGCCCCCTCGC  
AGAGCAGCACATCTGATGAGGAGCCTGGGGCCTACTGGAATGGAAAGCTACTCCGTTCCCACTCCCAGGC  
CTCACTGGCAGGCCCTGGCCCAGTGGATCCTAGTAACAGAAGCAACAGCATGCTGGAGCTAGCCCCGAAA  
GTGGCTTCCCCAGGTAGCACCATTGACACTGCTCCCCTGTCTTCAGTGGACTCACTCATCAACAAGTTTG  
ACAGTCAACTTGGAGGCCAGGCCCGGGTTCGACTGGCCGCCGAACACGGATGCTACCCCTGAACAGCG  
CAAACGGAGCAAGAGCCTGGACAGCCGCCTCCACGGGACACCTTTGAGGAACGGGAGCGCCAGTCCACC  
AACCACTGGACCTCTAGCACAAAATATGACAACCATGTGGGCACTTCGAAGCAGCCAGCCAGAGCCAGA

ACCTGAGTCCTCTCAGTGGCTTTAGCCGTTCTCGTCAGACTCAGGACTGGGTCCTTCAGAGTTTTGAGGA  
GCCGCGGAGGAGTGCACAGGACCCACCATTGCTGCAGTTCAAATCAACTCCAGACCTCCTTCGAGACCAG  
CAGGAGGCAGCCCCACCAGGCAGTGTGGACCATATGAAGGCCACCATCTATGGCATCCTGAGGGAGGGAA  
GCTCAGAAAGTGAACCTCTGTGAGGAGGAAGGTTAGTTTTGGTGCTGGAGAAGATGCAGCCTCTAGTGAT  
GGTTTTCTTCTGTTTCTACTAAGGCCGTGGCAGGGCAGGGTGAGCTTACCCGAAAAGTGGAGGAGCTACAG  
CGAAAGCTGGATGAAGAGGTGAAGAAGCGGCAGAAGCTAGAGCCATCCCAAGTTGGGCTGGAGCGGCAGC  
TGAGGAGAGAAAACAGAAGAGTGCAGCCGACTGCAGGAGCTGCTGGAGAGGAGGAAGGGGGAGGCCCCAGCA  
GAGCAACAAGGAGCTCCAGAACATGAAGCGCCTCTTGGACCAGGGTGAAGATTTACGACATGGGCTGGAG  
ACCCAGGTGATGGAGCTGCAGAACAAGCTGAAACATGTCCAGGGTCCTGAGCCTGCTAAGGAGGTGTTAC  
TGAAGGACCTGTTAGAGACCCGGGAACCTTCTGGAAGAGGTCTTGGAGGGGAAAACAGCGAGTAGAGGAGCA  
GCTGAGGCTGCGGGAGCGGGAGTTGACAGCCCTGAAGGGGGCCCTGAAAGAGGAGGTAGCCTCCCGTGAC  
CAGGAGGTGGAACATGTCCGGCAGCAGTACCAGCCAGACACAGAGCAGCTCCGCAGGAGCATGCAAGATG  
CAACCCAGGACCATGCAGTGTGGAGGCCGAGAGGCAGAAGATGTCAGCCCTTGTGCGAGGGCTGCAGAG  
GGAGCTGGAGGAGACTTCAGAGGAGACAGGGCATTGGCAGAGTATGTTCCAGAAGAACAAGGAGGATCTT  
AGAGCCACCAAGCAGGAACCTCTGCAGCTGCGAATGGAGAAGGAGGAGATGGAAGAGGAGCTTGGAGAGA  
AGATAGAGGTCTTGCAGAGGGAATTAGAGCAGGCCCCGAGCTAGTGCTGGAGATACTCGCCAGGTTGAGGT  
GCTCAAGAAGGAGCTGCTCCGGACACAGGAGGAGCTTAAGGAACTGCAGGCAGAACGGCAGAGCCAGGAG  
GTGGCTGGGCGACACCGGGACCGGGAGTTGGAGAAGCAGCTGGCGGTCTGAGGGTTCGAGGCTGATCGAG  
GTCCGGGAGCTGGAAGAACAGAACCTCCAGCTACAAAAGACCCTCCAGCAACTGCGACAGGACTGTGAAGA  
GGCTTCCAAGGCTAAGATGGTGGCCGAGGCAGAGGCAACAGTGTGGGGCAGCGGCGGGCCGAGTGGAG  
ACGAGCGTTCCGGGAGACCCAGGAGGAAAATGACGAATTCGCGCGGCATCCTGGGTTTGGAGCAGCAGC  
TGAAGGAGACTCGAGGTCTGGTGGATGGTGGGGAACGGTGGAGGCAACGACTACGGGACAGGACTGCAGCG  
GCTGGAGGCAGAGAAACAGCAGCTGGAGGAGGCCCTGAATGCGTCCCAGGAAGAGGAGGGGAGTCTGGCA  
GCAGCCAAGCGGGCACTGGAGGCACGCCTAGAGGAGGCTCAGCGGGGGCTGGCCCGCTGGGGCAGGAGC  
AGCAGACACTGAACCGGGGCCCTGGAGGAGGAAGGGAAGCAGCGGGAGGTGCTCCGGCGAGGCAAGGCTGA  
GCTGGAGGAGCAGAAGCGTTTGTGGACAGGACTGTGGACCGACTGAACAAGGAGTTGGAGAAGATCGGG  
GAGGACTCTAAGCAAGCCCTGCAGCAGCTCCAGGCCCCAGCTGGAGGATTATAAGGAAAAGGCCCGCGGG  
AGGTGGCAGATGCCAGCGCCAGGCCAAGGATTGGGCCAGTGAGGCTGAGAAGACCTCTGGAGGACTGAG  
CCGACTTCAGGATGAGATCCAGAGGCTGCGGCAGGCCCTGCAGGCATCCCAGGCTGAGCGGGACACAGCC  
CGGCTGGACAAAGAGCTACTGGCCCAGCGACTGCAGGGCTGGAGCAAGAGGCAGAGAAACAAGAGCGTT  
CCCAGGACGACAGGGCCCCGCGAGCTGAAGGTTCTCAGGAAAAAGTCTCACGGCTGGAACAGAGTTAGA  
TGAGGAGAAGAACACCGTGGAGCTGCTAACAGATCGGGTGAATCGTGGCCGGGACCAGGTGGATCAGCTG  
AGGACAGAGCTCATGCAGGAAGGTCTGCTCGGCAGGACCTGGAGTGTGACAAAATCTCCTTGGAGAGAC  
AGAACAAGGACCTGAAGACCCGGTTGGCCAGCTCAGAAGGCTTCCAGAAGCCTAGTGCCAGCCTCTCTCA  
GCTTGAGTCCCAGAATCAGTTGTTGCAGGAGCGGCTACAGGCTGAAGAGAGGGAGAAGACAGTTCTGCAG  
TCTACCAATCGAAAACCTGGAGCGGAAAGTTAAAGAACTATCCATCCAGATTGAAGACGAGCGGCAGCATG  
TCAATGACCAGAAAGACCAGCTAAGCCTGAGGGTGAAGGCTTTGAAGCGTCAGGTGGATGAAGCAGAAGA  
GGAAATTGAGCGACTGGACGGCTGAGGAAGAAGGCCAGCGTGAGGTGGAGGAGCAGCATGAGGTCAAT  
GAACAGCTCCAGGCCCCGATCAAGTCTCTGGAGAAGGACTCCTGGCGCAAAGCTTCCCGCTCAGCTGCTG  
AGTCAGCTCTCAAAACGAAGGGCTGAGCTCAGATGAGGAATTCGACAGTGTCTACGATCCCTCGTCCAT  
TGCATCACTGCTTACGGAGAGCAACCTACAGACCAGCTCCTGT**TAGCTCGTGGTCTCTCAAGGACTCAGAA**  
**ACCAGGCTCGAGGCCTATCCCAGCAAGTGTGCTCTGCTCTGCCCCACCCTGGGTTCTGCATTCTTATGGG**  
**TGACCCAATTATTTCAGACCTAAGACAGGGAGGGGTGAGAGTGATGGTGATAAAAAAAAAAATCATCAGC**  
**AATAAGCTGATAGATGGACTTTCCACTGTAGGAGTGACATTTCAAGCCAACTGAGCCTTTTCTCAAGT**  
**GCCGACACCTCCCTCATCTCTCTTATAGTGGAAGGATGGTCAGCATTAGGCTGATGGGGACTGAGAAGGA**  
**TAGGAAGGGATAGAAATTGCCATGTGTATAAAGCTTTATTCTTTAGCCCTTAACCCTAAGGCTCAGGGAA**  
**ATACCCTATGTTATTGTGCTCCCTGGATTCTGCAACTCATTTTCTTCCACTCTGGAGCAGGGTGAGGG**  
**GAATGTTATGGGTAACAGACATGCAGGCATGGCTCTACCCATTTCTTTGCACAAGTATGGGGCCCATGTG**  
**GTAGTCCCCATACCCCTCCAGTTCCATATATTTTGTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT**  
**GCAATTTTCTGTCAGTGCCTTAGCCAAGGCAAGGAGATAAGGATGCTCTTCTTCTTCTTCTTCTTCTTCTGCA**  
**CATTACATACCTCTCCAAAGACCAGCTTTTCCCGAGCCAGGGCCCTCAGCCTTCCCTGCTGCCCCAGTGAT**  
**TGATTGAGAGAGCTGTTGGGGTTTCTCTGCCAATGACCCCTGGGAGAGGGACTTTGGTAGGGTCATGATA**  
**AAGTGGCGGGGGTCTGGTCTGCTCAGGGTTTTCATCTTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT**  
**TGGTTATAAGGTGGTTGCACCTGGGAGCCCTGACAACTGGCTGCACAAATTCCAAAAGTAAAGGTGTCAG**  
**TCCCTGTGGCCTTCTTGGGGCTTCTCTGACCACATGTGCCAACTTCAATAAGAGAACCAAGGGACCCT**  
**CATTTTCTGAGGTGCTTGGCTCTGATTGAGGGCTTTGCAAGGGGTTAGAAGCTGACTGTAAAAATGGGAA**  
**GAGGCAACGGAAGACATTTATTTCTCTTTGGATTTTGGGGAGAACCAAGCCCTGGTAGGGAAGAGGTAA**  
**GGGGGATGATTACCTCCATATTTCTTAAGCAGGTGTATAGGGAGCCGGTGGCAGGAGGAAGGCTGTTT**  
**TCACAAATGACTGTAAATGTCGTGATTAAAAAAATTCCTATATTCTTCTGCAAATCAAACGTTCTTTCCC**  
**AATCCAATCCAGCCTTGGTTTTATTTAAATTAATTAATAATTAACACATTTATATTGAAAAAAAAAAAA**  
**AAAAAAAAAAAAAAAAAAAAA**



The start and stop codons are indicated in bold.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000271636 and has a sequence as in SEQ ID NO:66

```

MEQAPNMAEPRGPVDHGVQIRFITEPVSGAEMGTLRRGGRRPAK
DARASTYGVAVRVQGIAGQPFVVLNSGEKGGDSFGVQIKGANDQGASGALSSDLELPE
NPYSQVKGFAPSPQSSTSDEEPGAYWNGKLLRSHSQASLAGPGPVDPSNRSNSMLELA
PKVASPGSTIDTAPLSSVDSLINFDSQLGGQARGRTGRRTMLPPEQRKRKSLDSR
LPRDTFEERERQSTNHWTSSSTKYDNHVGTSKQPAQSQNLSPLSGFSRSRQTQDWVLQS
FEEPRRSAQDPTMLQFKSTPDLLRDQQEAAPPGSVDHMKATIYGILREGSSESETSVR
RKVSLVLEKMQPLVMVSSGSTKAVAGQGELTRKVEELQKRLDEEVKKRQKLEPSQVGL
ERQLEEKTEEC SRLQELLERRKGEAQSNKELQNMKRLLDQGEDLRHGLETQVMELQN
KLKHVQGPEPAKEVLLKDLLLETRELLEEVLEGGKQRVEEQLRLRERELTALKGALKEEV
ASRDQVEVHVRQQYQRDTEQLRRSMQDATQDHAVLEAERQKMSALVRGLQRELEETSE
ETGHWQSMFQKNKEDLRATKQELLQLRMEKEEMEEELGEKIEVLQRELEQARASAGDT
RQVEVLKKELLRTQEELEKELQAERQSQEVAGRHRDRELEKQLAVLRVEADRGRELEEQ
NLQLQKTLQQLRQDCEEASKAKMVAEAEATVLGQRRAAVETTLRETQEENDEFRRRIL
GLEQQKQKTRGLVDGGEAVEARLRDKLQRLEAEKQQLEELALNASQEEEGSLAAAKRAL
EARLEEAQRGLARLGQEEQQTINRALEEEGKQREVLRRGKAELEEQRLLDRTVDRLNK
ELEKIGEDSKQALQQLQAQLEDYKEKARREVADAQRQAKDWASEAEKTSGLSRLQDE
IQRRLQALQASQAERDTARLDKELLAQRLQGLEQEAENKKRSQDDRARQLKGLEEKVS
RLETDELDEEKNTVELLTDVRNVRGRDQVDQLRTELMQERSARQDLECDKISLERQNKDL
KTRLASSEGFQKPSASLSQLESQNQLLQERLQAEEREKTVLQSTNRKLERKVKELSIQ
IEDERQHVNDQKDQLSLRVKALKRQVDEAEIEERLDGLRKKQAQREVEEQHEVNEQLQ
ARIKSLEKDSWRKASRSAAESALKNEGLSSDEEFDSVYDPSSIASLLTESNLQTSSC

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Primers for amplifying the sequence CGN can be designed using primer design software such as Oligo Calc. Examples of primer pairs for amplifying CGN include those in

Forward SEQ ID NO:67 GCTTTAGCCGTTCTCGTCA  
Reverse SEQ ID NO:68 CTGGTCTCGAAGGAGGTCTG

Forward SEQ ID NO:69 CAGACCTCCTTCGAGACCAG  
Reverse SEQ ID NO:70 TTCCTCCTCACAGAGGTTTCA

Forward SEQ ID NO:71 TACAGCGAAAGCTGGATGAA  
Reverse SEQ ID NO:72 AGTCGGCTGCACTCTTCTGT

Forward SEQ ID NO:73 TGCAGAACAAGCTGAAACAT  
Reverse SEQ ID NO:74 GCTGCTCCTCTACTCGCTGT

Forward SEQ ID NO:75 GGGCATTGGCAGAGTATGTT  
Reverse SEQ ID NO:76 TTCCATCTCCTCCTTCTCCA

Forward SEQ ID NO:77 CAGCAACTGCGACAGGACT  
Reverse SEQ ID NO:78 CATTTTCCTCCTGGGTCTCC

Forward SEQ ID NO:79: CTGAGCTGGAGGAGCAGAAAG  
Reverse SEQ ID NO:80 TGCAGGGCTTGCTTAGAGTC

Forward SEQ ID NO:81 TGGAGCAAGAGGCAGAGAAC  
Reverse SEQ ID NO:82 ACTCTGTTTCCAGCCGTGAG

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting CGN can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include

SEQ ID NO:83 CAGGACTGGGTCCTTCAGAG  
SEQ ID NO:84 CAGGCAGTGTGGACCATATG  
SEQ ID NO:85 GCTAGAGCCATCCCAAGTTG  
SEQ ID NO:86 TGAGCCTGCTAAGGAGGTGT  
SEQ ID NO:87 TAGAGCCACCAAGCAGGAAC  
SEQ ID NO:88 TTCCAAGGCTAAGATGGTGG  
SEQ ID NO:89 GACAGGACTGTGGACCGACT  
SEQ ID NO:90 TGAAGGGTCTCGAGGAAAAA  
Probe from the array SEQ ID NO:91  
GGGAAGAGGTAAGGGGGATGATTACCTCCATATTCCTAAGCAGGTTGTAT  
AGGGAGCC

Antibodies to CGN include, but are not limited to Rabbit Anti-Human Cingulin (CGN) Polyclonal, Unconjugated Cat# LS-C22229-100, from lifespan bioscience (C-terminal region); and Mouse Anti-Human Cingulin (CGN) Monoclonal, Unconjugated, Clone 6a40 Cat# LS-C22230-100, from Lifespan Bioscience (C-terminal region).

#### Example 10: DDR1

DDR1 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that DDR1 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that DDR1 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Examples 2-4. Example 5 shows that DDR1 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to DDR1 is given in ENSEMBL accession no. ENST00000376570 and has a sequence as in SEQ ID NO:92

```
1  GTCTTCCCCTCGTGGGCGCTGAGCGGGACTGCAGCCAGCCCCCTGSGGGCGCCAGCTTTG
61  AGGCCCCCGACAGCTGCTCTCGGGAGCCGCTCCCGACACCCGAGCCCCGCGGGCGCCTC
121 CCGCTCCCGGCTCCCGGCTCCTGGCTCCCTCCGCTCCCCGCCCCCTCGCCCCGCGCC
181 AAGAGGCCCGCTCCCGGCTCGGACGCCCTGGGTCTGCCGGGAAGAGCGATGAGAGGTGTC
241 TGAAGGTGGCTATTCACTGAGCGATGGGGTTGGACTTGAAGGAATGCCAAGAGATGCTGC
301 CCCCACCCCTTAGGCCCCGAGGGATCAGGAGCTATGGGACCAGAGGCCCTGTCATCTTTA
361 CTGCTGCTGCTCTTGGTGCAAGTGGAGATGCTGACATGAAGGGACATTTTGATCCTGCC
421 AAGTGCCGCTATGCCCTGGGCATGCAGGACCGGACCATCCAGACAGTGACATCTCTGCT
481 TCCAGCTCCTGGTCAGATTCCACTGCCGCCCCGCCACAGCAGGTTGGAGAGCAGTGACGGG
541 GATGGGGCCTGGTGCCCCGAGGGTGGGTGTTTCCCAAGGAGGAGGAGTACTTGACAGGTG
601 CAGCTAGCAAGACTGCACCTGGTGGCTCTGGTGGGCACCCAGGGACGGCATGCCGGGGG
661 CTGGGCAAGGAGTTCTCCCGGAGCTACCGGCTGCGTTACTCCCGGGATGGTCGCCGCTGG
721 ATGGGCTGGAAGGACCGCTGGGGTCAGGAGGTGATCTCAGGCAATGAGGACCTGAGGGA
781 GTGGTGTGAAGGACCTTGGGCCCCCATGGTTGCCGACTGGTTGCTTCTACCCCCGG
841 GCTGACCGGGTCATGAGCGTCTGTCTGCGGGTAGAGCTCTATGGCTGCCTCTGGAGGGAT
901 GGACTCCTGTCTTACACCGCCCCCTGTGGGGCAGACAATGTATTTATCTGAGGCCGTGTAC
961 CTCACGACTCCACCTATGACGGACATACCGTGGGCGGACTGCAGTATGGGGGTCTGGGC
1021 CAGCTGGCAGATGGTGTGGTGGGGCTGGATGACTTTAGGAAGAGTCAGGAGCTGCGGGTC
1081 TGGCCAGGCTATGACTATGTGGGATGGAGCAACCACAGCTTCTCCAGTGGCTATGTGGAG
1141 ATGGAGTTTGAGTTTGACCGGCTGAGGGCCTTCCAGGCTATGCAGGTCCACTGTAACAAC
1201 ATGCACACGCTGGGAGCCGTCTGCCTGGCGGGGTGGAATGTCGCTTCCGGCGTGGGCCCT
1261 GCCATGGCCTGGGAGGGGGAGCCCCATGCCCCACAACCTAGGGGGCAACCTGGGGGACCCC
1321 AGAGCCCGGGCTGTCTCAGTGCCCCCTTGGCGGCCGTGTGGCTCGCTTTCTGCAGTGCCGC
1381 TTCTCTTTTGGGGGGCCTGGTTACTCTTACGCGAAATCTCCTTCATCTCTGATGTGGTG
1441 AACAATTCCTCTCCGGCACTGGGAGGCACCTTCCCGCCAGCCCCCTGGTGGCCGCTGGC
1501 CCACCTCCCAACCACTTCAGCAGCTTGGAGCTGGAGCCCAGAGGCCAGCAGCCGTGGCC
1561 AAGGCCGAGGGGAGCCCGACCGCCATCCTCATCGGCTGCCTGGTGGCCATCATCCTGCTC
1621 CTGCTGCTCATCATTGCCCTCATGCTCTGGCGGCTGCACTGGCGCAGGCTCCTCAGCAAG
1681 GCTGAACGGAGGGTGTGGAAGAGGAGCTGACGGTTACCTCTCTGTCCCTGGGGACACT
1741 ATCCTCATCAACAACCGCCAGGTCTTAGAGAGCCACCCCGTACCAGGAGCCCGGCCCT
1801 CGTGGGAATCCGCCCCACTCCGCTCCCTGTGCCCAATGGCTCTGCCTACAGTGGGGAC
1861 TATATGGAGCCTGAGAAGCCAGGCGCCCCGCTTCTGCCCCACCTCCCCAGAACAGCGTC
1921 CCCCATTATGCCGAGGCTGACATTGTTACCCTGCAGGGCGTCACCGGGGGCAACACCTAT
1981 GCTGTGCCTGCACTGCCCCAGGGGCACTCGGGGATGGGCCCCCAGAGTGGATTTCCTT
2041 GCTGTGCCTGCACTGCCCCAGGGGCACTCGGGGATGGGCCCCCAGAGTGGATTTCCTT
2061 CGATCTCGACTCCGCTTCAAGGAGAAGCTTGGCGAGGGCCAGTTTGGGGAGGTGCACCTG
2101 CGATCTCGACTCCGCTTCAAGGAGAAGCTTGGCGAGGGCCAGTTTGGGGAGGTGCACCTG
2161 TGTGAGGTGACAGCCCTCAAGATCTGGTTAGTCTTGATTTCCTTCAATGTGCGTAAG
2221 TGTGAGGTGACAGCCCTCAAGATCTGGTTAGTCTTGATTTCCTTCAATGTGCGTAAG
2281 GGACACCCCTTTGCTGGTAGCTGTCAAGATCTTACGGCCAGATGCCACCAAGAAATGCCAGG
2341 GGACACCCCTTTGCTGGTAGCTGTCAAGATCTTACGGCCAGATGCCACCAAGAAATGCCAGG
2401 AATGATTTCTGAAAGAGGTGAAGATCATGTGAGGCTCAAGGACCCAAACATCATTGCG
2461 AATGATTTCTGAAAGAGGTGAAGATCATGTGAGGCTCAAGGACCCAAACATCATTGCG
2521 CTGCTGGGCGTGTGTGTGACGAGACGACCCCTCTGCATGATTACTGACTACATGGAGAAC
2581 CTGCTGGGCGTGTGTGTGACGAGACGACCCCTCTGCATGATTACTGACTACATGGAGAAC
2641 GCGGACCTCAACCAAGTTCTCAGTGCCCACAGCTGGAGGACAAGGCAGCCGAGGGGGCC
2701 GCGGACCTCAACCAAGTTCTCAGTGCCCACAGCTGGAGGACAAGGCAGCCGAGGGGGCC
2761 CCTGGGGACGGGCAGGCTGCGCAGGGGGCCACCATCAGCTACCCAATGCTGCTGCATGTG
2821 CCTGGGGACGGGCAGGCTGCGCAGGGGGCCACCATCAGCTACCCAATGCTGCTGCATGTG
2881 CAGCCCCAGATCGCCTCCGGCATGCGCTATCTGGCCACACTCAACTTTGTACATCGGGAC
2941 GCAGCCCAGATCGCCTCCGGCATGCGCTATCTGGCCACACTCAACTTTGTACATCGGGAC
3001 CTGGCCACGCGGAAGTGCCTAGTTGGGGAAAATTTACCATCAAATCGCAGACTTTGGC
3061 CTGGCCACGCGGAAGTGCCTAGTTGGGGAAAATTTACCATCAAATCGCAGACTTTGGC
3121 ATGAGCCGGAACCTCTATGCTGGGGACTATTACCGTGTGCAGGGCCGGGCAGTGTGCC
3181 ATGAGCCGGAACCTCTATGCTGGGGACTATTACCGTGTGCAGGGCCGGGCAGTGTGCC
3241 ATCCGCTGGATGGCCTGGGAGTGCATCCTCATGGGGAAGTTACGACTGCGAGTGACGTG
3301 ATCCGCTGGATGGCCTGGGAGTGCATCCTCATGGGGAAGTTACGACTGCGAGTGACGTG
3361 TGGGCCCTTTGGTGTGACCTGTGGGAGGTGCTGATGCTCTGTAGGGCCAGCCCTTTGGG
3421 TGGGCCCTTTGGTGTGACCTGTGGGAGGTGCTGATGCTCTGTAGGGCCAGCCCTTTGGG
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2761 CAGCTCACCACGAGCAGGTGTCATCGAGAACGCGGGGGAGTTCTTCCGGGACCAGGGCCGG  
 2428 CAGCTCACCACGAGCAGGTGTCATCGAGAACGCGGGGGAGTTCTTCCGGGACCAGGGCCGG  
 2821 CAGGTGTACCTGTCCCGGCCGCTGCCTGCCCGCAGGGCCTATATGAGCTGATGCTTCGG  
 2488 CAGGTGTACCTGTCCCGGCCGCTGCCTGCCCGCAGGGCCTATATGAGCTGATGCTTCGG  
 2881 TGCTGGAGCCGGGAGTCTGAGCAGCGACCACCCCTTTTCCAGCTGCATCGGTTCTGGCA  
 2548 TGCTGGAGCCGGGAGTCTGAGCAGCGACCACCCCTTTTCCAGCTGCATCGGTTCTGGCA  
 2941 GAGGATGCACTCAACACGGTGTGAATCACACATCCAGCTGCCCCCTCCCTCAGGGAGCGAT  
 3001 CCAGGGGAAGCCAGTGACACTAAAACAAGAGGACACAATGGCACCTCTGCCCTTCCCCTC  
 3061 CCGACAGCCCATCACCTCTAATAGAGGCAGTGAGACTGCAGGTGGGCTGGGCCCCACCCAG  
 3121 GGAGCTGATGCCCCCTTCTCCCCCTTCTGGACACACTCTCATGTCCCCCTTCTGTTCTTCC  
 3181 TTCCTAGAAGCCCCCTGTGCCCCACCCAGCTGGTCTGTGGATGGGATCCTCTCCACCCTC  
 3241 CTCTAGCCATCCCTTGGGGAAGGGTGGGGAGAAATATAGGATAGACACTGGACATGGCCC  
 3301 ATTGGAGCACCTGGGCCCCACTGGACACACTGATTCTCTGGAGAGGTGGCTGCGCCCCCA  
 3361 GCTTCTCTCTCCCTGTACACACTGGACCCCACTGGCTGAGAATCTGGGGGTGAGGAGGA  
 3421 CAAGAAGGAGAGGAAAATGTTTCTTGTGCTGCTCCTGTACTTGTCTCAGCTTGGGCT  
 3481 TCTTCTCTCTCCATCACCTGAAACACTGGACCTGGGGGTAGCCCCGCCACGCCCTCAGT  
 3541 CACCCCCACTTCCCACTGTCAGTCTTGTAGCTAGAACTTCTCTAAGCCTATACGTTTCTG  
 3601 TGGAGTAAATATTGGGATTGGGGGGAAGAGGGAGCAACGGCCCATAGCCTTGGGGTTGG  
 3661 ACATCTCTAGTGTAGCTGCCACATTGATTTTCTATAATCACTTGGGGTTTGTACATTTT  
 3721 TGGGGGGAGAGACACAGATTTTACACTAATATATGGACCTAGCTTGAGGCAATTTTAAT  
 3781 CCCCTGCACTAGGCAGGTAATAATAAAGGTTGAGTTTTCC

The corresponding amino acid sequence is given in ENSEMBL accession no. EP0000365754 and has a sequence as in SEQ ID NO:93

1 MGPEALSSLLLLLVASGDADMKGHFDPKCRYALGMQDRTIPDSDISASSWSDDSTAAR  
 61 HSRLESSDGDGAWCPAGSVFPKEEYQLQDLQRLHLVALVGTQGRHAGGLGKEFSRSYRL  
 121 RYSRDGRWRWGWKDRWGQEVISGNEDPEGVVLKDLGPPMVARLVRFPYPRADRVMSVCLRV  
 181 ELYGCLWRDGLLSYAPVQTMYLSEAVYLNDSYDGHTVGGLYQYGLGLQADGVVGLDD  
 241 FRKSQELRVWPGYDYVGWSNHSFSSGYVEMEFEDRLRAFQAMQVHCNNMHTLGARLPGG  
 301 VECRFRRGFAMAWEGEPMRHNLGGLGDPARAVSVPLGGRVARFLQCRFLFAGPWLLFS  
 361 EISFISDVVNSSPALGGTFPPAPWPPGPPPTNFSLELEPRGQQPVAKAEGSPTAILI  
 421 GCLVAIILLLLLIALLMLWRLHWRLLSKAERRVLEEELTVHLSVPGDTILINNRPGPRE  
 481 PPPYQEPFRGNPPHSAPCVNPGSAYS GDYMEPEKPGAPLLPPPPQNSVPHYAEADIVTL  
 541 QGVTTGGNTYAVPALPPGAVGDGPPRVDFPRSLRFRFKEKLGEQGFGEVHLCEVDSPODLVS  
 601 LDFPLNVRKGHPLLVAVKILRPDATKNARNDLFKEVKIMSRLKDPNIIIRLLGVCVQDDPL  
 661 CMITDYMENGDLNQFLSAHQLEDKAAEGAPGDGQAAQGPTISYPMLLHVAAQIASGMRYL  
 721 ATLNLFVHRDLATRNCLVGENFTIKIADFGMSRNLVAGDYRVRQGRAVLPIRWMWECILM  
 781 GKFTTASDVWAFGVTLWEVLMLCRAQPFQQLTDEQVIENAGEFFRDQGRQVYLSRPPACF  
 841 QGLYELMLRCWSRESEQRPPFSQLHRFLAEDALNTV

Primers for amplifying the sequence DDR1 can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying DDR1 include those in

Forward SEQ ID NO:94 CATCTCTGCTTCCAGCTCCT  
Reverse SEQ ID NO:95 TACTCCTCCTCCTTGGGAAA

Forward SEQ ID NO:96 AGCTACCGGCTGCGTTACT  
Reverse SEQ ID NO:97 CTTCAGCACCACTCCCTCAG

Forward SEQ ID NO:98 CGTCTGTCTGCGGGTAGAG  
Reverse SEQ ID NO:99 CCGTCATAGGTGGAGTCGTT

Forward SEQ ID NO:100 CAACGACTCCACCTATGACG  
Reverse SEQ ID NO:101 TGCTCCATCCCACATAGTCA

Forward SEQ ID NO:102 TGACTATGTGGGATGGAGCA  
Reverse SEQ ID NO:103 CCAGCGTGTGCATGTTGTTA

Forward SEQ ID NO:104 TGTCTCAGTGCCCCTTGG  
Reverse SEQ ID NO:105 GTGCCGGAGAGGAATTGTT

Forward SEQ ID NO:106 ACCTCCCACCAACTTCAGC  
Reverse SEQ ID NO:107 CAGCAGGAGCAGGATGATG

Forward SEQ ID NO:108 CATCATCCTGCTCCTGCTG  
Reverse SEQ ID NO:109 CCAGGGACAGAGAGGTGAAC

Forward SEQ ID NO:110 ACCGCCCAGGTCCTAGAG  
Reverse SEQ ID NO:111 CGGTAGGCTGGATTGGAGA

Forward SEQ ID NO:112 CACCCTTTGCTGGTAGCTGT  
Reverse SEQ ID NO:113 CGAATGATGTTTGGGTCCTT

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting DDR1 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include

SEQ ID NO:114 ACAGCAGGTTGGAGAGCAGT  
SEQ ID NO:115 GTCAGGAGGTGATCTCAGGC  
SEQ ID NO:116 CTCTATGGCTGCCTCTGGAG  
SEQ ID NO:117 GTGGGGCTGGATGACTTTAG  
SEQ ID NO:118 AGTTTGAGTTTGACCGGCTG  
SEQ ID NO:119 CCCTGGTTACTCTTCAGCGA  
SEQ ID NO:120 CTTGGAGCTGGAGCCCAG  
SEQ ID NO:121 AGGGTGTTGGAAGAGGAGCT  
SEQ ID NO:122 ACTCTGCTCCCTGTGTCCC  
SEQ ID NO:123 GCCAGGAATGATTTCTGAA

A probe used to detect the DDR1 nucleic acid that was used on the microarray has a sequence as in SEQ ID NO:124

ATTGGGATTGGGGGAAAGAGGGAGCAACGGCCCATAGCCTTGGGGTTGGACAT  
CTCTAG

Other probes to DDR1 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against DDR1 include, but are not limited to, Rabbit polyclonal antibody to MCK10 from abcam cat# ab5508 epitope: aa31-47; and Mouse Anti-Human DDR1 Polyclonal Antibody, Unconjugated from abnova cat# H00000780-A01 against full length.

#### Example 11: EPS8L2

EPS8L2 (EPS8-like 2 also known as AI042819, AW545405, Eps8l2\_predicted, Eps8l2\_predicted, EPS8R2, FLJ16738, FLJ21935, FLJ22171, MGC126530, MGC3088)

was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that EPS8L2 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that EPS8L2 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Examples 2-4. Example 5 shows that EPS8L2 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The EPS8L2 gene encodes a protein that is related to epidermal growth factor receptor pathway substrate 8 (EPS8), a substrate for the epidermal growth factor receptor. The eps8Ls define a novel family of proteins responsible for functional redundancy in the RTK-activated signaling pathway leading to actin remodeling. Members of this family link growth factor stimulation to actin organization. Members of the eps8 family share a modular organization consisting of a putative PTB domain, a central SH3 domain and a C-terminal effector region. The SH3 domains of eps8Ls display unique binding preferences for peptides containing a proline-X-X-aspartate-tyrosine (pXXDY) consensus and constitute a phylogenetically distinct subfamily within the SH3 domain family. (PMID: 14565974).

Although EPS8L2 function is unknown, gene expression analyses of breast and thyroid cancers identified Eps8, another member of the family, as a novel putative

oncogene and also it was implicated in tumor cell migration in fibrosarcoma cells.  
(PMID: 16618726) (PMID: 17075124) (PMID: 15289329)

The sequence of an mRNA corresponding to EPS8L2 is given in ENSEMBL  
accession no. ENST00000318562 and SEQ ID NO:125

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ACTCCGCAACCTGTCGCTCAGGTTCTCTCTCCCGGCCCCGCCCCGGCCCCGCCCCGCGAGCGTCCCA
CCCCCCCCGCGGGAGACCTGGCGCCCCGGCCGAGGCGCGAACAGACGGACGCACCGGCGAGCGCCGAGGGG
ACAGGCCGAGCGCGGGGCGCCGGAGGCGAGGTGTGGGACAGGCACTGGCCTCAGACCGGGGCCACACTGAG
GTCTGCCCTTCTCCCGCTGGCCGCCACCCAAGACACCAATGAGCCAGTCCGGGGCCGTGAGCTGCTGCCCCG
GGTGCCACCAATGGCAGCCTGGGCGCGTCCGACGGTGTGGCCAAGATGAGCCCCAAGGACCTGTTTGAGC
AGAGGAAGAAGTATTCCAACCTCCAACGTCATCATGCACGAGACCTCGCAGTACCACGTCCAGCACCTGGC
CACATTTCATCATGGACAAGAGCGAAGCCATCACGTCTGTGGACGACGCCATCCGGAAGCTGGTGCAGCTG
AGCTCCAAGGAGAAGATCTGGACCCAGGAGATGCTGCTGCAGGTGAACGACCAGTCGCTGCGGCTGCTGG
ACATCGAGTCACAGGAGGAGCTGGAAGACTTCCCGCTGCCCCAGGTGCAGCGCAGCCAGACGGTCCCTCAA
CCAGCTGCGCTACCCGTCTGTGCTGCTGCTGCTGCTGCGTGTGCCAGGACTCGGAGCAGAGCAAGCCGGATGTCCAC
TTCTTCCACTGCGATGAGGTGGAGGCAGAGCTGGTGCACGAGGACATCGAGAGCGCGTTGGCCGACTGCC
GGCTGGGCAAGAAGATGCGGCCGACAGCCCTGAAGGGACACCAGGAGAAGATTCGGCAGCGGCAGTCCAT
CCTGCCTCCTCCCCAGGGCCCCGGCGCCCATCCCTTCCAGCACCGCGCGGGGATTCCCCGGAGGCCAAG
AATCGCGTGGGCGCGAGGTGCCACTCAGCGAGCCAGGTTTCCGCCGTGCGGAGTCGAGGAGGAGCCGC
GGGCCGTGCTGGCTCAGAAGATAGAGAAGGAGACGCAAACTCCTCAACTGCGCCCTGGACGACATCGAGTG
GTTTGTGGCCCGGCTGCAGAAGGCAGCCGAGGCTTTCAAGCAGCTGAACCAGCGGAAAAAGGGGAAGAAG
AAGGGCAAGAAGGCGCCAGCAGAGGGCGTCTCACACTGCGGGCACGGCCCCCTCTGAGGGCGAGTTCA
TCGACTGCTTCCAGAAAATCAAGCTGGCGATTAACTTGCTGGCAAAGCTGCAGAAGCACATCCAGAACCC
CAGCGCCGCGGAGCTCGTGCACTTCCTTTCGGGCCTCTGGACCTGATCGTCAACACCTGCAGTGGCCCA
GACATCGCAGCTCCGTCTCCTGCCACTGCTCTCCCGAGATGCCGTGGACTTCTTGCGCGGCCACCTGG
TCCCTAAGGAGATGTGCTGTGGGAGTCACTGGGAGAGAGCTGGATGCGGCCCCGTTCAGAGTGGCCGCG
GGAGCCACAGGTGCCCCCTTACGTGCCCAAGTTCACAGCGGCTGGGAGCCTCCTGTGGATGTGCTGCAG
GAGGCCCCCTGGGAGGTGGAGGGGCTGGCGTCTGCCCCATCGAGGAGGTGAGTCCAGTGAGCCGACAGT
CCATAAGAAACTCCAGAAAGCACAGCCCCACTTCAGAGCCACCCCCCGGGGATGCCCTACCACAGT
CAGCTCCCCACATACTCACAGGGGCTACCAGCCAACACCAGCCATGGCCAAGTACGTCAAGATCCTGTAT
GACTTCACAGCCCCGAATGCCAACGAGCTATCGGTGCTCAAGGATGAGGTCTAGAGGTGCTGGAGGACG
GCCGCGAGTGGTGAAGCTGCGCAGCCGACGCGCCAGGCGGGGTACGTGCCCTGCAACATCCTAGGCGA
GGCGCGACCGGAGGACGCCGGCGCCCCGTTCGAGCAGGCCCGTCAAGTACTGGGGCCCCGCGAGCCCG
ACCCACAAGCTACCCCCAAGCTTCCCGGGGAACAAAGACGAGCTCATGCAGCACATGGACGAGGTCAACG
ACGAGCTCATCCGGAAAATCAGCAACATCAGGGCGCAGCCACAGAGGCACTTCCGCGTGGAGCGCAGCCA
GCCCGTGAGCCAGCCGCTCACCTACGAGTCGGGTCCGGACGAGGTCCGCGCCTGGCTGGAAGCCAAGGCC
TTCAGCCCGCGGATCGTGGAGAACCTGGGCATCCTGACCGGGCCGACGCTCTTCTCCCTCAACAAGGAGG
AGCTGAAGAAAGTGTGCGGCGAGGAGGGCGTCCGCGTGTAAGCCAGCTCACCATGCAGAAGGCCCTTCCT
GGAGAAGCAGCAAAAGTGGGTGCGAGCTGGAAGAACTCATGAACAAGTTTCATTCCATGAATCAGAGGAGG
GGGGAGGACAGCTTAGGCCCAGCTGCCTTGGGCTGGGGCCTGCGGAGGGGAAGCCCACCCACAATGCATGG
AGTATTATTTTATATGTGTATGTATTTTGTATCAAGGACACGGAGGGGTGTGGTGTGCTAGAGGTC
CCTGCCCCCTGTCTGGAGGCACAACGCCCATCCTTAGGCCAAACAGTACCCAAGGCCTCAGCCCACACCAA
GACTAATCTCAGCCAAACCTGCTGCTTGGTGGTGCCAGCCCCTTGTCACCTTCTCTTGAGGCCACAGAA
CTCCCTGGGGCTGGGGCCTCTTCTCTGGCCTCCCTGTGCACCTGGGGGGTCTTGCCCCCTGTGATGCT
CCCCCATCCCCACCCACTTCTACATCCATCCACACCCCAGGGTGAGCTGGAGCTCCAGGCTGGCCAGGCT
GAACCTCGCACACGACGAGAGTCTGCTCCCTGAGGGGGGCCCCGGGAGGGGCTCCAGCAGGAGGGCCGTGG
GTGCCATTTCGGGGAAAGTGGGGGAACGACACACACTTCACCTGCAAGGGCCGACAACGCAGGGGACACC
GTGCCGCTTCAGACACTCCAGCGCCACTCTTACAGGCCAGGACTGGAGCTTCTCTGAGGCAAGTTT
CAGGCCAATGATCCCCGCATGGTGTGGGGGTGCTGGTGTGCTTGGTGCCTGGACTTGAGTCTACCCCT
ACAGATGAGAGGTGGCTGAGGCACCAGGGCTAAGCAATTAAACCAGTTAAGTCTCCAGGAAAAAAAAA
AAAAAA

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The start and stop codons are indicated in bold as well as the position corresponding  
to the microarray probe.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000320828 and has a sequence as in SEQ ID NO:126

```
MSQSGAVSCCPGATNGSLGRSDGVAKMSPKDLFEQRKKYSNSNV
IMHETSQYHVQHLATFIMDKSEAITSVDDAIRKLVQLSSKEKIWTQEMLLQVNDQSLR
LLDIESQELEDPLPTVQRSQTVLNQLRYPVSVLLVLCQDSEQSKPDVHFFHCDEVEA
ELVHEDIESALADCRLGKKMRPQTLKGHQEKIRQRQSILPPPQGPAPIPFQHRGGDSP
EAKNRVGPQVPLSEPGFRRRESQEEPRAVLAQKIEKETQILNCALDDIEWFVARLQKA
AEAFKQLNQRKKGKKKKKAPAEGLVTLRARPPSEGEFIDCFQKIKLAINLLAKLQKH
IQNPSSAAELVHFLFGPLDLIVNTCSGPDIA RSVSCPLLSDAVDFLRGHLVPKEMSLW
ESLGESWMRPRSEWPREPQVPLYVPKFHSGWEPPVDVLQEAPWEVEGLASAPIEEVSP
VSRQSI RNSQKHSPTSEPTPPGDALPPVSSPHTRGYQPTPAMAKYVKILYDFTARNA
NELSVLKDEVLEVLEDGRQWWKLRSRSGQAGYVPCNILGEARPEAGAPFEQAGQKYW
GPASPTHKLPPSFPGNKDELMQHMDEVNDELIRKISNIRAQPQRHFRVERSQPVSQPL
TYESGPDEVRAWLEAKAFSPRIVENLGILTGQLFSLNKEELKKVCGEEGVRVYSQLT
MQKAFLEKQQSGSELEELMNKFHSMNQRRGEDS
```

Primers for amplifying the sequence ENST00000318562 can be designed using primer design software such as Oligo Calc and/or Primer 3. Examples of primer pairs for amplifying EPS8L2 include:

Forward SEQ ID NO:127 GAG ACC TGG CGC CCC GGC (Ex1)  
Reverse SEQ ID NO:128 GTG GCC CCG GTC TGA GGC (Ex2)

Forward SEQ ID NO:129 GAG CCA GTC CGG GGC CGT G (Ex2)  
Reverse SEQ ID NO:130 CTT GGG GCT CAT CTT GGC (Ex3)

Forward SEQ ID NO:131 CGA CGG TGT GGC CAA GAT GAG (Ex3)  
Reverse SEQ ID NO:132 CGT GGT ACT GCG AGG TC (Ex4)

Forward SEQ ID NO:133 CTCCAACGTCATCATGCAC (Ex4)  
Reverse SEQ ID NO:134 GATGGCGTCGTCCACAGAC (Ex5)

Forward SEQ ID NO:135 CAGTCGCTGCGGCTGCTGG (Ex5)  
Reverse SEQ ID NO:136 GGACCGTCTGGCTGCGCTG (Ex6)

Forward SEQ ID NO:137 GATGTCCACTTCTTCCACTGC (Ex6)  
Reverse SEQ ID NO:138 CCGAATCTTCTCCTGGTGTC (Ex8)

Forward SEQ ID NO:139 GAGGCCAAGAATCGCGTGGGC (Ex8)  
Reverse SEQ ID NO:140 GTCCAGGGCGCAGTTGAGG (Ex10)

Forward SEQ ID NO:141 CGACTGCTTCCAGAAAATC (Ex11)  
Reverse SEQ ID NO:142 CGAAGAGGAAGTGCACGAG (Ex12)

Forward SEQ ID NO:143 GATGTGCTGTGGGAGTCAC (Ex13)  
Reverse SEQ ID NO:144 GAGGGGCACCTGTGGCTC (Ex14)

Forward SEQ ID NO:145 GGTGGAGGGGCTGGCGTC (Ex14)



Reverse SEQ ID NO:146 GGCTCTGAAGTG GGGCTGTG (Ex15)

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting EPS8L2 can be derived from any number of sources depending on the desired use (e.g., using the primers described above and the appropriate reagents).

Examples of probes include:

SEQ ID NO:147

GCTTCCCGGGGAACAAAGACGAGCTCATGCAGCACATGGACGAGGTCAACG  
ACGAGCTCA

SEQ ID NO:148

GCAGAGCTGGTGCACGAGGACATCGAGAGCGCGTTGGCCGACTGCCGG

SEQ ID NO:149

GCCGTCGGGAGTCGCAGGAGGAGCCGCGGGCCGTGCTGGCTCAGAAGATAG

SEQ ID NO:150

GCTCGTGTGCCAGGACTCGGAGCAGAGCAAGCCGGATGTCCAC

SEQ ID NO:151

GTACAGCCAGCTACCATGCAGAAGGCCTTCCTGGAGAAGCAGCAAAG

Other probes to EPS8L2 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against EPS8L2 include, but are not limited to, Abnova Cat# H00064787-M01 which is a mouse monoclonal antibody raised against a partial recombinant EPS8L2 (615 a.a. ~ 715 a.a) and Abnova Cat# H00064787-B01 which is a mouse polyclonal antibody raised against a full-length human EPS8L2 protein.

Example 12: FASTKD1

FASTKD1 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that FASTKD1 was overexpressed in primary endometrial cancer tissue as compared to normal

endometrial tissue and it was surprisingly found that FASTKD1 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Examples 2-4. Example 5 shows that FASTKD1 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to FASTKD1 is given in ENSEMBL accession no. ENST00000260971 and has a sequence as in SEQ ID NO:152

```
1  ATAAACCCTGAGATATGAGGGTTGGGCGAGACATCCGAGCCTGTTTCGTTCCCGTGTGGG
61  ACCAGGAATAACCCTGACTTCTGAGCTTTCATAACCCGAGGATCCTCCAGAAAATTTGCG
121  GCGCGCTGAGGGAAAACCTTGCTGAAGCTGTACATTGGAATGCGTTTACAGTCATTGTAA
181  TGGAAAGCAAAATACATGAAGGAAAACTGTTATTTGTATCCCTGCTTATTGCACCTGACG
241  ACTAGTTGCAGATGGTTTTGTTTACCTAAGAAAACTTGTGATATAAATGAAAAAACACC
301  TGTTCCTAGAGTCATTGTTTACAAATATGCTTCGTCTAAGAGCTATTTGTCCATTCTC
361  CTGGAGAGTGTTCATTTTCGACCCATCAGTTGTGAACCACTAATTATTCAGATGAATAA
421  GTGTACAGATGAGGAGCAAATGTTTGGTTTTATTGAAAGAAACAAAGCCATACTTTCAGA
481  AAAGCAAGTGGGATGTGCATTTGATATGCTTTGGAAGCTTCAAAGCAGAAGACCAGCCT
541  GTTAAAAAATGCTGAGTATGTGAGAGACCATCCTCAATTTCTTACTCTTCATAATTTAGC
601  TACAAATAAATTCAAATTAATGAATGACGATACCCTGGTGAATGTGTTATACGTCACACA
661  ACAGTTTGCTGGTGAGGCCCATGACCCGCTAGTTGAAGCACTAGTTACAGAAGCATGGAG
721  AAGGCTAGAAAAGGTTTGATATTAACTGCTCTCAGAATTTTCCTCTTGCCCTAGCAGATCA
781  GCATTTGTATTTTAGTCCATTAATGGGAAAAATAGCTGATATTGTTTCATAGGAACTTGGG
841  AACCACACAGGACTTAAGTTCCTTGTCTGTCTTGATGGTCAACATATCTTCTTTAATATC
901  ACGACATTTTCAACAACAACTGGTGAACAAAACAGAACTCTTTTTGACACCATAGATTC
961  TTCTGAGGTCAACGTTGCAAAAAGCATAGCAAAGTTTCTTCGAAATGTTAGATATCGTTA
1021  TCAACCACTATTAGAAAGATGTAATAACGTATTTTTAAGTAATGTGGACCACCTTGATTT
1081  GGATTCATCAGTAAATACTTAGTGTATACAAATTTTACAATTTAATAGTTTGAATT
1141  TATTATAATGGCTAAAAAGAAGCTAACTGAAATGATTCCTCTGTGTAATCATCCTGCTAG
1201  CTTTGTAAAATTGTTTGTAGCATTGGGACCCATTGCAGGACCTGAAGAAAAGAAACAACT
1261  TAAATCAACTATGTTATTGATGTCAGAGGACCTAACTGGCGAGCAAGCCCTGGCAGTGTT
1321  GGGAGCAATGGGAGATATGGAAGCAGAACTCATGTCTGATTAAAAGAGTTACTTCAGT
1381  TCTGCATAAACATTTGGATGGCTATAAACCATTAGAGTTGTTGAAGATAACTCAAGAATT
1441  AACTTTTCTGCATTTCCAAAGGAAGGAGTTTTTTGCGAACTTAGAGAATTACTGCTTAG
1501  TTATTTGAAAAATAGTTTCATACCAACTGAGGTGCTGTTCTGGTCCGTGCTATTTCCCT
1561  GCTCCCTTCTCCTCACTTGGACGAAGTGGGGATATCCCGAATTGAAGCCGTTTTACCACA
1621  GTGTGACCTAAATAACCTGAGTAGTTTTGCCACATCTGTTTTAAGATGGATTACAGCATGA
1681  TCACATGTAATTTGGATAATATGACTGCGAAACAACTGAACTACTTCAAAAATTAGATCA
1741  CTATGGTCGTGAGAGACTACAACACAGCAACAGTTTGATCTGTTACGGAAGGAACCTTAA
1801  ATCTCTCAAAGGAAACACGTTTCTGAGTCACCTTCTTGAAGAAATGATTGCTACTTTACA
1861  GCATTTTCATGGATGATATTAATTACATAAATGTTGGGGAGATTGCATCTTTTATTTCTAG
1921  TACTGATTACCTCAGTACTTTGCTACTAGATAGGATAGCCTCAGTGGCTGTTACAGCAGAT
1981  TGAAGAGATCCATCCTTTTACAATCCCTGCTATTATTGCTCCATTACAGCGTATTGAACTA
2041  TGATCCACCTCAAAGGGATGAATTTTTGGGAACTTGGCTGCAACATCTTAATTCCTACTT
2101  AGGTATATTGGATCCTTTTATATTAGTGTTCCTTGGTTTTCTCTTTGGCCACACTTGAATA
2161  TTTTCCAGAAGATCTGCTAAAGGCAATTTTAAACATCAAATTCCTTAGCTAGATTGGATTTC
2221  TCAACTTGAAAGTATTGGTGGCATGGATGGAACACAACAGCAGATTTTTAAATGTTAGC
2281  AGAGGTACTAGGAGGAATCAATTGTGTAAAGCCCTCGGTTCTTACGCCTTATTACCACAA
2341  AGTAGATTTTGAAGTGTATCTTGGATAAAAGAAAAAACCTCTTCCGTATGGGAAGCATAA
2401  TATAGCATTGGGACAACTACCAGAAATGCCCTGGGAATCAATATCGAAATAGTTGGATC
2461  AAGGCTGCCACCAGGGGCTGAAAGGATTGCTTTGGAATTTTGGATTCAAAGCACTTTG
2521  TAGAAATATCCCTCACATGAAAGGAAAATCTGCTATGAAAAAACGACATTTGGAAATTC
2581  GGGGTATCGTGAATTCAGATTTCCAGTTTGAATGGAACCTATGGCACTGTCAACAAA
2641  GGATGCTCGGATGGACTACCTGAGAGAATGTATATTTGGAGAAGTCAAGTCATGTTTGTAA
2701  GTTTTTTATTTAAATGAATGTTATCGTGTGTACATTTGGACCTATTTTAATAAAGTGCC
2761  CTGTCTC
```

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000260971 and has a sequence as in SEQ ID NO:153

```

1  MKKTPVFLES LVTNMLRLRAICPFSWRVFQFRPISCEPLIIQMKNKCTDEEQMFGFIERNK
61  AILSEKQVGCAFDMLWLKQKQTSLLKNAEYVRDHPQFLTLHNLATNKFCLMNDLTVNV
121 LYVTQQFAGEAHDPLVEALVTEAWRRLERFDIKLLSEFSSCLADQHL YFSPLMGKIADIV
181 HRNLETTQDLSSLSVLMVNISLISRHFQQQLVNKTELLFD TIDSSEVNVAKSI AKFLRN
241 VRYRYQPLLERCNNVFLSNVDHLDLDSISKILSVYKFLQFNSFEFIIMAKKKLTEMIPLC
301 NHPASFVKLFVALGP IAGPEEKKQLKSTMLLMSEDLTGEQALAVLGAMGDMESRNSCLIK
361 RVTSVLHKHLDGYKPLELLKITQELTFLHFQKEFFAKLRELLLSYLKNSFIPTEVSVLV
421 RAISLLPSPHLDEVGISRIEAVLPQCDLNNLSSFATSVLRW IQHDHMYLDNMTAKQLKLL
481 QKLDHYGRQRLQHSNSLDLLRKELKSLKGNTPFESLLEEMIATLQHFMDDIN YINVGEIA
541 SFISSTDYLS TLLLDRIASVAVQQIEKIHPFTIPAIIRPFSVLNYDPPQRDEF LGTCVQH
601 LNSYLGILDPFILVFLGFSLATLEYFPEDLLKAIFNIKFLARLDSQLESIGGMDGTQQQI
661 FKMLAEVLGGINCVKASVLT PYYHKVDFECILDKRKKPLPYGSHNIALGQLPEMPWESNI
721 EIVGSRLP PGAERIALEFLDSKALCRNIPHMKGKSAMKKRHLEILGYRVIQISQFEWNSM
781 ALSTKDARMDYLRECIFGEVKSC L

```

Primers for amplifying a FASTKD1 nucleic acid sequence can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying a FASTKD1 nucleic acid include those in

Forward: SEQ ID NO:154 TGAATGACGATACCCTGGTG

Reverse: SEQ ID NO:155 AGCCTTCTCCATGCTTCTGT

Forward: SEQ ID NO:156 CCATGACCCGCTAGTTGAAG

Reverse: SEQ ID NO:157 TGATCTGCTAGGCAAGAGGAA

Forward: SEQ ID NO:158 TTCCTCTTGCCTAGCAGATCA

Reverse: SEQ ID NO:159 TGTTGACCATCAAGACAGACA

Forward: SEQ ID NO:160 TCCTCTGTGTAATCATCCTGCT

Reverse: SEQ ID NO:161 CTCGCCAGTTAGGTCCTCTG

Forward: SEQ ID NO:162 GGAGCAATGGGAGATATGGA

Reverse: SEQ ID NO:163 TTCCTTTGGAAATGCAGAAAA

Forward: SEQ ID NO:164 TGCATTTCCAAAGGAAGGAG

Reverse: SEQ ID NO:165 CAAGTGAGGAGAAGGGAGCA

Forward: SEQ ID NO:166 AAATGTTGGGGAGATTGCAT

Reverse: SEQ ID NO:167 TCAATACGCTGAATGGACGA

Forward: SEQ ID NO:168 GATCCACCTCAAAGGGATGA

Reverse: SEQ ID NO:169 GGCCAAAGAGAAACCAAGAA

Forward: SEQ ID NO:170 GTGTTTCTTGGTTTCTCTTTGG

Reverse: SEQ ID NO:171 CTGTTGTGTTCCATCCATGC

Forward: SEQ ID NO:172 GCATTGGGACAACTACCAGAA  
Reverse: SEQ ID NO:173 GTATGGGAGCGCAAAAGAAG

Forward: SEQ ID NO:174 TGTGTTGCTTCATATTTGTACCC  
Reverse: SEQ ID NO:175 CATAGCAGATTTTCCTTTCATGTG

Forward: SEQ ID NO:176 TGACCGCTTCTGTCAACAAT  
Reverse: SEQ ID NO:177 TGAATCCAAAAATTCCAAAGC

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting FASTKD1 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include

SEQ ID NO:178 GACCCGCTAGTTGAAGCACT  
SEQ ID NO:179 ACAGAAGCATGGAGAAGGCT  
SEQ ID NO:180 GAACTTGGAACACACAGGA  
SEQ ID NO:181 TTGTAGCATTGGGACCCATT  
SEQ ID NO:182 TGCATAAACATTTGGATGGC  
SEQ ID NO:183 TTCTGGTCCGTGCTATTTCC  
SEQ ID NO:184 GTGGCTGTTTCAGCAGATTGA  
SEQ ID NO:185 GAACTTGCGTGCAACATCTT  
SEQ ID NO:186 CCAGAAGATCTGCTAAAGGCA  
SEQ ID NO:187 TGCCCTGGGAATCAAATATC  
SEQ ID NO:188 GGATTGCTTTGGAATTTTGG  
SEQ ID NO:189 ATGGATGGAACACAACAGCA

A probe for detecting a FASTKD1 nucleic acid that was used on the microarray has a sequence as in SEQ ID NO:190  
TGAATGGAACTCTATGGCACTGTCAACAAAGGATGCTCGGATGGACTACCTG  
AGAGA

Other probes to FASTKD1 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against FASTKD1 include, but are not limited to, Mouse Anti-Human FLJ21901 Polyclonal Antibody Cat# H00079675-A01 against de N-terminal (from aa 2-100).

#### Example 13: IKBKE

IKBKE (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase epsilon) also known as IKK-I; IKKE; IKKI; KIAA0151; MGC125294; MGC125295;

MGC125297, was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that IKBKE was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that IKBKE was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that IKBKE can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

IKBKE is a member of the large I $\kappa$ B kinase complex capable of phosphorylating I $\kappa$ B. IKK phosphorylates only one of two serine residues in I $\kappa$ B $\alpha$  necessary for ubiquitination and degradation of I $\kappa$ B $\alpha$ . The degradation of I $\kappa$ B $\alpha$  exposes however, the nuclear localization signals on NF- $\kappa$ B, leading to its translocation to the nucleus, where it binds to specific promoters and activates transcription. (PMID: 10882136).

The sequence of an mRNA corresponding to IKBKE is given in ENSEMBL accession no. ENST00000367120 and has a sequence as in SEQ ID NO:191

```
GAGAGAGCTGAGAGCCAGGACTCAGTGCTGAGCTTGGTGTCCACCGCCACAAGGAGGCAGGGAAGAAAC
CCACTAGTCCCAGCTCCTGGGGTGGCACAGACATTGCAACTGGCCCTGCCTGTGGGTCTAGGGGGCCCTT
GGCTACCAGGAGGCTAAGAACACTGCTCATGAATGACAGTGAGCCCTGAAAGCTCTGGGGGTGTCACCCA
GTCCCACAAGCCTGCATCCCTGCAGTGAGATGGGCTCAGCTCCTGGACGTGCCACAGACAGAAAGCAT
AACATACACTCGCCAGGAAGAGCCTTTGCTGACTCAGGGCAGCTCAGAGTGTGGGGCAGAAGGTGACCA
GCCAGCTCAGGGCAGGAGATGTCAGAGCACAGCCAATTACCTGTGGCACACAGATGACCTGCTGGGGCAGG
GGGCCACTGCCAGTGTGTACAAGGCCCGCAACAAGAAATCCGGAGAGCTGGTTGCTGTGAAGGTCTTCAA
CACTACCAGCTACCTGCGGCCCGCGAGGTGCAGGTGAGGGAGTTTGAGGTCTCGCGAAGCTGAACCAC
CAGAACATCGTCAAGCTCTTTGCGGTGGAGGAGACGGGCGGAAGCCGGCAGAAGGTACTGGTGATGGAGT
ACTGCTCCAGTGGGAGCCTGCTGAGTGTGCTGGAGAGCCCTGAGAATGCCTTTGGGCTGCCTGAGGATGA
GTTCTTGGTGGTGTGCTGCGCTGTGTGGTGGCCGGCATGAACCACCTGCGGGAGAACGGCATTGTGCATCGC
GACATCAAGCCGGGGAACATCATGCGCCTCGTAGGGGAGGAGGGGCAGAGCATCTACAAGCTGACAGACT
TCGGCGCTGCCCCGGGAGCTGGATGATGATGAGAAGTTTCGTCTCGGTCTATGGGACTGAGGAGTACCTGCA
TCCCGACATGTATGAGCGGGCGGTGCTTCGAAAGCCCCAGCAAAAAGCGTTTCGGGGTGAAGTGTGGATCTC
TGGAGCATTGGAGTGACCTTGTACCATGCAGCCACTGGCAGCCTGCCCTTCATCCCCCTTTGGTGGGCCAC
GGCGGAACAAGGAGATCATGTACCGGATCACACGGGAAGCCGGCTGGGGCCATTGCAGGTGCCCCAGAG
GCGGGAGAACGGGCCCTGGAGTGGAGCTACACCTCCCCATCACCTGCCAGCTGTCACTGGGGCTGCAG
AGCCAGCTGGTGGCCATCCTGGCCAAACATCCTGGAGGTGGAGCAGGCCAAGTGTGGGGCTTCGACCAGT
TCTTTGCGGAGACCAGTGACATCCTGCAGCGAGTTGTGCTCCATGTCTTCTCCCTGTCCAGGCAGTCTT
GCACCACATCTATATCCATGCCCAACACGATAGCCATTTTCCAGGAGGCCGTGCACAAGCAGACCAGT
GTGGCCCCCGACACCAGGAGTACCTCTTTGAGGGTTCACCTCTGTGTCTCGAGCCCAGCGTCTCAGCAC
AGCACATCGCCACACGACGGCAAGCAGCCCCCTGACCCTCTTCAGCACAGCCATCCCTAAGGGGCTGGC
CTTCAGGGACCCTGCTCTGGACGTCCCCAAGTTTCGTCCCCAAAGTGGACCTGCAGGCGGATTACAACACT
GCCAAGGGCGTGTGGGGCGCCGGCTACCAGGCCCTGCGGCTGGCACGGGGCCCTGTCTGGATGGGCAGGAGC
TAATGTTTCGGGGGCTGCACTGGGTTCATGGAGGTGCTCCAGGCCACATGCAGACGGACTCTGGAAGTGGC
AAGGACATCCCTCCTCTACCTCAGCAGCAGCCTGGGAAGTGAAGGTTTCAGCAGCGTGGCTGGAACGCCT
GAGATCCAGGAAGTGAAGGCGGCTGCAGAACTGAGGTCCAGGCTGCGGACTCTAGCGGAGGTCTCTCCA
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GATGCTCCCAAAATATCACGGAGACCCAGGAGAGCCTGAGCAGCCTGAACCGGGAGCTGGTGAAGAGCCG  
 GGATCAGGTACATGAGGACAGAAGCATCCAGCAGATTGCTGCTGTTTGGACAAGATGAACCTTCATCTAC  
 AAACAGTTCAAGAAGTCTAGGATGAGGCCAGGGCTTGGCTACAACGAGGAGCAGATTACAAAGCTGGATA  
 AGGTGAATTTGAGTCATTTAGCCAAAAGACTCCTGCAGGTGTTCCAGGAGGAGTGCCTGCAGAAGTATCA  
 AGCGTCTTAGTCACACACGGCAAGAGGATGAGGGTGGTGCACGAGACCAGGAACCACTGCGCTGGTT  
 GGCTGTTCTGTGGCTGCCTGTAACACAGAAGCCCAGGGGGTCCAGGAGAGTCTCAGCAAGCTCCTGGAAG  
 AGCTATCTCACCAGCTCCTTCAGGACCGAGCAAAGGGGGCTCAGGCCTCGCCGCTCCCATAGCTCCTTA  
 CCCAGCCCTACACGAAAGGACCTGCTTCTCCACATGCAAGAGCTCTGCGAGGGGATGAAGCTGCTGGCA  
 TCTGACCTCCTGGACAACAACCGCATCATCGAACGGCTAAATAGAGTCCCAGCACCTCCTGATGTCT**AG**  
 CTCCATGGGGCACATGAGGCATCCTGAAGCATTAGAATGATTCCAACACTGCTCTTCTGCACCATGAGAC  
 CAACCCAGGGCAAGATCCCATCCCATCACATCAGCCTACCTCCCTCCTGGCTGCTGGCCAGGATGTCGCC  
 AGCATTACCTTCCACTGCCTTTCTCCCTGGGAAGCAGCACAGCTGAGACTGGGCACCAGGCCACCTCTGT  
 TGGGACCCACAGGAAAGAGTGTGGCAGCAACTGCCTGGCTGACCTTTCTATCTTCTCTAGGCTCAGGTAC  
 TGCTCCTCCATGCCCATGGCTGGGCCGTGGGGAGAAGAAGCTCTCATAACGCTTCCCACTCCCTCTGGTT  
 TATAGGACTTCACTCCCTAGCCAACAGGAGAGGAGGCCTCCTGGGGTTTCCCCAGGGCAGTAGGTCAAAC  
 GACCTCATCAGCTCTTCTTCTTCTTCAAGCGTTTCATGTTGAACACAGCTCTCTCCGCTCCCTTGTGA  
 TTTCTGAGGGTCAACACTGCCAGCCTCAGGCAACATAGAGAGCCTCCTGTTCTTTCTATGCTTGGTCTGA  
 CTGAGCCTAAAGTTGAGAAAATGGGTGGCCAAGGCCAGTGCCAGTGTCTTGGGGCCCTTTGGCTCTCCC  
 TCACTCTCTGAGGCTCCAGCTGGTCTGGGACATGCAGCCAGGACTGTGAGTCTGGGCAGGTCCAAGGCC  
 TGCACCTCAAGAAGTGAATAAATGTGGCCTTGTCTCTGTT

The start and stop codons are indicated in bold.

The corresponding amino acid sequence is given in ENSEMBL accession no.  
 ENSP00000356087 and has a sequence as in SEQ ID NO:192

MQSTANYLWHTDDLGLQGATASVYKARNKKSSELVAVKVFNTTS  
 YLRPREVQVREFEVLRLNHNQIVKLFAVEETGGSRQKVLVMEYCSSGSLLSVLESPE  
 NAFGLPEDEFLVLRVAGMNLRENGIVHRDIKPGNIMRLVGEQGSIYKLTDFGA  
 ARELDDDEKFVSIVGTEEYLHPDMEYRAVLKPKQKAFGVTVDLWSIGVTLYHAATGS  
 LPFIPFGGPRRNKEIMYRITTEKPAIAGAQRRENGPLEWSYTLPICTQLSLGLQSQ  
 LVPILANILEVEQAKCWGFDQFFAETSDILQRVVHVFSLSQAVLHHIYIHAHNTIAI  
 FQEAHVHKQTSVAPRHQEYLFEGHLCVLEPSVSAQHIAHTTASSPLTLFSTAIPKGLAF  
 RDPALDVPKFPVKVDLQADYNTAKGVLGAGYQALRLARALLDQELMFRGLHWVMEVL  
 QATCRRTLEVARTSLLYLSSSLGTERFSSVAGTPEIQELKAAAEALRSRLRLAEVLSR  
 CSQNTTETQESLSSLNRELVKSRDQVHEDRSIQIQCLDKMNFYKQFKKSRMRPGL  
 GYNEEQIHKLDKVNFSHLAKRLQLVFQEECVQKYQASLVTHGKMRVHVHETRNHLRLV  
 GCSVAACNTEAQGVQESLSKLEELSHQLLQDRAKGAQASPPPIAPYPSPTRKDLLLH  
 MQELCEGMKLLASDLLDNNRIIERLNRVPAPPDV

Primers for amplifying the sequence ENST00000367120 can be designed using  
 primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying IKBKE include:

Forward SEQ ID NO:193 GTGCCACAGACAGAAAGCATAAC (EX2)  
 Reverse SEQ ID NO:194 GGCTGTGCTCTGCATCTC (ex3)

Foward SEQ ID NO:195 GGGGCCACTGCCAGTGTG (ex3)  
 Reverse SEQ ID NO:196 GCAGGTAGCTGGTAGTGTGAAG (ex4)

Forward SEQ ID NO:197 GAGGTCCTGCGGAAGCTGAAC (ex4)

Reverse SEQ ID NO:198 CACTCAGCAGGCTCCCACTG (ex5)

Forward SEQ ID NO:199 CCTGAGGATGAGTTCCTGGTG (ex5)

Reverse SEQ ID NO:200 GTCGCGATGCACAATGCCGTTC (ex6)

Forward SEQ ID NO:201 GGATGATGATGAGAAGTTCGTCTC

Reverse SEQ ID NO:202 GAACGCTTTTTGCTGGGGC (ex7)

Forward SEQ ID NO:203 CATCCCCTTTGGTGGGCCAC (ex7)

Reverse SEQ ID NO:204 CCGTTCTCCCGCCTCTGG (ex8)

Forward SEQ ID NO:205 CCTGGAGTGGAGCTACACC (ex8)

Reverse SEQ ID NO:206 CACTTGGCCTGCTCCACCTC (ex9)

Forward SEQ ID NO:207 GTCCCAGGCAGTCCTGCAC (ex9)

Reverse SEQ ID NO:208 GACGCTGGGCTCGAGGACAC (ex10)

Forward SEQ ID NO:209 GACCCTCTTCAGCACAGCCAT C

Reverse SEQ ID NO:210 GCCGCAGGGCCTGGTAGC (ex12)

Forward SEQ ID NO:211 GATCCAGGAAGTGAAGGCGGC (ex14)

Reverse SEQ ID NO:212 CCTGATCCCGGCTCTTCAC (ex15)

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting IKBKE can be derived from any number of sources depending on the desired use (e.g., using the primers described above and the appropriate reagents).

Other examples of probes include:

SEQ ID NO:213

CTCCTGTTCTTTCTATGCTTGGTCTGACTGAGCCTAAAGTTGAGAAAATGGG  
TGGCCAAG

SEQ ID NO:214

CATCACCTGCCAGCTGTCACTGGGGCTGCAGAGCC

SEQ ID NO:215

CTATATCCATGCCACAACACGATAGCCATTTTCC

SEQ ID NO:216

GGACGTCCCAAGTTCGTCCCCAAAGTGGACCTGCAGGCG

SEQ ID NO:217

GGTCCAGGAGAGTCTCAGCAAGCTCCTGGAAGAGCTATCTCAC

Other probes to IKBKE are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against IKBKE include, but are not limited to, Abcam Cat# ab37596 which is a rabbit polyclonal antibody with an antigen that was a KLH conjugated synthetic peptide selected within a.a. 700-800 of human IKKE; and Abcam Cat# ab12142 which is a mouse monoclonal antibody against a synthetic peptide corresponding to a.a. residues 175-188, 525-540, or 567-580 of human IKK iota/IKK epsilon.

#### Example 14: PHKG2

PHKG2 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that PHKG2 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that PHKG2 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Examples 2-4. Example 5 shows that PHKG2 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to PHKG2 is given in ENSEMBL accession no. ENST00000328273 and has a sequence as in SEQ ID NO:218

```
1  AAGGTGAGCGACTGCAGGCAAACCCGGCGACAGCGCAGCTCGCGTCGACCCTGGCTCCTC
61  TGCCTGCCCCCTCAGGCCCGCCCTCCTTCAGGATGACGCTGGACGTGGGGCCGGAGGAT
121  GAGCTGCCCCACTGGGCCCGCCCAAAGAGTTTACCAGAAGTACGACCCTAAGGACGTC
181  ATCGCGAGAGGAGTGAGCTCTGTGGTCCGCCGTTGTGTTTCATCGAGCTACTGGCCACGAG
241  TTTGCGGTGAAGATTATGGAAGTGACAGCTGAGCGGCTGAGTCCTGAGCAGCTGGAGGAG
301  GTGCGGGAAGCCACACGGCGAGAGACACATCCTTCGCCAGGTGCGCCGCCACCCCCAC
361  ATCATCACCCCTCATCGATTCCTACGAGTCTTCTAGCTTCATGTTCTGTTGTTGACCTG
421  ATGCGGAAGGGAGAGCTGTTTGACTATCTCACAGAGAAGGTGGCCCTCTCTGAAAAGGAA
481  ACCAGGTCCATCATGCGGTCTCTGCTGGAAGCAGTGAGCTTTCTCCATGCCAACACATT
541  GTGCATCGAGATCTGAAGCCCGAGAATATTCTCCTAGATGACAATATGCAGATCCGACTT
601  TCAGATTTCCGGTTCTCCTGCCACTTGGAACTGGCGAGAAGCTTCGAGAGTTGTGTGGG
661  ACCCCAGGGTATCTAGCGCCAGAGATCCTTAAATGCTCCATGGATGAAACCCACCCAGGC
721  TATGSCAAGGAGGTGACCTCTGGGCCCTGTGGGTGATCTTGTTCACACTCCTGGCTGGC
781  TCGCCACCCCTTCTGGCACCGCGCGCAGATCCTGATGTTACGCATGATCATGGAGGGCCAG
841  TACCAGTTCAAGTTCCCCCGAGTGGGATGACCGTTCCAGCACTGTCAAAGACCTGATCTCC
901  AGGCTGCTGCAGGTGGATCCTGAGGCACGCCCTGACAGCTGAGCAGGCCCTACAGCACCCC
961  TTCTTTGAGCGTTGTGAAGGCAGCCAACCTGGAACCTCACCCCGCCAGCGGTTCCGG
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```

1021 GTGGCAGTGTGGACAGTGGCTGGCTGGACGAGTGGCCCTAAGCACCCATCGTGTACGG
1081 CCACTGACCAAGAAATGCACTGTTGAGGGACCCCTTATGCGCTGCGGTCACTGCGGCACCTC
1141 ATCGACAACCTGTGCCTTCCGGCTCTACGGGCACTGGGTAAAGAAAGGGAGCAGCAGAAC
1201 CGGGCGGCTCTCTTTCAGCACCGGCCCCCTGGGCCTTTTCCCATCATGGGCCCTGAAGAG
1261 GAGGGAGACTCTGCTGCTATAACTGAGGATGAGGCCGTGCTTGTGCTGGGCTAGGACCTC
1321 AACCCAGGGATTCCCAGGAAGCAGAACTCTCCAGAAGAAGGGTTTTGATCATTCCAGCT
1381 CCTCTGGGCTCTGGCCTCTGGCCTCAGGCCCACTAATGATCCTGCTACCCCTCTTGAAGAC
1441 CAGCCCGGTACCTCTCTCCCCACTGGCCAGGACTCTGAGATCAGAGCTGGGGTGGGAAGGG
1501 AGCCATTCTGAACGCCACGCCTGGCCCCGTGCTGCTGCATGCACTGCATATGAAATAAA
1561 ATCTGCTACACGCCAGGG

```

The start and stop codons are indicated in bold.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000329968 and has a sequence as in SEQ ID NO:219

```

1-  MTLDVGPEDLPDWAAAKEFYQKYDPKDVIGRVSSVVRRCVHRATGHEFAVKIMEVTAE
61  RLSPEQLEEVREATRRETHILRQVAGHPHII TLIDSYESSSFMFLVFDLMRKGELFDYLT
121 EKVALSEKETRSIMRSLLEAVSFLHANNIVHRDLKPENILLDDNMQIRLSDFGFSCHLEP
181 GEKRLRELCGTPGYLAPEILKCSMDETHPGYGKEVDLWACGVILFTLLAGSPPFWHRRIIL
241 MLRMIMEGQYQFSSPEWDDRSSTVKDLISRLQVDPEARLTAEQALQHPFFERCEGSQPW
301 NLTPRQRFRAVAVWTVLAAGRVALSTHRVRPLTKNALLRDPYALRSVRHLIDNCAFRLYGH
361 WVKKGEQQNRAALFQHRPPGPFPI MGPEEEGDSAAITEDEAVLVLG

```

Primers for amplifying the sequence PHKG2 can be designed using primer design software such as Oligo Calc.

Examples of primer pairs for amplifying PHKG2 include those in

forward SEQ ID NO:220 CCGCCAAAGAGTTTTACCAG

reverse SEQ ID NO:221 TCCATAATCTTCACCGCAAA

forward SEQ ID NO:222 GGCGAGAGACACACATCCTT

reverse SEQ ID NO:223 CAAACACCAGGAACATGAAGC

forward SEQ ID NO:224 GCTTCATGTTCTGCTGGTGTGTTG

reverse SEQ ID NO:225 TTTTCAGAGAGGGCCACCTT

forward SEQ ID NO:226 GGAAGGGAGAGCTGTTTGACT

reverse SEQ ID NO:227 TGTTGTTGGCATGGAGAAAG

forward SEQ ID NO:228 TCAGATTTCTGGGTTCTCCTG

reverse SEQ ID NO:229 ATAGCCTGGGTGGGTTTCAT

forward SEQ ID NO:230 ATGAAACCCACCCAGGCTAT

reverse SEQ ID NO:231 TGCGTAAACATCAGGATCTGC

forward SEQ ID NO:232 CGTTCCAGCACTGTCAAAGA

reverse: SEQ ID NO:233 CCTTCACAACGCTCAAAGAA

forward SEQ ID NO:234 ACCCCTTCTTTGAGCGTTGT

reverse SEQ ID NO:235 CGTACACGATGGGTGCTTAG

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting PHKG2 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include

SEQ ID NO:236 CCGTTGTGTTTCATCGAGCTA  
SEQ ID NO:237 CATCACCTCATCGATTCTT  
SEQ ID NO:238 GGAAGGGAGAGCTGTTTGACT  
SEQ ID NO:239 AGGAAACCAGGTCCATCATG  
SEQ ID NO:240 CAGGGTATCTAGCGCCAGAG  
SEQ ID NO:241 CCTGTGGGGTGATCTTGTTT  
SEQ ID NO:242 ACAGCTGAGCAGGCCCTAC  
SEQ ID NO:243 GTTGTGGCAGTGTGGACAGT

A probe for detecting a PHKG2 nucleic acid that was used on the microarray has a sequence as in

SEQ ID NO:244  
CTCAACCCCAGGGATTCCCAGGAAGCAGAACTCTCCAGAAGAAGGGTTTTGATCA  
TTCCA

Other probes to PHKG2 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against PHKG2 include, but are not limited to, Mouse monoclonal antibody Anti-PHKG2 against full length protein Cat# WH0005261M1 from SIGMA; PHKG2 antibody - N-terminal Cat# ab71129 from abcam; and PHKG2 antibody Cat# ab28642 against a region between amino acids 8-57 of human PHKG2 from abcam.

#### Example 15: P4HB

P4HB was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that P4HB was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue and it was surprisingly found that P4HB was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial

cancer by the method described in Examples 2-4. Example 5 shows that P4HB can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to P4HB is given in ENSEMBL accession no. ENST00000331483 and has a sequence as in SEQ ID NO:245

```

1  GAGCCTCGAAGTCCGCGGCCAATCGAAGGCGGGCCCCAGCGGCGCGTGC GCGCCGCGGC
61  CAGCGCGCGCGGGGCGGGGGGCGAGGCGCGCCCCGGACCCAGGATTTATAAAGGCGAGGCC
121 GGGACCGGCGCGCGCTCTCGTCGCCCCCGCTGTCCCGGCGGCGCCAACCGAAGCGCCCCG
181 CCTGATCCGTGTCCGACATGCTGCGCCGCGCTCTGCTGTGCCTGGCCGTGGCCGCCCTGG
241 TGC GCGCCGACGCCCCCGAGGAGGAGGACACGTCTGCTGCTGCGGAAAAGCAACTTCG
301 CGGAGGCGCTGGCGGCCCCACAAGTACCTGCTGGTGGAGTTCTATGCCCTTGCTGTGGCC
361 ACTGCAAGGCTCTGGCCCCCTGAGTATGCCAAAGCCGCTGGGAAGCTGAAGGCAGAAGGTT
421 CCGAGATCAGGTTGGCCAAGGTGGACGCCACGGAGGAGTCTGACCTGGCCAGCAGTACG
481 GCGTGC GCGGCTATCCACCATCAAGTTCTTCAGGAATGGAGACACGGCTTCCCCCAAGG
541 AATATACAGCTGGCAGAGAGGCTGATGACATCGTGAAGTGGCTGAAGAAGCGCACGGGCC
601 CGGCTGCCACCACCCTGCCTGACGGCGCAGCTGCAGAGTCCTTGGTGGAGTCCAGCGAGG
661 TGGCTGTCATCGGCTTCTTCAAGGACGTGGAGTCGGACTCTGCCAAGCAGTTTTTGCAGG
721 CAGCAGAGGCCATCGATGACATACCATTGGGATCACTTCCAACAGTGACGTGTTCTCCA
781 AATACCAGCTCGACAAAGATGGGGTGTCTCTTTAAGAAGTTTGATGAAGGCCGGAACA
841 ACTTTGAAGGGGAGGTCACCAAGGAGAACCTGCTGGACTTTATCAAACACAACAGCTGC
901 CCCTTGTCATCGAGTTCACCGAGCAGACAGCCCCGAAGATTTTTGGAGGTGAAATCAAGA
961 CTCACATCCTGCTGTTCTTGCCCCAAGAGTGTGTCTGACTATGACGGCAAACCTGAGCAACT
1021 TCAAACAGCAGCCGAGAGCTTCAAGGGCAAGATCCTGTTTCATCTTCATCGACAGCGACC
1081 ACACCGACAACCAGCGCATCCTCGAGTTCTTTGGCCTGAAGAAGGAAGAGTGCCCGGCCG
1141 TGCGCCTCATCACCTGGAGGAGGAGATGACCAAGTACAAGCCCGAATCGGAGGAGCTGA
1201 CGGCAGAGAGGATCACAGAGTTCTGCCACCGCTTCTGGAGGGCAAATCAAGCCCCACC
1261 TGATGAGCCAGGAGCTGCCGAGGACTGGGACAAGCAGCCTGTCAAGGTGCTTGTGGGA
1321 AGAAGTTTGAAGACGTGGCTTTTGATGAGAAAAAAACGTCTTTGTGGAGTCTATGCCC
1381 CATGGTGTGGTCACTGCAAACAGTTGGCTCCCATTTGGGATAAACTGGGAGAGACGTACA
1441 AGGACCATGAGAACATCGTCATCGCCAAGATGGACTCGACTGCCAACGAGGTGGAGGCCG
1501 TCAAAGTGACAGCTTCCCCCACTCAAGTTCTTTCTGCCAGTGCCGACAGGACGGTCA
1561 TTGATTACAACGGGGAACGCACGCTGGATGGTTTTAAGAAATTCCTGGAGAGCGGTGGCC
1621 AGGATGGGGCAGGGGATGATGACGATCTCGAGGACCTGGAAGAAGCAGAGGAGCCAGACA
1681 TGGAGGAAGACGATGATCAGAAAGCTGTGAAAGATGAAGTGATAATACGCAAAGCCAGACC
1741 CGGGCGCTGCCGAGACCCCTCGGGGGCTGCACACCCAGCAGCAGCGCACGCCTCCGAAGC
1801 CTGCGGCCTCGCTTGAAGGAGGGCGTCGCCGGAACCCAGGGAACCTCTCTGAAGTGACA
1861 CCTCACCCCTACACACCGTCCGTTCAACCCCGTCTCTTCTCTGCTTTTCGGTTTTTGG
1921 AAAGGGATCCATCTCCAGGCAGCCACCCCTGGTGGGGCTTGTTCCTGAAACCATGATGT
1981 ACTTTTTATACATGAGTCTGTCCAGAGTGCTTGCTACCGTGTTCCGAGTCTCGCTGCCT
2041 CCTCCCGCGGGAGGTTTCTCCTCTTTTGAATAATCCGTCTGTGGGATTTTGTAGACATT
2101 TTTGCACATCAGGGTATTTGTTCCACCTTGGCCAGGCCTCCTCGGAGAAGCTTGTCCCCC
2161 GTGTGGGAGGGACGGAGCCGACTGGACATGGTCACTCAGTACCGCCTGCAGTGTGCCCA
2221 TGAATGATCATGGCTCTTGCAATTTTGGGTAAATGGAGACTTCCGGATCCTGTGAGGGTG
2281 TCCCCCATGCCTGGAAGAGGAGCTGGTGGCTGCCAGCCCTGGGGCCCGGCACAGGCCTGG
2341 GCCTTCCCCTTCCCTCAAGCCAGGGCTCCTCCTCCTGTGCTGGGCTCATTGTGACCACTG
2401 GCCTCTCTACAGCACGGCTGTGGCCTGTTCAAGGCAGAACCACGACCCCTGACTCCCGG
2461 GTGGGGAGGTGGCCAAGGATGCTGGAGCTGAATCAGACGCTGACAGTTCTCAGGCATTT
2521 CTATTTCAATCGGAATTGAACACATTGGCCAAATAAAGTTGAAATTTTACCACCTGT

```

The start and stop codons are indicated in bold as well as the position corresponding to the microarray probe.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000327801 and has a sequence as in SEQ ID NO:246

```

1 MLRRALLCLAVAALVRADAPEEEDHVLVLRKSNFAEALAAHKYLLVEFYAPWCGHCKALA
61 PEYAKAAGKLKAEGSEIRLAKVDATEESDLAQYGVRGYPTIKFFRNGDTASPKKEYTAGR
121 EADDIVNWLKKRTGPAATTLPGAAAESLVESSEVAVIGFFKDVEDSAKQFLQAAEAID
181 DIPFGITSNSDVFSKYQLDKDGVVLFKKFDEGRNNFEGEVTKENLLDFIKHNQLPLVIEF
241 TEQTAPKIFGGEIKTHILLFLPKSVSDYDGKLSNEKTAAESFKGKILFIFIDSDHTDNQR
301 ILEFFGLKKEECPAVRLITLEEEMTKYKPESEELTAERITEFCHRFLEGKIKPHLMSQEL
361 PEDWDKQPVKVLVGKNFEDVAFDEKKNVFVEFYAPWCGHCKQLAPIWDKLGETYKDHENI
421 VIAKMDSTANEVEAVKVHSFPTLKFFPASADRTVIDYNGERTLDGFKKFLESQGQDGAGD
481 DDDLEDLEEAEPPMEEDDDQKAVKDEL

```

Primers for amplifying the sequence P4HB can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying P4HB include those in

Forward SEQ ID NO:247: GCTGCGGAAAAGCAACTTC  
Reverse SEQ ID NO:248 CTGATCTCGGAACCTTCTGC

Forward SEQ ID NO:249 GGCTATCCCACCATCAAGTT  
Reverse SEQ ID NO:250 TCTTCAGCCAGTTCACGATG

Forward SEQ ID NO:251 GCAGAGTCCTTGGTGGAGTC  
Reverse SEQ ID NO:252 TGGAAGTGATCCCAAATGGT

Forward SEQ ID NO:253 ACCATTTGGGATCACTTCCA  
Reverse SEQ ID NO:254 GGTGACCTCCCCTTCAAAGT

Forward SEQ ID NO:255 CCCCTTGTCATCGAGTTCAC  
Reverse SEQ ID NO:256 TGCTCAGTTTGCCGTCATAG

Forward SEQ ID NO:257 TCACATCCTGCTGTTCTTGC  
Reverse SEQ ID NO:258 GTCGCTGTCGATGAAGATGA

Forward SEQ ID NO:259 GACGGCAGAGAGGATCACAG  
Reverse SEQ ID NO:260 TTCTTCCCAACAAGCACCTT

Forward SEQ ID NO:261 AGCCTGTCAAGGTGCTTGTT  
Reverse SEQ ID NO:262 CAAATGGGAGCCAACTGTTT

Forward SEQ ID NO:263 ACAGCTTCCCCACACTCAAG  
Reverse SEQ ID NO:264 CACCGCTCTCCAGGAATTT

Forward SEQ ID NO:265 GCACGCTGGATGGTTTTAAG  
Reverse SEQ ID NO:266 TCATCGTCTTCTCCATGTCT

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting P4HB can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include

SEQ ID NO:267 CACAAGTACCTGCTGGTGGGA  
SEQ ID NO:268 GGCTTCCCCCAAGGAATATA  
SEQ ID NO:269 GCTTCTTCAAGGACGTGGAG  
SEQ ID NO:270 CTCGACAAAGATGGGGTTGT  
SEQ ID NO:271 TCACATCCTGCTGTTCTTGC  
SEQ ID NO:272 CTATGACGGCAAACCTGAGCA  
SEQ ID NO:273 AAAATCAAGCCCCACCTGAT  
SEQ ID NO:274 TGAAGACGTGGCTTTTGATG  
SEQ ID NO:275 GGTCATTGATTACAACGGGG  
SEQ ID NO:276 ATGACGATCTCGAGGACCTG

A probe for detecting a P4HB nucleic acid that was used on the microarray has a sequence as in

SEQ ID NO:277  
GGCATTCTATTTCACAATCGAATTGAACACATTGGCCAAATAAAGTTGAAATT  
TCCCC

Other probes to P4HB are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against P4HB include, but are not limited to, anti P4HB Cat# ab31811 de abcam (rabbit polyclonal) against residues 400 to 500; and PDI (P4HB) Mouse anti-Human Monoclonal Antibody from Lifespan Biosciences Cat# LS-C38385.

#### Example 16: P2RX4

P2RX4 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that P2RX4 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that P2RX4 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example

5 shows that P2RX4 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

## P2RX4

(also known as P2X4; P2X4R; P2RX4)

P2X purinoceptor 4 (P2X4)(ATP receptor)(Purinergic receptor)

ENSG00000135124

The sequence of an mRNA corresponding to P2RX4 is given in ENSEMBL accession no. ENST00000337233 and has a sequence as in SEQ ID NO:278

```

1  AAGTGCTGGGATGACAGGTGTGAGCCACCGCCCCCGGCCCTCGCCCGCCTTTTGAAGGA
   61  GCCTTTCGTCTCTCAAGGGCGAGGCCACTCCCCCCCCGCGAGTTCCATGCCCCCTAGAGGG
  121  TCATCGTTCCCGACGGGGAGGTGGCGCCCTCCCCCGGGCCCCGGGCCCCGACCGCCCGT
  181  CTGCTCTCTTCCGGGCCCCCTCTCCGCGATGACGGCGCCGCCAGCAGGCCAGGCGGACTGG
  241  GCGGGGCTCCGAGCGGGGACTGGGACCCAGACCGACTAGGGGACTGGGAGCGGGCGGCGC
  301  GGCCATGGCGGGGCTGCTGCGCCGCGCTGGCGGCCTTCCTGTTGAGTACGACACGCCGCG
  361  CATCGTGCTCATCCGCAGCCGCAAAGTGGGGCTCATGAACCGCGCCGTGCAACTGCTCAT
  421  CCTGGCTACGTCATCGGGTGGGTGTTTGTGTGGGAAAAGGGCTACCAGGAACTGACTC
  481  CGTGCTCAGCTCCGTTACGACCAAGGTCAAGGGCGTGGCTGTGACCAACACTTCTAAACT
  541  TGGATTCCGGATCTGGGATGTGGCGGATTATGTGATACCAGCTCAGGAGGAAACTCCCT
  601  CTTGCTCATGACCAACGTGATCCTCACCATGAACCAGACACAGGGCCTGTGCCCGAGAT
  661  TCCAGATGCGACCACTGTGTGTAAATCAGATGCCAGCTGTACTGCCGGCTCTGCCGCGAC
  721  CCACAGCAACCGAGTCTCAACAGGCAGGTGCGTAGCTTTCAACGGGTCTGTCAAGACGTG
  781  TGAGGTGGCGGCCTGGTGCCCGGTGGAGGATGACACACACGTGCCACAACCTGCTTTTTT
  841  AAAGGCTGCAGAAAACCTCACTCTTTTGGTTAAGAACAACATCTGGTATCCCAAATTTAA
  901  TTTCAAGCAAGAGGAATATCCTTCCCAACATCACCCTACTTACCTCAAGTCGTGCATTTA
  961  TGATGCTAAAACAGATCCCTTCTGCCCCATATTCCGTCTTGGCAAAATAGTGGAGAACGC
 1021  AGGACACAGTTTCCAGGACATGGCCGTGGAGGGAGGCATCATGGGCATCCAGGTCAACTG
 1081  GGACTGCAACCTGGACAGAGCCGCTCCCTCTGCTTGCCAGGTAAGTCTCTCCGCGCCT
 1141  CGATACACGGGACGTTGAGCACAACGTATCTCTGGCTACAATTTCAAGGTTTGCCAAAGTA
 1201  CTACAGAGACCTGGCTGGCAACGAGCAGCGCAGCTCATCAAGGCCTATGGCATCCGCTT
 1261  CGACATCATTGTGTTTGGGAAGGCAGGGAAATTTGACATCATCCCCACTATGATCAACAT
 1321  CGGCTCTGGCCTGGCACTGCTAGGCATGGCGACCGTGCTGTGTGACATCATAGTCTCTA
 1381  CTGCATGAAGAAAAGACTCTACTATCGGGAGAAGAAATATAAATATGTGGAAGATTACGA
 1441  GCAGGCTCTTGCTAGTGAGCTGGACCACTGAGGCCTACCCACACCTGGGCTCTCCACAG
 1501  CCCCATCAAAGAACAGAGAGGAGGAGGAGGGAGAAATGGCCACCACATCACCCAGAGAA
 1561  ATTTCTGGAATCTGATTGAGTCTCCACTCCACAAGCACTCAGGGTTCCCCAGCAGCTCCT
 1621  GTGTGTTGTGTGCAGGATCTGTTTGCCCACTCGGCCCAGGAGGTCAGCAGTCTGTTCTTG
 1681  GCTGGGTCAACTCTGCTTTTCCCGCAACCTGGGGTTGTGCGGGGAGCGCTGGCCCGACGC
 1741  AGTGGCACTGCTGTGGCTTTCAGGGCTGGAGCTGGCTTTGCTCAGAAGCCTCCTGTCTCC
 1801  AGCTCTCTCCAGGACAGGCCAGTCTCTGAGGCACGGCGGCTCTGTTCAAGCACTTTAT
 1861  GCGGCAGGGGAGGCCGCTGGCTGCACTAGACTTGTAGCAGGCCTGGGCTGCAGGC
 1921  TTCCCCCGACCATTCCTGCGAGCCATGCGGCAGAGCTGGCATTTCTCCTCAGAGAAGCG
 1981  CTGTGCTAAGGTGATCGAGGACCAGACATTAAAGCGTGATTTTCTT

```

The start and stop codons are indicated in bold as well as the position corresponding to the microarray probe.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000336607 and has a sequence as in SEQ ID NO:279

```

1  MAGCCAALAAFLFEYDTPRIVLIRSRKVGLMNRVQLLILAYVIGWVFVWEKGYQETDSV
61  VSSVTTKVKGVAVTNTSKLGFRIWDVADYVIPAQEENSLFVMTNVILTMNQTGGLCPEIP
121 DATTVCKSDASCTAGSAGTHSNGVSTGRCVAFNGSVKTC EVAAWCPVEDDTHVPQPAFLK
181 AAENFTLLVKNNIWYPKENFNSKRNLPNITTTTLKSCIYDAKTD PFCPIFRLGKIVENAG
241 HSFQDMAVEGGIMGIQVNWDCNLDRAASLCLPRYSFRRLDTRDVEHNVSPGYNFRFAKYY
301 RDLAGNEQRTLKAYGIRFDIIVFGKAGKFDI IPTMINIGSGLALLGMATVLCDIIVLYC
361 MKKRLLYYREKKYKYVEDYEQGLASELDQ

```

ENST00000359949

ENSP00000353032

SEQ ID NO:280

```

1  MAGCCAALAAFLFEYDTPRIVLIRSRKVGLMNRVQLLILAYVIGWVFVWEKGYQETDSV
61  VSSVTTKVKGVAVTNTSKLGFRIWDVADYVIPAQEENSLFVMTNVILTMNQTGGLCPEIP
121 DATTVCKSDASCTAGSAGTHSNVCTLI PAFLKAAENFTLLVKNNIWYPKENFNSKRNL P
181 NITTTTLKSCIYDAKTD PFCPIFRLGKIVENAGHSFQDMAVEGGIMGIQVNWDCNLDRAA
241 SLCLPRYSFRRLDTRDVEHNVSPGYNFRFAKYYRDLAGNEQRTLKAYGIRFDIIVFGKA
301 GKFDI IPTMINIGSGLALLGMATVLCDIIVLYCMKKRLLYYREKKYKYVEDYEQGLASELD
361 Q

```

Examples of primer pairs for amplifying P2RX4 include:

Forward SEQ ID NO:281 AACTGCTCATCCTGGCCTAC

Reverse SEQ ID NO:282 GTCGTAACGGAGCTGACCAC

Forward SEQ ID NO:283 GGATGTGGCGGATTATGTG

Reverse SEQ ID NO:284 CCTGTGTCTGGTTCATGGTG

Forward SEQ ID NO:285 AGATTCCAGATGCGACCACT

Reverse SEQ ID NO:286 CAGACCCGTTGAAAGCTACG

Forward SEQ ID NO:287 TCTGTCAAGACGTGTGAGGTG

Reverse SEQ ID NO:288 CCAAAGAGTGAAGTTTTCTGC

Forward SEQ ID NO:289 TTTTGGTTAAGAACACATCTGG

Reverse SEQ ID NO:290 ATATGGGGCAGAAGGGATCT

Forward SEQ ID NO:291 CGCTTCGACATCATTGTGTT

Reverse SEQ ID NO:292 TAGCAGTGCCAGGCCAGAG

Forward SEQ ID NO:293 GAAAAGACTCTACTATCGGGAGAA

Reverse SEQ ID NO:294 CTGTTCTTTGATGGGGCTGT

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting P2RX4 derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include:

SEQ ID NO:295 TTGTGTGGGAAAAGGGCTAC  
SEQ ID NO:296 TTCGTCATGACCAACGTGAT  
SEQ ID NO:297 TCAGATGCCAGCTGTACTGC  
SEQ ID NO:298 GTGGAGGATGACACACACGT  
SEQ ID NO:299 TCCTTCCCAACATCACCACT  
SEQ ID NO:300 GAAGGCAGGGAAATTTGACA  
SEQ ID NO:301 GGGTCTTGCTAGTGAGCTGG

A probe for detecting a P2RX4 nucleic acid that was used on the microarray has a sequence as in

SEQ ID NO:302  
CTCCTCAGAGAAGCGCTGTGCTAAGGTGATCGAGGACCAGACATTAAAGCGTGA  
TTTTCT

Other probes to P2RX4 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies to P2RX4, include, but are not limited to, Mouse Anti-Human P2RX4 Maxpab polyclonal, unconjugated from Novus Biologicals, P2RX4 (1 a.a. ~ 388 a.a) full-length human protein, H00005025-B01, and Goat Anti-P2RX4 polyclonal, unconjugated from Novus Biologicals, NBP1-00141, Synthetic peptide, SEQ ID NO:303 YREKKYKYVEDYEQ, representing the C Terminus of the sequence according to NP\_002551.2

#### Example 17: PPFIBP2

PPFIBP2 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that PPFIBP2 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that PPFIBP2 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that PPFIBP2 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.



## PPPFIBP2

The sequence of an mRNA corresponding to PPPFIBP2 is given in ENSEMBL accession no. ENST00000299492 and has a sequence as in SEQ ID NO:304

```
1 GCAGGCTTCTTCGGTGCCCGAGAGGGAGCGGGTGCCCAAGGGGGTGGTCCCTGTGGCAGG
61 TCCCGGGGTGGGGGCGCGCGCTCCGGGAAGAGCCTTCCGCAGGTCCCCGCCCCGTACAG
121 TGGGCGCCGGCCCCGGCCGCTGCGGTGCGTCCGCTGGTTGGTCGGGCGCTTGGTCCGGCA
181 GTTGGTCGGTGGGCCAGTGGCCCGTTCGCTCGCTTCTGGGCTCTCATGTTTGAAGGTGGGA
241 GGGACACGGGAGCGGCCCGCACACCTGAGCCGCCCGGAGAGGAGCCTCGGCCCCGTACCC
301 AGTAAGAAGAGGAGGAGGCCAGGCAGGCAAAAGGAGTCATGGCCTTCTGATGCTAGTCATG
361 CGCTGGAAGCTGCCCTGGAGCAAATGGACGGGATCATTGCAGGCACTAAAACAGGTGCAG
421 ATCTTAGTGATGGTACTTGTGAGCCTGGACTGGCTTCCCGGCCCTCCTACATGAACCCCT
481 TCCCGGTGCTCCATCTCATCGAGGACTTGAGGCTGGCCTTGGAGATGCTGGAGCTTCCTC
541 AGGAGAGAGCAGCCCTCCTGAGCCAGATCCCTGGCCCAACAGCTGCCTACATAAAGGAAT
601 GGTTTGAAGAGAGCTTGTCCAGGTAAACCACCACAGTGCTGCTAGTAATGAAACCTACC
661 AGGAACGCTTGGCACGTCTAGAAGGGGATAAAGGAGTCCCTCATATTGCAGGTGAGTGTCC
721 TCACAGACCAAGTAGAAGCCAGGGAGAAAAGATTTCGAGACCTGGAAGTGTGTCTGGAAG
781 GACACCAGGTGAAACTCAATGCTGCTGAAGAGATGCTTCAACAGGAGCTGCTAAGCCGCA
841 CATCTCTTGAGACCCAGAAGCTCGATCTGATGACTGAAGTGTCTGAGCTGAAGCTCAAGC
901 TGGTTGGCATGGAGAAGGAGCAGAGAGAGCAGGAGGAGAAGCAGAGAAAAGCAGAGGAGT
961 TACTGAAGAGCTCAGGCACCTCAAAATCAAAGTGAAGAGTTGGAAAATGAAAGGAATC
1021 AGTATGAATGGAAGCTAAAGGCCACTAAGGCTGAAGTCGCCAGCTGCAAGAACAGGTGG
1081 CCCTGAAAGATGCAGAAATTGAGCGTCTGCACAGCCAGCTCTCCCGGACAGCAGCTCTCC
1141 ACAGTGAGAGTCACACAGAGAGAGACCAAGAAATTCACGCTTGAAAATGGGGATGGAAA
1201 CTTTGCTGCTTGCCAATGAAGATAAGGACCGTCGGATAGAGGAGCTTACGGGGCTGTAA
1261 ACCAGTACCGGAAGGTAAAGGAGATTGTGATGGTCACTCAAGGGCCTTCGGAGAGAACTC
1321 TCTCAATCAATGAAGAAGAACCAGGAGGGAGGTTTCAGCAAGTGGAACGCTACAAATAAGG
1381 ACCCTGAAGAATTATTTAAACAAGAGATGCCTCCAAGATGTAGCTCTCCTACAGTGGGGC
1441 CACCTCCATTGCCACAGAAATCACTGGAAACCAGGGCTCAGAAAAAGCTCTCTTGATGTC
1501 TAGAAGACTTGAGAAGTGAATCTGTGGATAAGTGTATGGATGGGAACCAGCCCTTCCCGG
1561 TGTTAGAACCACAGGACAGCCCTTTCTTGGCGGAGCACAAATATCCACTTTACCTGGGA
1621 AGCTTTTCAGGAGCCACGCCCAATGGAGAGGCTGCCAAATCTCCTCCACCATCTGCCAGC
1681 CTGACGCCACGGGAGCAGCCTGCTGAGGCTGAGAGACACAGAAAGTGCTGGGACGACA
1741 CTGCTGTGGTCAATGACCTCTCATCCACATCATCGGGCACTGAATCAGGTCTCAGTCTC
1801 CTCTGACACCAGATGGTAAACGGAATCCCAAAGGCATTAAGAAGTTCTGGGGAAAATCC
1861 GAAGAACTCAGTCAGGAAATTTCTACACTGACACGCTGGGGATGGCAGAGTTTCGACGAG
1921 GTGGGCTCCGGGCAACCGCAGGGCCAAGACTCTCTAGGACCAGGGACTCCAAGGGACAGA
1981 AAAGTGACGCCAATGCCCCCTTTGCCAGTGGAGCACAGAGCGTGTGTGTCATGGCTGG
2041 AGGACTTTGGCCTGGCTCAGTATGTGATCTTTGCCAGGCACTGGGTATCTTCTGGCCACA
2101 CCTTATTGACAGCCACCCCTCAGGACATGGAAAAGGAGCTAGGAATTAAGCACCACCTCC
2161 ACAGGAAGAAGCTTGTTTTAGCAGTGAAAGCCATCAACACCAAACAGGAGGAGAAGTCTG
2221 CACTGCTAGACCACATTTGGGTGACAAGGTGGCTTGATGATATTGGCTTACCCCAGTACA
2281 AAGACCAGTTTCATGAATCTAGAGTTGACAGACGAATGCTGCAATACCTAACTGTGAACG
2341 ATTTACTCTTCTTAAAAGTCACCAGCCAACTACATCATCTCAGCATCAAATGTGCCATTC
2401 ACGTGCTGCATGTCAACAAGTTCAACCCCCACTGCCTGCACCGCGGCCAGCTGATGAGA
2461 GTAACCTTTCTCCTTCAGAAGTTGTACAGTGGTCCAACCACAGGGTGATGGAGTGGTTAC
2521 GATCTGTGGACCTGGCAGAGTATGCACCCAATCTTCGAGGGAGTGGAGTCCATGGAGGCC
2581 TCATTATCCTGGAGCCACGCTTCACTGGGGACACCCTGGCTATGCTTCTCAACATCCCCC
2641 CACAAAAGACGCTCCTCAGGCGCCACCTGACCACCAAGTTCAATGCCTTGATTGTCGGG
2701 AGGCTGAACAGGAGAAGCGAGAGAAAATGGCCTCACCAGCTTACACACCACTGACCACA
2761 CAGCCAAAGTCCGGCCAAGGAACTAGGATTTTACACTTCGGAACATAAGAAAAAAGA
2821 AGTTCGATGAATCGACGGACTACATTTGCCCAATGGAGCCCAGTGACGGTGTGAGTGATA
2881 GTCACAGGGTCTACAGTGGCTACCGGGGCTCAGCCCCCTTGATGCCCTGAACTGGATG
2941 GGCTGGACCAGGTGGGACAGATTAGCTGTGATGCCCTTGTCACCTGCCCTCTGTGCACCCTG
3001 AGAGCTCACAGTAACACTGTGTGTGTCACCATATAACTGCACCTCACCCCCGCACGTGTG
3061 CATGACTCGCAGAGAATATTCAGCAATTGTGTACCCCTGGGCCAGTCTCTTTGAACCTT
3121 GAGGGTGGCCAGGATCTGGAGCTGCATCTCTAAGGGGCCAGGCTTTGGGGACCATTGCCA
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3181 AAGGTGGACTCAGGAGGAAAGACACTTAAAGACACTTTTACATGTCTAGTAATTCTTGAT  
 3241 GTTCATCTTCAGCACCACTGGAAACACATGAAGTTCGATGCAGGTCCAGAGACCATGGAC  
 3301 ACTCCACGAGGCTCAGCTCTCAGGCACCCCTACACTTCAGTTGAGGGAAAAGCTCAAG  
 3361 TGCCTTAGGCCCGTGGACCACAGTCTTGGCTGAGATCAAAGGGATGAGCAACAGGGACTT  
 3421 CTGCCACAGTGACAATGGAATTGTGTTGTCCTTACTTCAGAGGTGGTCTCTTCTTTCTT  
 3481 GTAATAAAAGCAATATTTATGC

The start and stop codons are indicated in bold as well as the position corresponding to the microarray probe.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000299492 and has a sequence as in SEQ ID NO:305

1 MASDASHALEAALEQMDGIIAGTKTGADLSDGTCEPGLASPASYMNPFPVLHLIEDLRLA  
 61 LEMLELPQERAALLSQIPGPTAAYIKWFEESSLQVNHHSAAASNETYQERLARLEGDKES  
 121 LILQVSVLTDQVEAQGEKIRDLEVCLEGHQVKLNAAEMLQQELLSRTSLETQKLDLMTE  
 181 VSELKCLKVGMEKEQREQEEKQKAEELLQELRHLKIKVEELENERNQYEWKLKATKAEV  
 241 AQLQEQVALKDAEIERLHSQLSRTAALHSESTERDQEIQRLKMGMETLLLANEDKDRI  
 301 EELTGLLNQYRKVKEIVMTQGPSERTLSINEEEPEGGFSKWNATNKDPEELFKQEMPPR  
 361 CSSPTVGPPLPQKSLETRAQKKLSCSLEDLRSESVDKCMDGNQPFVLEPKDSPFLAEH  
 421 KYPTLPGLKSGATPNGEAAKSPPTICQPDATGSSLLRLRDTESGWDDTAVVNDLSSTSSG  
 481 TESGPQSPLTPDGKRNPKGIKKFWGKIRRTQSGNFYDTLGMAEFRRGLRATAGPRLSR  
 541 TRDSKGQKSDANAPFAQWSTERVCAWLEDFGLAQYVIFARQWVSSGHTLLTATPDMEKE  
 601 LGIKHPLHRKKLVLAVKAINTKQEEKSALLDHIWVTRWLDDIGLPQYKDQFHESRVDRM  
 661 LQYLTVNDLLFLKVTSQLHHLSTKCAIHVLHVNFNPHCLHRRPADESNLSPSEVVQWSN  
 721 HRVMEWLRSVDLAEYAPNLRGSGVHGGLIILEPRFTGDTLAMLNIPPQKTLRRHLTTK  
 781 FNALIGPEAEQEKREKMASPAYTPLTTTAKVRPRKLGFSHFGNIRKKKFDESTDYICPME  
 841 PSDGVSDSHRVYSGYRGLSPLDAPELDGLDQVGQIS

Primers for amplifying the sequence ENST00000299492 can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying PPFIBP2 include:

- 1) Forward SEQ ID NO:306 GCTAGTCATGCGCTGGAAG  
Reverse SEQ ID NO:307 GAAGCTCCAGCATCTCCAAG
- 2) Forward SEQ ID NO:308 CCCAGGTAAACCACACAGT  
Reverse SEQ ID NO:309 CTGGTGTCTTCCAGACACA
- 3) Forward SEQ ID NO:310 TGTGTCTGGAAGGACACCAG  
Reverse SEQ ID NO:311 TCCTCCTGCTCTCTCTGCTC
- 4) Forward SEQ ID NO:312 AAGAGCTCAGGCACCTCAAA  
Reverse SEQ ID NO:313 CTCCTGTGGAGAGCTGCTG
- 5) Forward SEQ ID NO:314 AACTTTGCTGCTTGCCAAT  
Reverse SEQ ID NO:315 TTGAGTGACCATCACAATCTCC
- 6) Forward SEQ ID NO:316 TCTCTCAATCAATGAAGAAGAACC  
Reverse SEQ ID NO:317 TCCAGTGATTTCTGTGGCAAT

- 7) Forward SEQ ID NO:318 GCCTCCAAGATGTAGCTCTCC  
Reverse SEQ ID NO:319 TCCACAGATTCACCTTCTCAAGTC
- 8) Forward SEQ ID NO:320 CGGAGCACAAATATCCCACT  
Reverse SEQ ID NO:321 CTTTGGGATTCCGTTTACCA
- 9) Forward SEQ ID NO:322 TGGTAAACGGAATCCCAAAG  
Reverse SEQ ID NO:323 TTGGAGTCCCTGGTCCTAGA
- 10) Forward SEQ ID NO:324 TCTAGGACCAGGGACTCCAA  
Reverse SEQ ID NO:325 GGGTGGCTGTCAATAAGGTG

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting PPFIBP2 derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include:

Probe:

SEQ ID NO:326 CAGGCACTAAAACAGGTGCA  
 SEQ ID NO:327 AGGGGATAAGGAGTCCCTCA  
 SEQ ID NO:328 TTGAGACCCAGAAGCTCGAT  
 SEQ ID NO:329 GAAATTGAGCGTCTGCACAG  
 SEQ ID NO:330 TTACGGGGCTGTAAACCAG  
 SEQ ID NO:331 CAGCAAGTGGAACGCTACAA  
 SEQ ID NO:332 TGCCACAGAAATCACTGGAA  
 SEQ ID NO:333 ACACAGAAAGTGGCTGGGAC  
 SEQ ID NO:334 TTCTACACTGACACGCTGGG  
 SEQ ID NO:335 GGCCTGGCTCAGTATGTGAT

A probe for detecting PPFIBP2 nucleic acid that was used on the microarray has a sequence as in SEQ ID NO:336

AGATCAAAGGGATGAGCAACAGGGACTTCTGCCACAGTGACAATGGAATTGTGTTGTGCC

Other probes to PPP1R16A are known in the art and/or can be readily designed by the skilled artisan.

- 1) Antibodies:
- 2) Mouse Anti-Human PPFIBP2 Monoclonal Antibody, Unconjugated, Clone 3A5, Abnova Corporation, PPFIBP2 (NP\_003612, 1 a.a. ~ 101 a.a) partial recombinant protein with GST tag. MW of the GST tag alone is 26 KDa.

- 3) Rabbit Anti-Human PPFIBP2 Purified - MaxPab Polyclonal Antibody, Unconjugated, Abnova Corporation, PPFIBP2 (NP\_003612.1, 1 a.a. ~ 876 a.a) full-length human protein.

#### Example 18: PPP1R16A

PPP1R16A (protein phosphatase 1, regulatory (inhibitor) subunit 16A) also known as MGC14333 and MYPT3 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that PPP1R16A was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that PPP1R16A was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that PPP1R16A can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

PPP1R16A, also named Myosin phosphatase targeting subunit 3 (MYPT3) is a membrane located protein which having 524 amino acid residues, in which five Ankyrin repeats and a consensus PP1 binding site are located within the N-terminal 300 amino acid residues. The C-terminal region with 224 residues contains two possible Src homology 3 binding sites and a prenylation motif (CaaX). These structural features suggest that R16A could be a scaffold protein regulating protein-protein interactions as well as cellular signalling. (PMID: 18202305)

The sequence of an mRNA corresponding to PPP1R16A is given in ENSEMBL accession no. ENST00000292539 and has a sequence as in SEQ ID NO:337

```
GTGAAAAGAGGACTCTCAGGGGCTCACAGGGGCTCTCACTGCTGGTTGGCCCTGCCCTCCCTTCCCCCTC
AGCAGGGTGCCCGGAAGCTGGAACCTTGTTATCTGGGTAATTAGTTTCAGACCCTGCACTGAGGCCGGCC
AGGTCTCGGGGCTGCCTCCCATAGGTTGTGCACCCTGACCCCGAGAGGGAGGCGAGGCGCTGCTTGTCGA
CAGCTAGAGGCTGGCCTGGGGAGCAGGTTTGGGGTGCCCTCCACACTGCCCTCCCTGCCCGGCCCATG
CCCCCAGGGCTGCCTGGGCCTGGTTATTGTGTGGGGCCTCCTGACCCAGCCAAGGGCACGAAGCTCTGG
GAAGGGGATGCCCGAGGGTGCCAGTCCAGTAGCTGCCCCACCCCTCAGGCCAGCCTGGCCCCCAAG
CTCCCCACTCTGGTGCCCCGAGCAGCCCTGTGGGCAAGCAGCCGCCGCCATGGCCGAGCACCTGGAGCTG
CTGGCAGAGATGCCCATGGTGGGCAGGATGAGCACACAGGAGCGGCTGAAGCATGCCAGAAGCGGCGCG
CCCAGCAGGTGAAGATGTGGGCCCAGGCTGAGAAGGAGGCCAGGGCAAGAAGGGTCCTGGGGAGCGTCC
CCGGAAGGAGGCAGCCAGCCAAGGGCTCCTGAAGCAGGTCTCTTCCCTCCAGTGTTGTCCTTCTGGAG
GCCGTGCCCCGAAATGACCTGGAAGAAGTCCGCCAGTTCCTTGGGAGTGGGGTCAGCCCTGACTTGGCCA
ACGAGGACGGCCTGACGGCCCTGCACCAGTGTGTCATTGATGATTTCCGAGAGATGGTGCAGCAGCTCCT
GGAGGCTGGGGCCAACATCAATGCCTGTGACAGTGAGTGCTGGACGCCTCTGCATGCTGCGGCCACCTGC
GGCCACCTGCACCTGGTGGAGCTGCTCATCGCCAGTGGCGCCAATCTCCTGGCGGTCAACACCGACGGGA
ACATGCCCTATGACCTGTGTGATGATGAGCAGACGCTGGACTGCCTGGAGACTGCCATGGCCGACCGTGG
```

CATCACCCAGGACAGCATCGAGGCCGCCCGGGCCGTCGCCAGAACTGCGCATGCTGGACGACATCCGGAGC  
 CGGCTGCAGGCCGGGGCAGACCTCCATGCCCCCTGGACCACGGGGCCACGCTGCTGCACGTCGCAGCCG  
 CCAACGGGTTTCAGCGAGGCGGCTGCCCTGCTGCTGGAACACCGAGCCAGCCTGAGCGCTAAGGACCAAGA  
 CGGCTGGGAGCCGCTGCACGCCGCGGCCTACTGGGGCCAGGTGCCCTGGTGGAGCTGCTCGTGGCGCAC  
 GGGGCCGACCTGAACGCAAAGTCCCTGATGGACGAGACGCCCTTGATGTGTGCGGGGACGAGGAGGTGC  
 GGGCCAAGCTGCTGGAGCTGAAGCACAAGCACGACGCCCTCCTGCGCGCCAGAGCCGCCAGCGCTCCTT  
 GCTGCGCCGCGCACCTCCAGCGCCGGCAGCCGCGGAAGGTGGTGAAGCGGGTGAGCCTAACCCAGCGC  
 ACCGACCTGTACCGCAAGCAGCACGCCAGGAGGCCATCGTGTGGCAACAGCCGCCGCCACCAGCCCGG  
 AGCCGCCCGAGGACAACGATGACCGCCAGACAGGCGCAGAGCTCAGGCCGCCGCCCGGGAGGAGGACAA  
 CCCGAAGTGGTCAGGCCGCACAATGGCCGAGTAGGGGGCTCCCCAGTGCGGCATCTATACTCCAAGCGA  
 CTAGACCGGAGTGTCTCCTACCAGCTGAGCCCCCTGGACAGCACCACCCCCACACCCTGGTCCACGACA  
 AGGCCCCACCACACCCTGGCTGACCTGAAGCGCCAGCGAGCTGCTGCCAAGCTGCAGCGACCCCCACCTGA  
 GGGCCCCGAGAGCCCTGAGACAGCTGAGCCTGGCCTGCCTGGTGACACGGTGACCCCCCAGCCTGACTGT  
 GGCTTCAGGGCAGGCGGGGACCCACCCCTGCTCAAGCTCACAGCCCCGCGCGGTGGAGGCTCCCGTGGAGA  
 GGAGGCCGTGCTGCCTGCTCATGT**AGAGGCTGT**GCTCAGCATGCAGGGGCCCTGTCGCGGGCACAGCCCA  
 AGGCTGCCTCCCCACGGTGCGTGCCCTGGTGTGCGGGTGACGACGGAACCCCGGCT**TCTACTGTACA**  
**GGACACTGGCCCCCTCTCAGGTGAGAAGACATGCCTGGAGGGATGTCTGGCTGCAAAGACTATTTTTATCC**  
 TGCAACTCTTGATAAAGGGCTGTTTTGCCATGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  
 AAAAAAAAAAAAAAAAAA

The start and stop codons are indicated in bold as well as the position corresponding to the microarray probe.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000292539 and has a sequence as in SEQ ID NO:338

MAEHLELLAEMPMVGRMSTQERLKHAKRRAQQVKMWAQAEKEA  
 QGKKGPGERPRKEAASQGLLKQVLFPPSVVLEAAARNDL EEVRQFLGSGVSPDLANE  
 DGLTALHQCCIDDFREM VQQLLEAGANINACDSECWTP LHAAATCGHLHLVELLIASG  
 ANLLAVNTDGNMPYDLCDD EQLDCL ETAMADRGITQDSIEAARAVPELRMLDDIRSR  
 LQAGADLHAPLDHGATLLHVAANGFSEAAALLLEHRASLSAKDQDGWEPLHAAAYWG  
 QVPLVELLLVAHGADLNAKSLMDETPLDVC GDEEVRAKLLELKHKHDALLRAQSRQ RSL  
 LRRRTSSAGSRGKVVRRVSLTQRTDLYRKQHAQEAI VWQPPPTSPEPPEDNDDRQTG  
 AELRPPPPPEEDNPEVVRPHNGRVGGSVVRHLYSKRLDRSVSYQLSPLDSTTPHTLVHD  
 KAHHTLADLKRQRAAAKLQRPPPEGPE SPETAEPGLPGDVTVPQPD CGFRAGGDPPLL  
 KLTAPAVEAPVERRPCCLLM

Primers for amplifying the sequence ENST00000292539 can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying PPP1R16A include:

Forward SEQ ID NO:339 GTGTTGTCCTTCTGGAGGCCG (Ex2)  
 Reverse SEQ ID NO:340 GCCGTCAGGCCGTCCTCGTTG (Ex3)

Forward SEQ ID NO:341 GCTGCCCCGAAATGACCTGG (Ex3)  
 Reverse SEQ ID NO:342 CGGAAATCATCAATGCAGC (Ex5)

Forward SEQ ID NO:343 GACGCCTCTGCATGCTGCGG (Ex5)  
 Reverse SEQ ID NO:344 CACAGGTCATAGGGCATGTTC (Ex6)

Forward SEQ ID NO:345 GATGAGCAGACGCTGGACTG (Ex6)  
Reverse SEQ ID NO:346 CTCCGGATGTCGTCCAGC (Ex7)

Forward SEQ ID NO:347 CAGGCCGGGGCAGACCTC  
Reverse SEQ ID NO:348 GGCTCGGTGTTCCAGCAGCAG

Forward SEQ ID NO:349 GGGAGCCGCTGCACGCC  
Reverse SEQ ID NO:350 CCCGCACCTCCTCGTCCC

Forward SEQ ID NO:351 CTGCGCGCCCAGAGCCGC  
Reverse SEQ ID NO:352 GCGTGCTGCTTGCGGTAC

Forward SEQ ID NO:353 GCCAGACAGGCGCAGAGCTC  
Reverse SEQ ID NO:354 CTACTCGGCCATTGTGCG

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting PPP1R16A derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include:

SEQ ID NO:355  
TCTACTGTACAGGACACTGGCCCCTCTCAGGTCAGAAGACATGCCTGGAGGG  
ATGTCTGGCTGCAAAGACTATTTTATCC

SEQ ID NO:356  
CTGACGGCCCTGCACCAGTGCTGCATTGATGATTTC

SEQ ID NO:357  
GACTGCCATGGCCGACCGTGGCATCACCCAG

SEQ ID NO:358  
GCTCGTGGCGCACGGGGCCGACCTGAACGC

SEQ ID NO:359  
GCGCCGGCAGCCGCGGGAAGGTGGTGAGG

Other probes to PPP1R16A are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against PPP1R16A include, but are not limited to, Abnova Corporation Cat# H00084988-M06 which is a mouse monoclonal antibody raised against a partial

recombinant PPP1R16A: 429 a.a. ~ 529 a.a; and from Abnova Cat# H00084988-B01 which is a mouse polyclonal raised against a full-length human PPP1R16A protein.

#### Example 19: RASSF7

RASSF7, Ras association (RalGDS/AF-6) domain family (N-terminal) member 7 also known as 2400009B11RIK, AW210608, C11ORF13, HRAS1, HRC1, MGC126069, MGC126070, and RGD1306244 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that RASSF7 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that RASSF7 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that RASSF7 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

RASSF7 is a member of a new Ras effector family characterise for the presence of a RA domain in their sequence. Although they interact either directly or indirectly with activated Ras, their role in mediating its biological effects remains unclear. What is clear is that they seem to modulate some of the growth inhibitory responses mediated by Ras and may serve as tumour suppressor genes. In fact, it is been described that members of the family are silenced in tumours by methylation of their promoters. (PMID: 17692468).

The sequence of an mRNA corresponding to RASSF7 is given in ENSEMBL accession no. ENST00000344375 and has a sequence as in SEQ ID NO:360

```
GAATTCTGGGGGGAGGGGGCAGTGTCTCCGAGCCAGGACAGGCATGTTGTTGGGACTGGCGGCCATGGAG
CTGAAGGTGTGGGTGGATGGCATCCAGCGTGTGGTCTGTGGGGTCTCAGAGCAGACCACCTGCCAGGAAG
TGGTCATCGCACTAGCCCAAGCAATAGGCCAGACTGGCCGCTTTGTGCTTGTGCAGCGGCTTCGGGAGAA
GGAGCGGCAGTTGCTGCCACAAGAGTGTCCAGTGGGCGCCAGGCCACCTGCGGACAGTTTGCCAGCGAT
GTCCAGTTTGTCTGAGGCGCACAGGGCCAGCCTAGCTGGGAGGCCCTCCTCAGACAGCTGTCCACCCC
CGGAACGCTGCCTAATTCGTGCCAGCCTCCCTGTAAAGCCACGGGCTGCGCTGGGCTGTGAGCCCCGCAA
AACACTGACCCCCGAGCCAGCCCCAGCCTCTCACGCCCTGGGCCTGCGGCCCTGTGACACCCACACCA
GGCTGCTGCACAGACCTGCGGGGCTGGAGCTCAGGGTGCAGAGGAATGCTGAGGAGCTGGGCCATGAGG
CCTTCTGGGAGCAAGAGCTGCGCCGGGAGCAGGCCCGGGAGCGAGAGGGACAGGCACGCCTGCAGGCACT
AAGTGGCGCCACTGCTGAGCATGCCGCCGGCTGCAGGCCCTGGACGCTCAGGCCGTGCCCTGGAGGCT
GAGCTGCAGCTGGCAGCGGAGGCCCTGGGCCCTCACCTATGGCATCTGCCACTGAGCGCCTGCACC
AGGACCTGGCTGTTTCAAGAGCGGCAGAGTGCGGAGGTGCAGGGCAGCCTGGCTCTGGTGAGCCGGGCCCT
GGAGGCAGCAGAGCGAGCCTTGCAGGCTCAGGCTCAGGAGCTGGAGGAGCTGAACCGAGAGCTCCGTCAG
```

TGCAACCTGCAGCAGTTTCATCCAGCAGACCGGGGCTGCGCTGCCACCGCCCCACGGCCTGACAGGGGCC  
 CTCCTGGCACTCAGGGCCCTCTGCCTCCAGCCAGAGAGGAGTCCCTCCTGGGCGCTCCCTCTGAGTCCCA  
 TGCTGGTGGCCAGCCTAGGCCCCGAGGTGGCCCCCATGACGCAGAAGTCCCTGGAGGTAGCAGCAGCTCCT  
 GCCCCAGAGTGGTGTCTCTGGCAGCCAGCCCCAGGCTCTGTGACAGCCTAGTGAGGGCTGCAAGACCA  
 TCCTGCCCCGACCACAGAAGGAGAGTTGGCGGTACAGAGGGCTCCTCTGCCAGGCAGTGGGAAGCCCTG  
 GGTTCGGCCTCAGGAGCTGGGGGTGCAGTGGGGGACTGCCCTAGTCCTTGCCAGGTGCCCCAGCACCCCTG  
 GAGAAGCATGGGGCGTAGCCAGCTCGGAAGTTGCCAGGCCCCAAAGGCCACGACTGCCTGTTGGGGACAG  
 GAGATGCATGGACAGTGTGCTCAAGCTGTGGGCATGTGCTTGCCCTGCGGGAGAGGTCTTCACTGTGTGT  
 ACACAGCAAGAGCATGTGTGTGCCACTTCCCCTACCCCAACGTGAAAACCTCAATAAACTGCCCGAAGC

The corresponding amino acid sequence is given in ENSEMBL accession no.  
 ENSP00000344226 and has a sequence as in SEQ ID NO:361

MLLGLAAMELKVVWDGIQRVVCGVSEQTTTQEVVIALAQAIGQTGRFVLVQRLREKERQLLPQECFVGAQ  
 ATCGQFASDVQFVLRRTGPSLAGRPSSDSCPPPERCLIRASLPVKPRAALGCEPRKTLTPEPAPSLSRPG  
 PAAPVTPTPGCCTDLRGLRLVQRNAEELGHEAFWEQELRREQAREREGQARLQALSAATAEHAARLQAL  
 DAQARALEAEELQLAAEAPGPPSPMASATERLHQDLAVQERQSAEVQGSLLVSRALAAERLQAQAEEL  
 EELNRELRLQCNLQQFIQQTGAALPPPPRPDRGPPGTQGPLPPAREESLLGAPSESHAGAQRPRRGPHDA  
 ELLEVAAAPAPEWCPLAAQPQAL

Primers for amplifying the sequence ENST00000344375 can be designed using  
 primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying RASSF7 include:

Forward SEQ ID NO:362 CTGCCAGGAAGTGGTCAT C (Ex1)  
 Reverse SEQ ID NO:363 GCCGCTGCACAAGCACA (ex2)

Forward SEQ ID NO:364 CATGGAGCTGAAGGTG (ex1)  
 Reverse SEQ ID NO:365 CTCAGGACAACTGGAC (ex2)

Forward SEQ ID NO:366 GCCACTGAGCGCCTGC (Ex2)  
 Reverse SEQ ID NO:367 GTCTGCTGGATGAACTG (EX3)

Forward SEQ ID NO:368 CAG CAG AGC GAG CCT TGC AG  
 Reverse SEQ ID NO:369 CTG AGT GCC AGG AGG GC (Ex3)

Forward SEQ ID NO:370 CAC GGC CTG ACA GGG GCC (Ex3)  
 Reverse SEQ ID NO:371 GCC TAG GCT GGG CAC (EX4)

Forward SEQ ID NO:372 CTCTGAGTCCCATGCTGG (EX4)  
 Reverse SEQ ID NO:373 GACACCACTCTGGGGC (EX5)

Forward SEQ ID NO:374 TGCCCAGCCTAGGCCC (EX4)  
 Reverse SEQ ID NO:375 GCCAGAGGACACCACTC (EX5)

Other sets of primers can be readily designed by the skilled artisan and/or are known  
 in the art.



Probes for detecting RASSF7 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include:

SEQ ID NO:376

GAGAGGTCCTTCACTGTGTGTACACAGCAAGAGCATGTGTGTGCCACTTC

SEQ ID NO:377

AGTGTCCTCCGAGCCAGGACAGGCATGTTGTTGGGACTGGCGGCCATGGAG

SEQ ID NO:378

GAGCCGGGCCCCTGGAGGCAGCAGAGCGAGCCTTGCAGGCTCAGGCTCAGGA  
GCTG

SEQ ID NO:379

CGGCCTGACAGGGGCCCTCCTGGCACTCAGGGCCCTCTGCCTCCAGCCAGAG  
AGGAG

SEQ ID NO:380

GAGGAGCTGGGCCATGAGGCCTTCTGGGAGCAAGAGCTGCGCCGGGAGCAG  
GCCCCGGGAG

Other probes to RASSF7 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against RASSF7 include, but are not limited to, LifeSpan BioSciences. Cat# LS-C31793-100 which is a rabbit polyclonal antibody; and from Novus Biologivals Cat#NB100-93434 , which is a goat polyclonal anti-RASSF7 against the epitope SEQ ID NO:381 CTDLRGLELRVQRN.

Example 20: RNF183

RNF183 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that RNF183 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that RNF183 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that RNF183 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to RNF183 is given in ENSEMBL accession no. ENST00000297894 and has a sequence as in SEQ ID NO:382

```
CGATTGAGGGGAGGGAGCAACTGGAGCCTCAGGCCCTCCAGAGTAGTCTGCCTGACCACCTGGAGCCCA
CAGAAGCCCAGGACGTCTCCCGCGAAGCCTCCCCGTGTGTGGCTGAGGATGGCTGAGCAGCAGGGCCGGG
AGCTTGAGGGCTGAGTGCCCCGTCTGCTGGAACCCCTTCAACAACACGTTCCATACCCCCAAAATGCTGGA
TTGCTGCCACTCCTTCTGCGTGGAATGTCTGGCCACCTCAGCCTTGTGACTCCAGCCCGGCGCCGCTG
CTGTGCCACTCTGTGCGCCAGCCACAGTGCTGGCCTCAGGGCAGCCTGTCACTGACTTGCCCACGGACA
CTGCCATGCTCGCCCTGCTCCGCCTGGAGCCCCACCATGTTCATCCTGGAAGGCCATCAGCTGTGCCTCAA
GGACCAGCCCAAGAGCCGCTACTTCCTGCGCCAGCCTCAAGTCTACACGCTGGACCTTGCCCCCAGCCT
GGGGGCCAGACTGGGCGGCCCCAGACACGGCCTCTGCCACCGTGTCTACGCCCATCCTCATCCCCAGCC
ACCACTCTTTGAGGGAGTGTTCGCAACCCTCAGTTCGCATCTTTGCCTACCTGATGGCCGTCATCCT
CAGTGTCACTCTGTTGCTCATATTCTCCATCTTTTGACCAAGCAGTTCCTTTGGGGTGTGGGGTGAGTG
CTGTTCCCAGACAAGAAACCAACCTTTTCGGTTGCTGCTGGGTATGGTGACTACGGAGCCTCATTTGG
TATTGTCTTCCTTTGTAGTGTGTTTATTTACAATCCAGGGATTGTTTCAGGCCATGTGTTTGCTTCTGG
GAACAATTTTAAAAAAAACAAAAAACGAAAAGCTTGAAGGACTGGGAGATGTGGAGCGACCTCCGGGT
GTGAGTGTGGCGTCATGGAAGGGCAGAGAAGCGGTTCTGACCACAGAGCTCCACAGCAAGTTGTGCCAAA
GGGCTGCACAGTGGTATCCAGGAACCTGACTAGCCCCAAATAGCAAGTTGCATTTCTCACTGGAGCTGCTT
CAAAATCAGTGACATATTTTTTTGAGTTGCTCTTTTACTATGGGTTGCTAAAAAAAATAATTGGGA
AGTGAGCTTCAATTCTGTGGGTAAATGTGTGTTTCTCTTTGAATGTCTTGCCACTGGTTGCAGTAA
AAGTGTCTGTATTTCATTAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
```

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000297894 and has a sequence as in SEQ ID NO:383

```
MAEQQGRELEAECPVCWNPFNNTFHTPKMLDCCSHFCVECLAHLSLVTPARRRLLCPLCRQPTVLASGQPVTDLP
TDTAMLALLRLPHHVILEGHQLCLKDQPKSRYFLRQPVYTLDLGPQPGGQTGPPPDASATVSTPILIPSHS
LRECFRNPQFRIFAYLMAVILSVTLLLFISIFWTKQFLWGVG
```

Primers for amplifying the sequence RNF183 can be designed using primer design software such as Oligo Calc.

Examples of primer pairs for amplifying RNF183 include those in

Forward SEQ ID NO:384 GAGAAGCTGGGCTGGAG (EXON3)  
Reverse SEQ ID NO:385 CAGCCACACACGGGGA (EXON4)

Forward SEQ ID NO:386 CAGCTGTGTGCTAAGAACAAAG (EXON3)  
Reverse SEQ ID NO:387 GCCCTGCTGCTCAGCCATC (EXON4)

Forward SEQ ID NO:388 GCAGAAGGCAGCGAGGAC (EXON3)  
Reverse SEQ ID NO:389 GGCAGCAATCCAGCATTTTG (EXON4)

Forward SEQ ID NO:390 CTGCGTGGAATGTCTGGCC (EXON4)  
Reverse SEQ ID NO:391 CAAGTCAGTGACAGGCTGC (EXON4)

Forward SEQ ID NO:392 GTCTACACGCTGGACCTTG (EXON4)  
Reverse SEQ ID NO:393 GATGCGGAACTGAGGGTTG (EXON4)

Forward SEQ ID NO:394 CTACCTGATGGCCGTCATC (EXON4)  
Reverse SEQ ID NO:395 CCAGCAGCAACCGAAAAAG (EXON4)

Forward SEQ ID NO:396 CATGCGTGCAGGGCTGCA (EXON1)

Reverse SEQ ID NO:397 GTGCTGCTCTCCCAGGG (EXON2)

Forward SEQ ID NO:398 CCG TGG AATCGATTCCCAG (EXON2)

Reverse SEQ ID NO:399 CTGTTTCTCATATGGGTCATTCG (EXON3)

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting RNF183 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include

SEQ ID NO:400 ATGGCTGAGCAGCAGGGCCGGGAGCTTGAGGCTGAGTGCCC

SEQ ID NO:401 GCCCACGGACACTGCCATGCTCGCCCTGCTCC

SEQ ID NO:402 GGACCAGCCCAAGAGCCGCTACTTCCTGCGCCAGCCT

SEQ ID NO:403 CGCTGGACCTTGGCCCCCAGCCTGGGGGGCCAG

SEQ ID NO:404 GTTCCTTTGGGGTGTGGGGTGAGTGCTG

A probe for detecting RNF183 nucleic acid that was used on the microarray has a sequence as in SEQ ID NO:405

CAGTGGTATCCAGGAACCTGACTAGCCCAAATAGCAAGTTGCATTTCTCACT  
GGAGCTGC

Other probes to RNF183 are known in the art and/or can be readily designed by the skilled artisan.

#### Example 21: SIRT6

SIRT6 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that SIRT6 was overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that SIRT6 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that SIRT6 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to SIRT6 is given in ENSEMBL accession no. ENST00000269860 and has a sequence as in SEQ ID NO:406

```

1  GCTTCCGGCGGAAGCGGCCTCAACAAGGGAAACTTTATTGTTCCCGTGGGGCAGTCGAGG
61  ATGTCGGTGAATTACGCGGCGGGGCTGTGCGCGTACGCGGACAAGGGCAAGTGCGGCCTC
121 CCGGAGATCTTCGACCCCCCGGAGGAGCTGGAGCGGAAGGTGTGGGAAGTGGCGAGGCTG
181 GTCTGGCAGTCTTCAGTGTGGTGTTCACACGGGTGCCGGCATCAGCACTGCCTCTGGC
241 ATCCCCGACTTCAGGGACAACTGGCAGAGCTCCACGGGAACATGTTTGTGGAAGAATGT
301 GCCAAGTGTAAGACGCAGTACGTCCGAGACACAGTCGTGGGCACCATGGGCCTGAAGGCC
361 ACGGGCCGGCTCTGCACCGTGGCTAAGGCAAGGGGGCTGCGAGCCTGCAGGGGAGAGCTG
421 AGGGACACCATCCTAGACTGGGAGGACTCCCTGCCCGACCGGGACCTGGCACTGCGCGAT
481 GAGGCCAGCAGATCCGCCCCAGCGGGAACCTGCCGCTGGCTACCAAGCGCCGGGAGGCC
541 GCCTGGTCATCGTCAACCTGCAGCCCCACCAAGCACGACCGCCATGCTGACCTCCGCATCC
601 ATGGCTACGTTGACGAGGTCATGACCCGGCTCATGAAGCACCTGGGGCTGGAGATCCCCG
661 CCTGGGACGCGCCCCCTGTGCTGGAGAGGGCGCTGCCACCCCTGCCCGCCCCGCCACCC
721 CCAAGCTGGAGCCCCAAGGAGGAATCTCCACCCGGATCAACGGCTCTATCCCCGCCGGCC
781 CCAAGCAGGAGCCCTGCGCCCAGCACACGGCTCAGAGCCCGCCAGCCCCAACCGGGAGC
841 GGCCACACAGCCCTGCCCCCCACAGACCCCCCAAAGGGTGAAGGCCAAGGCGGTCCCCA
901 GCTGACCAGGGTGCTTGGGGAGGGTGGGGCTTTTTGTAGAACTGTGGATTCTTTTTCTC
961 TCGTGGTCTCACTTTGTTACTTGTCTTCTGTCCCCGGGAGCCTCAGGGCTCTGAGAGCTGT
1021 GCTCCAGGCCAGGGGTTACACCTGCCCTCCGTGGTCCCTCCCTGGGCTCCAGGGGCCTCT
1081 GGTGCGGTTCGCGGAAGAAGCCACCCCCAGAGGTGACAGGTGAGCCCCCTGCCACACCCC
1141 AGCCTCTGACTTGCTGTGTTGTCCAGAGGTGAGGCTGGGCCCTCCCTGGTCTCCAGCTTA
1201 AACAGGAGTGAACCTCCTCTGTCCCCAGGGCCTCCCTTCTGGGCCCCCTACAGCCACCC
1261 TACCCCTCCTCCATGGGCCCTGCAGGAGGGGAGACCCACCTGAAAGTGGGGGATCAGTAG
1321 AGGCTTGCACTGCCTTTGGGGCTGGAGGGGAGACGTGGGTCCACCAGGCTTCTGGAAAAGT
1381 CCTCAATGCAATAAAACAATTTCTTTCTTGCA

```

The start and stop codons are indicated in bold as well as the position corresponding to the microarray probe.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000269860 and has a sequence as in SEQ ID NO:407

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1  MSVNYAAGLSPYADKGKCGLPEIFDPPEELERKVVWELARLVWQSSSVVFHTGAGISTASG
61  IPDFRDKLAELHGNMFVEECAKCKTQYVRDVTVGTMGLKATGRLCTVAKARGLRACRGEL
121  RDTILDWEDSLPDRDLALADEASRSGPAGTCRWLPSAGEAAWSSSTCSPPSTTAMLTSA
181  MATLTRS

```

Primers for amplifying the sequence SIRT6 can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying SIRT6 include those in

Forward SEQ ID NO:408 TTGTGGAAGAATGTGCCAAG  
Reverse SEQ ID NO:409 CCTTAGCCACGGTGCAGAG

Forward SEQ ID NO:410 TCTTCCAGTGTGGTGTTCCTCA  
Reverse SEQ ID NO:411 TTGGCACATTCTTCCACAAA

Forward SEQ ID NO:412 AGCTGAGGGACACCATCCTA  
Reverse SEQ ID NO:413 GCAGGTTGACGATGACCAG

Forward SEQ ID NO:414 GCTTCCTGGTCAGCCAGA  
Reverse SEQ ID NO:415 ATGTACCCAGCGTGATGGAC

Forward SEQ ID NO:416 GCTTCCTGGTCAGCCAGA  
Reverse SEQ ID NO:417 CTAGGATGGTGTCCCTCAGC

Forward SEQ ID NO:418 GAGAGCTGAGGGACACCATC  
Reverse SEQ ID NO:419 GTACCCAGCGTGATGGACAG

Forward SEQ ID NO:420 AGGATGTCTGGTGAATTACGC  
Reverse SEQ ID NO:421 AAAGGTGGTGTCTGAACTTGG

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting SIRT6 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include

SEQ ID NO:422 TGTAAGACGCAGTACGTCCG  
SEQ ID NO:423 GACTTCAGGGACAACTGGC  
SEQ ID NO:424 ACTGGGAGGACTCCCTGC  
SEQ ID NO:425 TGTAAGACGCAGTACGTCCG  
SEQ ID NO:426 TGTAAGACGCAGTACGTCCG  
SEQ ID NO:427 TAGACTGGGAGGACTCCCTG  
SEQ ID NO:428 GAGTCTGGACCATGGAGGAG

A probe to detect SIRT6 nucleic acid that was used on the microarray has a sequence as in SEQ ID NO:429

GAAGTGGGGGATCAGTAGAGGCTTGCACTGCCTTTGGGGCTGGAGGGAGA

Other probes to SIRT6 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against SIRT6 include, but are not limited to, Rabbit polyclonal anti-SIRT6 against de C-terminal Cat# 2590 from Cell Signalling Technology; and Mouse monoclonal antibody raised against a partial recombinant SIRT6 141 a.a. ~ 251 a.a Catalog #:H00051548-M01 from abnova.

#### Example 22: TJP3

TJP3, tight junction protein 3 (zona occludens 3) also known as MGC119546, ZO-3, ZO3 was found to be overexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that TJP3 was

overexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that TJP3 was overexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that TJP3 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

TJP3 (ZO-3) was first identified as a 130 kDa protein that coimmunoprecipitates with ZO-1. It is a member of the MAGUK proteins (MEMBRANE-associated guanylate kinase-like homologues). These proteins are implicated in the formation and maintenance of supramolecular complexes at specific areas of the cell surface called tight junctions. Tight junctions locate at the most apical part of lateral membranes of simple epithelial cells, and are considered to be involved in barrier and fence functions.

Cloning and sequencing cDNAs encoding MAGUK proteins showed that all have three PDZ domains (PDZ1 to -3), one SH3 domain, and one guanylate kinase-like (GUK) domain in this order from their NH2 termini (PMID: 10966866). Among these domains, PDZ domains bind to COOH-terminal ends of various proteins, especially integral membrane proteins, most of which end in valine. Thus, MAGUKs can cross-link multiple integral membrane proteins at the cytoplasmic surface of plasma membranes to establish specialized membrane domains. ZO-3 has also been reported to associate with ZO-1, but not with ZO-2, although the domains responsible for ZO-3/ZO-1 interaction remain unidentified. ZO-3 was also shown to directly bind to the cytoplasmic domain of occludin (Haskins et al. 1998).

The sequence of an mRNA corresponding to TJP3 is given in ENSEMBL accession no. ENST00000262968 and has a sequence as in SEQ ID NO:430

```
ATGAACCTGTGTGGCCTCATGCCCATCTTCCCCGCTCCCCTCGACCAGGTGGCTGACATGGAGGAGCTGA
CCATCTGGGAACAGCACACGGCCACACTGTCCAAGGACCCCCGCCGGGGCTTTGGCATTGCGATCTCTGG
AGGCCGAGACCGGCCCGGTGGATCCATGCTTGTATCTGACGTGGTACCTGGAGGGCCGCGGAGGGCAGG
CTACAGACAGGCGACCACATCGTCAATGGTGAACGGGGTTTCCATGGAGAATGCCACCTCCGCGTTTGCCA
TTCAGATACTCAAGACCTGCACCAAGATGGCCAAACATCACAGTGAAACGTCCCCGGAGGATCCACCTGCC
CGCCACCAAAGCCAGCCCCCTCCAGCCCAGGGCGCCAGGACTCGGATGAAGACGATGGGCCCCAGCGGGTG
GAGGAGGTGGACCAGGGCCGGGGCTATGACGGCGACTCATCCAGTGGCTCCGGCCGCTCCTGGGACGAGC
GCTCCCCGCCGGCCGAGGCCCTGGTCCGGGGCCGGGGCCGGCAGCCATGGGCGTAGGAGCCCAGGTGGTGG
CTCTGAGGCCAACGGGCTGGCCCTGGTGTCCGGCTTTAAGCGGCTGCCACGGCAGGACGTGCAGATGAAG
CCTGTGAAGTCAGTGCTGGTGAAGAGGAGAGACAGCGAAGAGTTTGGCGTCAAGCTGGGCAGTCAGATCT
TCATCAAGCACATTACAGATTCCGGGCCCTGGCTGCCCCGCCACCGTGGGCTGCAGGAAGGAGATCTCATTCT
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ACAGATCAACGGGGTGTCTAGCCAGAACCTGTCACTGAACGACACCCGGCGACTGATTGAGAAGTCAGAA  
 GGGAAAGCTAAGCCTGCTGGTGTCTGAGAGATCGTGGGCAGTTCTTGGTGAACATTCCGCGCTGCTGTCAGTG  
 ACAGCGACAGCTCGCCATTGGAGGAAGGCGTGACCATGGCTGATGAGATGTCTCTCCCCCTGCAGACAT  
 CTCGGACCTCGCCTCGGAGCTATCGCAGGCACCAACATCCCACATCCCACCACCACCCCGGCATGCTCAG  
 CGGAGCCCCGAGGCCAGCCAGACCGACTCTCCCGTGGAGAGTCCCCGGCTTCGGCGGGAAAGTTTCACTAG  
 ATTCAGAACCATCTCGGAACAGATGAGCAACGGTCAGAGTTGCCAGGGAAAGCAGCTATGACATCTA  
 CAGAGTGCCAGCAGTCAGAGCATGGAGGATCGTGGGTACAGCCCCGACACGCGTGTGGTCCGCTTCCTC  
 AAGGGCAAGAGCATCGGGCTGCGGCTGGCAGGGGGCAATGACGTGGGCATCTTCGTGTCCGGGGTGCAGG  
 CGGGCAGCCCCGGCCAGGGGCAGGGCATCCAGGAGGGAGATCAGATTCTGCAGGTGAATGACGTGCCATT  
 CCAGAACCTGACACGGGAGGAGGCAGTGCAGTTCTTGTCTGGGGCTGCCACCAGGCGAGGAGATGGAGCTG  
 GTGACGCAGAGGAAGCAGGACATTTTCTGGAATAATGGTGAGTCCCGCGTGGGTGACTCCTTCTACATCC  
 GCACTCACTTTGAGCTGGAGCCCAGTCCACCGTCTGGCCTGGGCTTCACCCGTGGCGACGTCTTCCACGT  
 GCTGGACACGCTGCACCCCGGCCCCGGGCAGAGCCACGCACGAGGAGGCCACTGGCTGGCGGTGCGCATG  
 GGTCGTGACCTGCGGGAGCAAGAGCGGGGCATCATTCCTCAACAGAGCAGGGCGGAGCAGCTGGCCAGCC  
 TGGAAAGCTGCCAGAGGGCCGTGGGAGTGGGGCCCGCTCCTCCGCGGGCTCCAATGCTCGGGCCGAGTT  
 CTGGCGGCTGCGGGGTCTTCGTGAGGAGCCAAGAAGACCACTCAGCGGAGCCGTGAGGACCTCTCAGCT  
 CTGACCCGACAGGGCCGCTACCCGCCCTACGAACGAGTGGTGTTCGAGAAAGCCAGTTTCAAGCGCCCGG  
 TAGTGATCCTGGGACCCGTGGCCGACATTGCTATGCAGAAGTTGACTGCTGAGATGCCTGACCAAGTTTGA  
 AATCGCAGAGACTGTGTCCAGGACCGACAGCCCCCTCCAAGATCATCAAACTAGACACCGTGCGGGTGATT  
 GCAGAAAAGAGCAAGCATGCGCTCCTGGATGTGACCCCTCCGCCATCGAGCGCTCAACTATGTGCAGT  
 ACTACCCCATTTGAGTCTTCTTCATCCCGAGAGCCGGCCCGCCCTCAAGGCACTGCGCCAGTGGCTGGC  
 GCCTGCCTCCCGCCGACGACCCGTGCGCTCTACGCACAAGCCCAGAAGCTGCGAAAACACAGCAGCCAC  
 CTCTTCACAGCCACCATCCCTCTGAATGGCAGAGTGACACCTGGTACCAGGAGCTCAAGGCCATCATTC  
 GAGAGCAGCAGACGCGGCCCATCTGGACGGCGGAAGATCAGCTGGATGGCTCCTTGGAGGACAACCTAGA  
 CCTCCCTCACACGGCCCTGGCCGACAGTCCGCTGACCTCAGCTGCGACAGCCGCGTTAACAGCGACTAC  
 GAGACGGACGGCGAGGGCGGCGCGTACACGGATGGCGAGGGCTACACAGACGGCGAGGGGGGGCCCTACA  
 CGGATGTGGATGATGAGCCCCCGGCTCCAGCCCTGGCCCGGTCTCGGAGCCCGTGCAGGCAGATGAGTC  
 CCAGAGCCCCGAGGGATCGTGGGAGAAATCTCGGCTCATCAGGGGGCCAGGTGGACAGCCGCCACCCCCAG  
 GGACAGTGGCGACAGGACAGCATGCGAACCTATGAACGGGAAGCCCTGAAGAAAAAGTTTATGCGAGTAC  
 ATGATGCGGAGTCTCCGATGAAGACGGCTATGACTGGGGTCCGGCCACTGACCTGTGA

The corresponding amino acid sequence is given in ENSEMBL accession no.  
 ENSP00000262968 and has a sequence as in SEQ ID NO:431

MNLCGLMPIFPAPLDQVADMEELTIWEQHTATLSKDPRRGFGIA  
 ISGGRDRPGGSMVVDVPPGPAEGRQLTGDHIVMNVGSMENATSAFAIQILKTCTK  
 MANITVKRPRRIHLPATKASPSSPGRQSDDEDDGPQVVEVDQGRGYDGDSSSGSGRS  
 WDESRRRPRPGRRGRAGSHGRRSPGGGSEANGLALVSGFKRLPRQDVQMKPVKSVLVK  
 RRDSEEFVGLGSGIFIKHITDSGLAARHRLQEGDLILQINGVSSQNLSLNDTRRLI  
 EKSEGLSLLLVRDRGQFLVNIIPAVSDSDSSPLEEGVTMADEMSSPPADISDLASEL  
 SQAPPSHIPPPRHAQRSPEASQTDSPVESPRLRRESSVDSRTISEPDEQRSELPRES  
 SYDIYRVPSSQSMEDRGYSPDTRVVRFLKGKISIGRLLAGGNDVGI FVSGVQAGSPADG  
 QGIQEGDQILQVNDVPFQNLTREEAVQFLGLFPGEEMELVTQRKQDIFWKMVQSRVG  
 DSFYIRTHFELEPSPPSGLGFTRGDVPHVLDLTHPGPGQSHARGGHWLAVRMGRDLRE  
 QERGIIPNQSRAEQLASLEAAQRAVGVPGSSAGSNARAEFWRLRGLRRGAKKTTQRS  
 REDLSALTRQGRYPYERVVLRASFKRPVILGPVADIAMQKLTAEMPDOFEIAETV  
 SRTDPSKIIKLDTVRVIAEKDKHALLDVTPSAIERLNVYQYYPIVVFPIPESRPALK  
 ALRQWLAPASRRSTRRLYAQAQKLKSHSLFTATIPLNGTSDTWYQELKAIIREQQT  
 RPIWTAEDQLDGSLEDNLDLPHHGLADSSADLSCDSRVNSDYETDGEAGYTDEGYT  
 DGEAGPYTDVDEPPAPALARSSEPVQADESQSPDRGRISAHQGAQVDSRHPQGWQRQDSMRTYEREALKKKFM  
 RVHDAESSDEDDGYDWGPATDL

Primers for amplifying the sequence ENST00000262968 can be designed using primer design software such as Oligo Calc and/or Primer 3.

Examples of primer pairs for amplifying TJP3 include:

Forward SEQ ID NO:432 CCCTCGACCAGGTGGCTGAC (Exon1)  
 Reverse SEQ ID NO:433 CCTCCAGAGATCGCAATGC (Exon2)

Forward SEQ ID NO:434 GTATCTGACGTGGTACCTG (Exon2)  
Reverse SEQ ID NO:435 GGCAAACGCGGAGGTGGCATT C (Exon3)

Forward SEQ ID NO:436 CGGGGTTTCCATGGAGAATG (Exon3)  
Reverse SEQ ID NO:437 GCGGGCAGGTGGATCCTCC (Exon4)

Forward SEQ ID NO:438 GCAGGACGTGCAGATGAAGC (Exon4)  
Reverse SEQ ID NO:439 CCCGAATCTGTAATGTGCTTG (Exon5)

Forward SEQ ID NO:440 GTGGGCTGCAGGAAGGAGATC (Exon5)  
Reverse SEQ ID NO:441 GAACTGCCCACGATCTCTCAGC (Exon6)

Forward SEQ ID NO:442 GATCGTGGGCAGTTCCTGG (Exon6)  
Reverse SEQ ID NO:443 GATGTCTGCAGGGGGAGAGG (Exon7)

Forward SEQ ID NO:444 CACCCCGGCATGCTCAGCG (Exon7)  
Reverse SEQ ID NO:445 CCGAGATGGTTCTGGAATC (Exon8)

Forward SEQ ID NO:446 GAGTCCCCGGCTTCGGCGG (Exon8)  
Reverse SEQ ID NO:447 CGATCCTCCATGCTCTGACTG (Exon9)

Forward SEQ ID NO:448 GTG CAG GCG GGC AGC CCG (Exon10)  
Reverse SEQ ID NO:449 GTC CTG CTT CCT CTG CGT C (Exon11)

Forward SEQ ID NO:450 CGAGAGCAGCAGACGCGGCC  
Reverse SEQ ID NO:451 GAGGTCAGCGGAGCTGTCG

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting TJP3 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include:

SEQ ID NO:452  
CAGGGACAGTGGCGACAGGACAGCATGCGAACCTATGAACGGGAAGCCCTG  
AAGAAAAAG

SEQ ID NO:453  
GAACAGCACACGGCCCACTGTCCAAGGACCCCCGCCGGGGC

SEQ ID NO:454  
ACCAAGATGGCCAACATCACAGTGAAACGTCCCCGGAGGATCCACCTGCCCC  
GCC

SEQ ID NO:455



CAGTGACAGCGACAGCTCGCCATTGGAGGAAGGCGTGACCATGGCTGATGA  
GAT

SEQ ID NO:456

CGAGTGGTGTGCGAGAAGCCAGTTTCAAGCGCCCGGTAGTGATCCTGGGA  
CCC

Other probes to TJP3 are known in the art and/or can be readily designed by the skilled artisan.

Antibodies against include, but are not limited to, TJP3 are commercially available from e.g., Abnova Cat# H00027134-A01 which is a mouse polyclonal antibody raised against a partial recombinant TJP3 having the sequence SEQ ID NO:457 DEPPAPALARSEPVQADESQSPRDRGRISAHQGAQVDSRHPQGQWRQDS MRTYEREALKKKFMRVHDAESSDEDGYDWGPATDL (NP\_055243, 868 a.a. ~ 953 a.a); from LifeSpanBiosciences Cat# LS-C18593 which is a rabbit polyclonal against a synthetic peptide derived from the C-terminus of the human TJP3 (ZO-3) protein; and from LifeSpanBiosciences Cat#LS-C50518 which is a rabbit polyclonal against a synthetic peptide derived from the C-terminus of the human TJP3 (ZO-3) protein.

#### Example 23: EFEMP2

EFEMP2 also known as FBLN4, MBP1, and UPH1 was found to be underexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that EFEMP2 was underexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that EFEMP2 was underexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that EFEMP2 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

ENSG00000172638: Just one transcript

The sequence of an mRNA corresponding to EFEMP2 is given in ENSEMBL accession number ENST00000307998 and has a sequence as in SEQ ID NO:458.

GGGGCG

CTTCCTGGGGCCGCGCGTCCAGGGAGCTGTGCCGTCCGCCCCTCCGTCTGCCCCGAGGCATTGCCCCGAG  
C  
CAGCCGAGCCGCCAGAGCCGCGGGCCGCGGGGTGTGCGGGGCCCAACCCAGGATGCTCCCCTGCGCC  
T  
CCTGCCTACCCGGGTCTCTACTGCTCTGGGCGCTGCTACTGTTGCTCTTGGGATCAGCTTCTCCTCAGG  
A  
TTCTGAAGAGCCCGACAGCTACACGGAATGCACAGATGGCTATGAGTGGGACCCAGACAGCCAGCACTG  
C  
CGGGATGTCAACGAGTGTCTGACCATCCCTGAGGCCTGCAAGGGGGAAATGAAGTGCATCAACCACTAC  
G  
GGGGCTACTTGTGCCTGCCCCGCTCCGCTGCCGTCAACGACCTACACGGCGAGGGACCCCCGCCAC  
C  
AGTGCCTCCCGCTCAACACCCCAACCCCTGCCACCAGGCTATGAGCCCGACGATCAGGACAGCTGTGT  
G  
GATGTGGACGAGTGTGCCAGGCCCTGCACGACTGTGCCCCAGCCAGGACTGCCATAACTTGCCTGGC  
T  
CCTATCAGTGCACCTGCCCTGATGGTTACCGCAAGATCGGGCCCGAGTGTGTGGACATAGACGAGTGCC  
G  
CTACCGCTACTGCCAGCACCGCTGCGTGAACCTGCCTGGCTCCTTCCGCTGCCAGTGCAGCCGGGCTT  
C  
CAGCTGGGGCCTAACAACCGCTCCTGTGTTGATGTGAACGAGTGTGACATGGGGGCCCATGCGAGCAG  
C  
GCTGCTTCAACTCCTATGGGACCTTCCTGTGTGCTGCCACCAGGGGCTATGAGCTGCATCGGGATGGCT  
T  
CTCCTGCAGTGATATTGATGAGTGTAGCTACTCCAGCTACCTCTGTCAGTACCGCTGCGTCAACGAGCC  
A  
GGCCGTTTCTCCTGCCACTGCCCACAGGGTTACCAGCTGCTGGCCACACGCCTCTGCCAAGACATTGAT  
G  
AGTGTGAGTCTGGTGGCACCAGTGCTCCGAGGCCCAAACCTGTGTCAACTTCCATGGGGGCTACCGCT  
G  
CGTGGACACCAACCGCTGCGTGGAGCCCTACATCCAGGTCTCTGAGAACCGCTGTCTCTGCCCGGCCTC  
C  
AACCCTCTATGTCGAGAGCAGCCTTCATCCATTGTGCACCGCTACATGACCATCACCTCGGAGCGGAGC  
G  
TGCCCGCTGACGTGTTCCAGATCCAGGCGACCTCCGTCTACCCCGGTGCCTACAATGCCTTTTCAATCC  
G  
TGCTGGAAACTCGCAGGGGGACTTTTACATTAGGCAAATCAACAACGTCAGCGCCATGCTGGTCCTCGC  
C  
CGGCCGGTGACGGGGCCCCGGGAGTACGTGCTGGACCTGGAGATGGTCACCATGAATTCCCTCATGAGC  
T  
ACCGGGCCAGCTCTGTACTGAGGCTCACCGTCTTTGTAGGGCCTACACCTTCTGAGGAGCAGGAGGGA  
G  
CCACCCTCCCTGCAGCTACCCTAGCTGAGGAGCCTGTTGTGAGGGGCAGAATGAGAAAGGCAATAAAGG  
G  
AGAAAGAAAGTCTGTTGGCTGAGGTGGGCGGGTCACTGCAGGAAGCCTCAGGCTGGGGCAGGGTGG  
C  
ACTTGGGGGGCAGGCCAAGTTCACCTAAATGGGGGTCTCTATATGTTTCAGGCCAGGGGCCCCCATTG  
A  
CAGGAGCTGGGAGCTCTGCACCACGAGCTTCAGTCACCCGAGAGGAGAGGAGGTAACGAGGAGGGCGG  
A  
CTCCAGGCCCCGGCCCAGAGATTTGGACTTGGCTGGCTTGCAGGGGTCTTAAGAACTCCACTCTGGAC  
A  
GCGCCAGGAGGCCCTGGGTTCATTCCTAACTCTGCCTCAAACGTACATTTGGATAAGCCCTAGTAGT  
T  
CCCTGGGCCTGTTTTTCTATAAAACGAGGCAACTGGACTGTT

The corresponding amino acid sequence is given in ENSEMBL accession no.  
ENSP00000309953 and has a sequence as in SEQ ID NO:459

MLPCASCLPGSLLLWALLLLLLLGSASPQDSEEPDSYTECTDGYE  
 WDPDSQHCRDVNECLTIPEACKGEMKCINHYGGYLCLPRSAVINDLHGEGPPPPVPP  
 AQHPNCPPPGYEPDDQDSCVDVDECAQALHDCRPSQDCHNLPGSYQCTCPDGYRKIGP  
 ECVDIDECRYRYCQHRCVNLPGSFRCQCEPGFQLGPNNRSCVDVNECDMGAPCEQRCF  
 NSYGTFLCRCHQGYELHRDGFSCSDIDECSYSSYLCQYRCVNEPGRFSCHCPQGYQLL  
 ATRLCQDIDECESGAHQCEAQTVCNHFHGGYRCVDTNRCVEPYIQVSENRCCLCPASNP  
 LCREQPSSIVHRYMTITSERVPAADVFIQATSVYPGAYNAFQIRAGNSQGDFYIRQI  
 NNVSAMLVLARPVGTGPREYVLDLEMTMNSLSYRASSVLRLTVFVGAYTF

Examples of primer pairs for amplifying EFEMP2 include those in

Forward SEQ ID NO:460 TGCTCTTGGGATCAGCTTCT  
 Reverse SEQ ID NO:461 CCTCAGGGATGGTCAGACAC

Forward SEQ ID NO:462 TGCCCACCAGGCTATGAG  
 Reverse SEQ ID NO:463 CAGGCAAGTTATGGCAGTCC

Forward SEQ ID NO:464 AACTTGCTGGCTCCTATCA  
 Reverse SEQ ID NO:465 GTGCTGGCAGTAGCGGTAG

Forward SEQ ID NO:466 GGCCTAACAACCGCTCCT  
 Reverse SEQ ID NO:467 CGACACAGGAAGGTCCCATA

Forward SEQ ID NO:468 TATGGGACCTTCCTGTGTCTG  
 Reverse SEQ ID NO:469 GATGCAGCGGTACTGACAGA

Forward SEQ ID NO:470 GTCAGTACCGCTGCATCAAC  
 Reverse SEQ ID NO:471 CGCACCAGACTCACACTCAT

Forward SEQ ID NO:472 GTGGAGCCCTACATCCAGGT  
 Reverse SEQ ID NO:473 TCCGAGGTGATGGTCATGTA

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting EFEMP2 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include

The probe used on the microarray has a sequence as in SEQ ID NO:474  
 TTCATCCATTGTGCACCGCTACATGACCATCACCTCGGAGCGGAGCGTGC  
 SEQ ID NO:475 GAAGAGCCCGACAGCTACAC  
 SEQ ID NO:476 CAGGCAAGTTATGGCAGTCC  
 SEQ ID NO:477 CCTGATGGTTACCGCAAGAT  
 SEQ ID NO:478 GTGAACGAGTGTGACATGGG  
 SEQ ID NO:479 ATGGCTTCTCCTGCAGTGAT  
 SEQ ID NO:480 ACGCCTCTGCCAAGACATT  
 SEQ ID NO:481 ATGTCGAGAGCAGCCTTCAT

Antibodies to EFEMP2 include Mouse Anti-Human EFEMP2 MaxPab® Polyclonal Antibody, Unconjugated Cat# H00030008-B01 against full length human EFEMP2; Anti-EFEMP2 Monoclonal Antibody, Unconjugated, Clone 2C8 Cat# H00030008-M01 against a partial protein , 26aa-443aa; and Rabbit Anti-Human EFEMP2 Polyclonal Antibody, Unconjugated Cat# ab74873 against a Synthetic peptide derived from an internal region of human EFEMP2.

#### Example 24: SOCS2

SOCS2 also known as CIS2, Cish2, SOCS-2, SSI-2, SSI2, and STATI2 was found to be underexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that SOCS2 was underexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that SOCS2 was underexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that SOCS2 can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

The sequence of an mRNA corresponding to SOCS2 is given in ENSEMBL accession number ENST00000340600 and has a sequence as in SEQ ID NO:482

```

1  AGCCGCGGCCTCAACTAAAAGTGGCCATTGACCTTTCAAGCTTTGAGCAGTGATGCAAT
61  AGAATAGTATTTCAAAGAAAAATGCTTATCGAAATTTTGGATCCGGTTTTCCCGTGATTG
121  TTAAGGGTTTCTTTTAAAAAGTAGGTCACATTTCAAGTAGGTCATATTTGGGGGCGGGT
181  GCGCAGACAAGGAGATGAGTTTCCACTAAGGCCAGGGGGCCTCCAACGGGGTTGGAGGTG
241  AGAATCCCAGGTAGGGTAGAGGTGCCGAGATCCTTCCGAATCCCAGCCCTGGGGCGTCAG
301  CCCTGCAGGGAATGGCAGAGACACTCTCCGGACTGAGGGAACCGAGGCCAGTCACCAAGC
361  CCCTTCCGGGCGCGCAGGCGATCAGTGGGTGACCGCGGCTGCGAGGGACTTTGTTCATCCG
421  TCCTCCAGGATCTGGGGAGAAAAGAGCCCCATCCCTTCTCTCTCTGCCACCATTTTCGGACA
481  CCCCAGGACTCGTTTTGGGATTGCGCACTGACTTCAAGGAAGGACGCGAACCCTTCTC
541  TGACCCAGCTCGGGCGGCCACCTGTCTTTGCCGCGGTGACCCTTCTCTCTATGACCCTGC
601  GGTGCCTTGAGCCCTCCGGGAATGGCGGGGAAGGGACGCGGAGCCAGTGGGGGACCGCGG
661  GGTGCGCGGAGGAGCCATCCCCGAGGCGGCGCGTCTGGCGAAGGCCCTGCGGGAGCTCG
721  GTCAGACAGGATGGTACTGGGGAAGTATGACTGTTAATGAAGCCAAAGAGAAATTAAG
781  AGGCACCAGAAGGAACCTTTCTTGATTAGAGATAGCTCGCATTGAGACTACCTACTAACA
841  TATCTGTTAAACATCAGCTGGACCAACTAATCTTCGAATCGAATACCAAGACGGAAT
901  TCAGATTGGACTCTATCATATGTGTCAAATCCAAGCTTAAACAATTTGACAGTGTGGTTC
961  ATCTGATCGACTACTATGTTTCAGATGTGCAAGGATAAGCGGACAGGTCCAGAACGCCCC
1021  GGAACGGCACTGTTACCTTTATCTGACCAAAACCGCTCTACACGTCAGACCATCTCTGC
1081  AGCATCTCTGTAGGCTCACCATTAAACAAATGTACCGGTGCCATCTGGGGACTGCCTTTAC
1141  CAACAAGACTAAAAGATTACTTGAAGAATATAAATTCAGGTATAAATGTTTCTCTTTT
1201  TTTAAACATGTCTCACATAGAGTATCTCCGAATGCAGCTATGTAAAGAGAACCAAACT
1261  TGAGTGCTCTGGATAACTATATGGAATGCTTTCTAAGAACAGCTGAAGCTAATCTAATTT
1321  AAATTTAACAGCTTGAAGAGGTAGCTAGGTGTTTAAAGTTCCTCCAGATACTTTTACCTG
1381  AGTGATGCTTCCCTTCCTAAGGCTGACCAAGACCTGTTGATCCTTTTAGATTAAAAATAA

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1441 AATGTCGCATGTAAAGGCTGAAGTCGCGTTTTATCAGAATGCCTTGCCTTCTTAGGTTCT
1501 TTTCCATTATGTCAAAGGTCAGGCTCCAGTAGGAGAGAAAGAACTCCTCATAGGAATAC
1561 TGAAGAAGTGGGAAGGAACCAAGCTGACACAGGCCTCACTGCAATTTGATATGCCTGCTG
1621 ATCAGAGTCTCTTGGGCATTTTATATTTTGCATTCTGATGTACCTAGGAGTTTTGTTAA
1681 CAGATGATGTATGTGAGTATTTATCCCATTTTATGCAATTAACCAAATCAACCAAAAAA
1741 GTGACCATGAAGTCCTGTATTTGTCTTTTTACTACATGTAGGAACCTCTCATGTGAATGAG
1801 TACTGTAGTAATCCATTCTATGGGAGCCTTATTTTCAAGAAATATTTCAAACCTGGTGCAAT
1861 GGAAAAGACTTTCTCTTTTCTTTTAAAGCTAAAGACAAGAATATCATGCTATACAGGTGC
1921 AACTCAATCCCCGTTAATAAAAACCAATGTAGGTATAGGCATTCTACCCCTTTGAAATAGC
1981 TGTGTCCCAACCTGTTGCCATTGATTTTTTGGAAATGGCTTTAGAAATATCCAAGTTGTC
2041 CTTGAATTGTCTAACCATGGACATAAACAGTTGTCTCCCTTCTACTGTGTAGAATACTTT
2101 GACTTAATTTTCTTCCAGATACAGGGGGATACCTGCCTGTTTTTCAAAGTGTTTATTTAC
2161 TGCTGTTACTATTTGATTAGAATGTATTAATAAAAAAACCTGATTTCT

```

The start and stop codons are indicated in bold.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000339428 and has a sequence as in SEQ ID NO:483

```

1  MTLRCLEPSGNGGEGTRSQWGTAGSAEESPQAARLAKALRELGQTGWYWGSMTVNEAKE
61  KLKEAPEGTFLIRDSSHSYLLTISVKTSAGPTNLRIEYQDGKFRLDISIICVKSCLKQFD
121 SVVHLIDYYVQMCKDKRTGPEAPRNGTVHLYLTKPLYTSAPSLQHLCLRTINKCTGAIWG
181 LPLPTRLKDYLEEYKFQV

```

Examples of primer pairs for amplifying SOCS2 include those in

Forward SEQ ID NO:484 AGTCACCAAGCCCCTTCC

Reverse SEQ ID NO:485 GCTCTTTCTCCCCAGATCCT

Forward SEQ ID NO:486 GGGACTGCCTTTACCAACAA

Reverse SEQ ID NO:487 TTTACATAGCTGCATTCCGGAGA

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art (e.g., using Oligo Calc and/or Primer 3).

Probes for detecting SOCS2 can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents).

Other examples of probes include

The probe used on the microarray has a sequence as in SEQ ID NO:488

AGTGTGGTTCATCTGATCGACTACTATGTTTCAAGATGTGCAAGGATAAGCGGA  
CAGGTCCA

SEQ ID NO:489 GACTTTGTTCATCCGTCCTCC

SEQ ID NO:490 ACTTGAAGAATATAAATTCAGGT

Antibodies to SOCS2 include, but are not limited to, Mouse Anti-Human SOCS2 Polyclonal Antibody, Unconjugated Cat# H00008835-A01 against a partial protein: 99aa-198aa; Mouse Anti-Human SOCS2 Monoclonal Antibody, Unconjugated, Clone 3E7 Cat# H00008835-M01 against a partial protein: 99aa-198aa; Rabbit Anti-Human

SOCS2 Polyclonal Antibody, Unconjugated Cat# ab74533 against the C-terminal part of the protein.

#### Example 25: DCN

DCN also known as CSCD, DSPG2, PG40, PGII, PGS2, and SLRR1B was found to be underexpressed in endometrial cancer primary tissue as compared to normal endometrial tissue by the microarray experiment described in Example 1. Further studies using RT-PCR demonstrated that DCN was underexpressed in primary endometrial cancer tissue as compared to normal endometrial tissue as described in Example 2. It was surprisingly found that DCN was underexpressed in samples obtained from uterine fluid (e.g., aspirates) from patients having endometrial cancer by the method described in Example 4. Example 5 shows that DCN can be combined with other biomarkers to give excellent predictive power for diagnosis of endometrial cancer.

Six transcripts from gene ENSG00000011465 but only 4 of them hybridize with our array probe, the following ones:

The sequence of an mRNA corresponding to DCN is given in ENSEMBL accession number ENST00000052754 and has a sequence as in SEQ ID NO:491

```
1 GAATCTACAATAAGACAAATTTCAAATCAAGTTGCTCCACTATACTGCATAAGCAGTTTA
61 GAATCTTAAGCAGATGCAAAAAGAATAAAGCAAATGGGAGGAAAAAAGGCCGATAAAG
121 TTTCTGGCTACAATAACAAGAGACATATCATTACCATATGATCTAATGTGGGTGTGAGCCG
181 GATTGTGTTTCATTGAGGGAAACCTTATTTTTTAACTGTGCTATGGAGTAGAAGCAGGAGG
241 TTTTCAACCTAGTCACAGAGCAGCACCTACCCCTCCTCCTTTCCACACCTGCAAACTCT
301 TTTACTTGGGCTGAATATTTAGTGTAAATTACATCTCAGCTTTGAGGGCTCCTGTGGCAAA
361 TTCCCGGATTAAAGGTTCCCTGGTTGTGAAAATACATGAGATAAATCATGAAGGCCACT
421 ATCATCCTCCTTCTGCTTGCACAAGTTTCCTGGGCTGGACCGTTTCAACAGAGAGGCTTA
481 TTTGACTTTATGCTAGAAGATGAGGCTTCTGGGATAGGCCCAGAAGTTCCTGATGACCGC
541 GACTTCGAGCCCTCCCTAGGCCCAGTGTGCCCCCTCCGCTGTCAATGCCATCTTCGAGTG
601 GTCCAGTGTTCTGATTGGGTCTGGACAAAGTGCCAAAGGATCTTCCCCCTGACACAAC
661 CTGCTAGACCTGCAAAACAACAAAATAACCGAAATCAAAGATGGAGACTTTAAGAACCTG
721 AAGAACCTTCACGCATTGATTCTTGTCAACAATAAAATTAGCAAAGTTAGTCCTGGAGCA
781 TTTACACCTTTGGTGAAAGTTGGAACGACTTTATCTGTCCAAGAATCAGCTGAAGGAATTG
841 CCAGAAAAAATGCCCAAACTCTTCAGGAGCTGCGTGCCCATGAGAATGAGATCACCAAA
901 GTGCGAAAAGTTACTTTCAATGGACTGAACCAGATGATTGTCATAGAAGTGGGCACCAAT
961 CCGCTGAAGAGCTCAGGAATTGAAAATGGGGCTTTCCAGGGAATGAAGAAGCTCTCCTAC
1021 ATCCGCATTGCTGATACCAATATCACCAGCATTCCCTCAAGGTCTTCCTCCTTCCCTTACG
1081 GAATTACATCTTGATGGCAACAAAATCAGCAGAGTTGATGCAGCTAGCCTGAAAGGACTG
1141 AATAATTTGGCTAAGTTGGGATTGAGTTTCAACAGCATCTCTGCTGTTGACAATTGGCTCT
1201 CTGGCCAATACGCCTCATCTGAGGGAGCTTCACTTGGACAACAACAAGCTTACCAGATA
1261 CTTGGTGGGCTGGCAGAGCATAAGTACATCCAGGTTGTCTACCTTCATAACAACAATATC
1321 TCTGTAGTTGGATCAAGTGACTTCTGCCCACCTGGACACAACACCAAAAAGGCTTCTTAT
1381 TCGGGTGTGAGTCTTTTCAGCAACCCGGTCCAGTACTGGGAGATACAGCCATCCACCTTC
1441 AGATGTGTCTACGTGCGCTCTGCCATTCAACTCGGAACTATAAGTAATTCTCAAGAAAG
1501 CCCTCATTTTTATAACCTGGCAAAATCTTGTTAATGTCATTGCTAAAAAATAAATAAAG
```

1561 CTAGATACTGGAAACCTAACTGCAATGTGGATGTTTTACCCACATGACTTATTATGCATA  
 1621 AAGCCAAATTTCCAGTTTAAGTAATTGCCTACAATAAAAAGAAATTTTGCCTGCCATTTT  
 1681 CAGAATCATCTTTTGAAGCTTTCTGTTGATGTTAACTGAGCTACTAGAGATATTCTTATT  
 1741 TCACTAAATGTAAATTTGGAGTAAATATATATGTCAATATTTAGTAAAGCTTTTCTTTT  
 1801 TTAATTTCCAGGAAAAAATAAAAAGAGTATGAGTCTTCTGTAATTCATTGAGCAGTTAGC  
 1861 TCATTTGAGATAAAGTCAAATGCCAAACACTAGCTCTGTATTAATCCCCATCATTACTGG  
 1921 TAAAGCCTCATTTGAATGTGTGAATTCAATACAGGCTATGTAAAATTTTACTAATGTCA  
 1981 TTATTTTGA AAAAATAAATTTAAAAATACATTCAAATTTACTATTGTATACAAGCTTAAT  
 2041 TGTTAATATTCCCTAAACACAATTTTATGAAGGGAGAAGACATTGGTTTGTGACAATAA  
 2101 CAGTACATCTTTTCAAGTTCTCAGCTATTTCTTCTACCTCTCCCTATCTTACATTTGAGT  
 2161 ATGGTAACTTATGTCATCTATGTTGAATGTAAGCTTATAAAGCACAAAGCATACATTTCC  
 2221 TGA CTGGTCTAGAGAACTGATGTTTCAATTTACCCCTCTGCTAAATAAATATTTAAACTA  
 2281 TCATGTG

The stop codon is indicated in bold as well as the position corresponding to the microarray probe.

The corresponding amino acid sequence is given in ENSEMBL accession no. ENSP00000052754 and has a sequence as in SEQ ID NO:492

1 MKATIILLLLAQVSWAGPFQQRGLFDFMLEDEASGIGPEVPDDRDFEPSLGPVCPFRQCQ  
 61 HLRVVQCSLDGLDKVPKDLPPDTLLDLQNNKITEIKDGDGFKNLKNLHALILVNNKISKV  
 121 SPGAFTPLVKLERLYLSKNQLKELPEKMPKTLQELRAHENEITKVRKVTFNGLNQMIVIE  
 181 LGTNPLKSSGIENGAFQGMKKLSYIRIADTNITSIPQGLPPSLTELHLDGNGKISRVDAA  
 241 LKGLNNLAKLGLSFNSISAVDNGSLANTPHLRELHLDNNKLTRVPGGLAEHKYIQVVYLH  
 301 NNNISVVGSSDFCPPGHNTKKASYSGVSLFSNPVQYWEIQPSTFRVCYVRSAILGLQNYK

Primers for amplifying the sequence DCN can be designed using primer design software such as Oligo Calc and/or Primer 3. Examples of primer pairs for amplifying DCN include those in

Forward SEQ ID NO:493 AGCTTTGAGGGCTCCTGTG  
 Reverse SEQ ID NO:494 GCAAGCAGAAGGAGGATGAT

Forward SEQ ID NO:495 AATGCCATCTTCGAGTGGTC  
 Reverse SEQ ID NO:496 TGCAGGTCTAGCAGAGTTGTG

Forward SEQ ID NO:497 AACCGAAATCAAAGATGGAGA  
 Reverse SEQ ID NO:498 GTCCAGGTGGGCAGAAAGTC

Forward SEQ ID NO:499 AATGCCATCTTCGAGTGGTC  
 Reverse SEQ ID NO:500 CTGCTGATTTTGTTGCCATC

Forward SEQ ID NO:501 TGGCAACAAAATCAGCAGAG  
 Reverse SEQ ID NO:502 GCCATTGTCAACAGCAGAGA

Forward SEQ ID NO:503 GGGCTGGCAGAGCATAAGTA  
 Reverse SEQ ID NO:504 GTCCAGGTGGGCAGAAAGTC

Forward SEQ ID NO:505 AACCGAAATCAAAGATGGAGA  
 Reverse SEQ ID NO:506 CCAAAGGTGTAAATGCTCCAG

Forward SEQ ID NO:507 GAGATCACCAAAGTGCGAAA  
Reverse SEQ ID NO:508 AAAGCCCCATTTTCAATTCC

Forward SEQ ID NO:509 AATGCCATCTTCGAGTGGTC  
Reverse SEQ ID NO:510 AAAGCCCCATTTTCAATTCC

Other sets of primers can be readily designed by the skilled artisan and/or are known in the art.

Probes for detecting DCN can be derived from any number of sources depending on the desired use (e.g., using the above described primers and appropriate reagents). Other examples of probes include

The probe used on the microarray has a sequence as in SEQ ID NO:511  
TTTAACTGTGCTATGGAGTAGAAGCAGGAGGTTTTCAACCTAGTCACAGAGCAGC  
ACC

SEQ ID NO:512 TTCCCGGATTAAAAGGTTCC  
SEQ ID NO:513 AAGTGCCAAAGGATCTTCCC  
SEQ ID NO:514 CCTGAAGAACCTTCACGTTG  
SEQ ID NO:515 TCCTCCTTCCCTTACGGAAT  
SEQ ID NO:516 ATGCAGCTAGCCTGAAAGGA  
SEQ ID NO:517 CATCCAGGTTGTCTACCTTCA  
SEQ ID NO:518 TGAAGAACCTTCACGCATTG  
SEQ ID NO:519 TGTCATAGAACTGGGCACCA  
SEQ ID NO:520 GTTCTGATTTGGAAGTGGGC

Antibodies to DCN include, but are not limited to, Mouse Anti-Human Decorin Monoclonal Antibody, Unconjugated Cat# ab54728, against recombinant full length protein; and Anti-DCN Monoclonal Antibody, Unconjugated, Clone 2B5-G5 Cat# H00001634-M02, against recombinant full length protein.

Additional primers for the biomarkers of the invention:

ACAA1  
SEQ ID NO:521 tcacgggagaagcaggatac  
SEQ ID NO:522 cttgctctgggctcttgc

SEQ ID NO:523 ccagagattgcctgattcct  
SEQ ID NO:524 cctgcttctcccgtgaaat

SEQ ID NO:525 agctgggggacatctgtgt  
SEQ ID NO:526 cactcagaaactgggcgatt



## AP1M2

SEQ ID NO:527 cacatcgaagaatgccaatg

SEQ ID NO:528 gtccttgaagtattcgcaga

SEQ ID NO:529 tgctcttcgagctcactgg

SEQ ID NO:530 cacgcactggtggaatttt

SEQ ID NO:531 gtctgctacatcacccagagt

SEQ ID NO:532 gtaaggaagccccgtgttc

## CGN

SEQ ID NO:533 gagcttaccgaaaagtgga

SEQ ID NO:534 tctagcttctgccgttctt

SEQ ID NO:535 ggagatactgccaggttga

SEQ ID NO:536 ccttaagctcctctgtgtcc

SEQ ID NO:537 cctctgtgaggaggaagggttag

SEQ ID NO:538 ttagtagaaccagaagaaccatcac

## DDR1

SEQ ID NO:539 tagagagccacccccgta

SEQ ID NO:540 ccatatagtcacctgtaggc

SEQ ID NO:541 ccactctgctccctgtgtc

SEQ ID NO:542 ctggcttctcaggctccata

SEQ ID NO:543 tggggactattaccgtgtgc

SEQ ID NO:544 acgtcactcgagtcgtg

## EPS8L2

SEQ ID NO:545 gcagctcttctccctcaaca

SEQ ID NO:546 cccactttgtgttctcc

SEQ ID NO:547 caagatgagccccaaggac

SEQ ID NO:548 tgatgacgttgagttggaa

SEQ ID NO:549 caaggatgaggtcctagagggtg

SEQ ID NO:550 gatgttgcagggcacgta

## FASTKD1

SEQ ID NO:551 tggaaattctggggtatcgt

SEQ ID NO:552 gcaccccttgttgacagtgc

SEQ ID NO:553 cctgggaatcaaatacgaaatag

SEQ ID NO:554 ccaaaaattccaagcaatcc

SEQ ID NO:555 aagaattaactttctgcattcca

SEQ ID NO:556 cagaacagacacctcagttggt

## GMIP

SEQ ID NO:557 aaccctggccatggagac

SEQ ID NO:558 ccgccacttctcaatctcag

SEQ ID NO:559 cccagcaccacagtaccc

SEQ ID NO:560 ctctgtggagttggaatctcg

SEQ ID NO:561 ctggtggcccatctgttc

SEQ ID NO:562 ggttggttgccagacatctgt

## IKBKE

SEQ ID NO:563 acagttcaagaagtctaggatgagg

SEQ ID NO:564 tggctaaatgactgaaattcacc

SEQ ID NO:565 ggacatccctcctctaccta

SEQ ID NO:566 ggatctcaggcgttccag

SEQ ID NO:567 ctgcctgaggatgagttcct

SEQ ID NO:568 gatgcacaatgccgttctc

## P2RX4

SEQ ID NO:569 ccgttacgaccaaggtcaag

SEQ ID NO:570 tgacgaagagggagttttcc

SEQ ID NO:571 tctgtcaagacgtgtgaggtg

SEQ ID NO:572 agtgaagttttctgcagccttta

SEQ ID NO:573 tctcctggctacaatttcagg

SEQ ID NO:574 atgcataggccttgatgag

## P4HB

SEQ ID NO:575 gcttcccccaaggaatataca

SEQ ID NO:576 tcttcagccagttcacgatg

SEQ ID NO:577 gcaggggatgatgacgat

SEQ ID NO:578 cgttctcctcatgtctgg

SEQ ID NO:579 ctggagggcaaaatcaagc

SEQ ID NO:580 ttcttccaacaagcacctt

## PHKG2

SEQ ID NO:581 gcagatccgactttcagatttc

SEQ ID NO:582 ggggtcccacacaactctc

SEQ ID NO:583 ttccagcactgtcaaagacct

SEQ ID NO:584 aaagaaggggtgctgtaggg

SEQ ID NO:585 aggctatggcaaggaggtc

SEQ ID NO:586 tgcgtaacatcaggatctgc

## PPFIBP2

SEQ ID NO:587 aggggataaggagtcctca

SEQ ID NO:588 ctggtgtccttcagacaca

SEQ ID NO:589 gaatggaagctaaaggccact

SEQ ID NO:590 atctttcaggccacctgtt

SEQ ID NO:591 aatcttcgaggagtgaggatc

SEQ ID NO:592 cagggtgtccccagtgaa

## PPP1R16A

SEQ ID NO:593 ccctcccagtggtgtcctt

SEQ ID NO:594 cccactcccaaggaact

SEQ ID NO:595 gagtgtggacgcctctg

SEQ ID NO:596 ttgaccgccaggagattg

SEQ ID NO:597 atgccctatgacctgtgtgat

SEQ ID NO:598 gatgtgtcctgggtgatg

## RASSF7

SEQ ID NO:599 cactagcccaagcaataggc

SEQ ID NO:600 cactcttggtgcagcaactg

SEQ ID NO:601 cagcctggctctggtgag

SEQ ID NO:602 ggagctctcggttcagctc

SEQ ID NO:603 tctgcctccagccagaga

SEQ ID NO:604 ctccaggagtctctgcgtcat

## RNF183

SEQ ID NO:605 tccagagtagtctgcctgacc

SEQ ID NO:606 catcctcagccacacacg

SEQ ID NO:607 tccagagtagtctgcctgacc

SEQ ID NO:608 tgtgttgaaggggttcag

SEQ ID NO:609 tctgccaccgtgtctacg

SEQ ID NO:610cggaacactccctcaaaga

## SIRT6

SEQ ID NO:611 agctgaggacaccatccta

SEQ ID NO:612 atgtaccagcgtgatggac

SEQ ID NO:613 aggatgtcggatgaattacgc

SEQ ID NO:614 agaccagcctcgccagtt

SEQ ID NO:615 ggtcagccagaacgtgga

SEQ ID NO:616 gtggagctctgccagtttgt

## TJP3

SEQ ID NO:617 gtgggcatcttcgtgtcc

SEQ ID NO:618 gaatggcacgtcattcacc

SEQ ID NO:619 atctggacggcggaagat

SEQ ID NO:620 ggtgagggaggtctaggttgt

SEQ ID NO:621 tcatcaagcacattacagattcg

SEQ ID NO:622 ggctagacaccccgttgat

## EFEMP2

SEQ ID NO:623 actcgcagggggacttttac

SEQ ID NO:624 catgaggggaattcatggtga

SEQ ID NO:625 atcgggatggcttctcct

SEQ ID NO:626 tgatgcagcgggtactgaca

SEQ ID NO:627 agtaccgctgcatcaacga

SEQ ID NO:628 cgcaccagactcacactcat

## SOCS2

SEQ ID NO:629 ggagctcggtcagacagg

SEQ ID NO:630 ctaatcaagaaagttccttctggtg

SEQ ID NO:631 cagtcaccaagccccttc

SEQ ID NO:632 aagggatggggtctttct

SEQ ID NO:633 ggagctcggtcagacagg

SEQ ID NO:634 gttccttctggtgcctctttt

## DCN

SEQ ID NO:635 ggagactttaagaacctgaagaacc

SEQ ID NO:636 cgttccaacttcaccaaagg

SEQ ID NO:637 ctgtcaatgccatcttcgag

SEQ ID NO:638 gatcctttggcactttgtcc

SEQ ID NO:639 caatatcaccagcattcctcaag

SEQ ID NO:640 ctgctgattttgttgccatc

All publications and patent applications mentioned in the specification are indicative of the level of those skilled in the art to which this invention pertains. All publications and patent applications are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference. The mere mentioning of the publications and patent applications does not necessarily constitute an admission that they are prior art to the instant application.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be obvious that certain changes and modifications may be practiced within the scope of the appended claims.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should be taken as an acknowledgement or admission or any form of suggestion that the prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

## CLAIMS

1. An in vitro diagnostic method for the diagnosis of endometrial cancer comprising detecting the level of the biomarker P4HB in a sample from a patient wherein an increased level of P4HB compared to a control value indicates the existence of endometrial cancer;  
wherein said patient is selected from the group comprising: a patient with abnormal uterine bleeding, a pre-menopausal patient, a peri-menopausal patient, or post-menopausal patient, a patient having an endometrium with increased thickness; or  
wherein said sample is chosen from the group consisting of a tissue sample, blood and/or serum, and uterine fluid.
2. The in vitro diagnostic method of claim 1, further comprising detecting the level of one or more of GMIP, IKBKE, or EFEMP2.
3. The in vitro diagnostic method of any one of claim 1 or claim 2, further comprising detecting the level of FASTKD1.
4. The in vitro diagnostic method of any one of claims 1 to 3, further comprising detecting the level of DDR1.
5. The in vitro diagnostic method of any one of claims 1 to 4, further comprising detecting the level of SIRT6.
6. The in vitro diagnostic method of any one of claims 1 to 5 further comprising detecting the level of PHKG2.
7. The in vitro diagnostic method of any one of claims 1 to 6, further comprising detecting the level of a biomarker chosen from ACAA1, AP1M2, EPS8L2, P2RX4, PPFIBP2, PPP1R16A, CGN, RASSF7, RNF183, TJP3, SOCS2, and DCN.

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8. The in vitro diagnostic method of any one of claims 1 to 7, wherein said patient has a risk factor for endometrial cancer or is being screened for endometrial cancer.
9. The in vitro diagnostic method of any one of claims 1 to 8, wherein said uterine fluid sample is obtained by aspiration.
10. The in vitro diagnostic method of any one of claims 1 to 9, wherein the level of the biomarker P4HB, and optionally, one biomarker chosen from GMIP, IKBKE, FASTKD1, DDR1, SIRT6, PHKG2, ACAA1, AP1M2, EPS8L2, P2RX4, PPFIBP2, PPP1R16A, CGN, RASSF7, RNF183, TJP3, EFEMP2, SOCS2, and DCN, is determined with an antibody.
11. The in vitro diagnostic method of any one of claims 1 to 9, wherein the level of the biomarker P4HB, and optionally, one biomarker chosen from GMIP, FASTKD1, DDR1EFEMP2, SIRT6, PHKG2, ACAA1, AP1M2, EPS8L2, IKBKE, P2RX4, PPFIBP2, PPP1R16A, CGN, RASSF7, RNF183, TJP3, SOCS2, and DCN, is determined by RT-PCR.
12. The in vitro diagnostic method of any one or claims 2 to 11, wherein from 2 to 20 markers are detected.
13. The in vitro diagnostic method of any one of claims 1 to 12, wherein one or more additional biomarkers are detected.
14. The in vitro diagnostic method of claim 13, wherein said one or more additional biomarkers are chosen from differential diagnosis biomarkers, prognostic biomarkers, biomarkers useful for detecting endometrial cancer, biomarkers for classifying endometrial cancer and auxiliary biomarkers for detecting endometrial cancer.
15. The method of any one of claims 1 to 14, wherein a combination of markers is detected wherein said combination comprises IKBKE and P4HB; IKBKE and SOCS2; P4HB and SOCS2; GMIP and IKBKE; GMIP and P4HB; GMIP,

SOCS2, and P4HB; GMIP, IKBKE, and P4HB; IKBKE,P4HB, and SOCS2; GMIP, IKBKE, P4HB, and SOCS2GMIP, SOCS2, P4HB, and EPS8L2; GMIP, IKBKE, P4HB, and EPS8L2; IKBKE, P4HB, SOCS2, and EPS8L2; GMIP, IKBKE, P4HB, SOCS2, and DDR1; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, and PPP1R16A; GMIP, IKBKE, P4HB, SOCS2, PHKG2, and RASSF7; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, and DDR1; GMIP, IKBKE, P4HB, SOCS2, EPS8L2, PPP1R16A, and DDR1; DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, RASSF7, SIRT6, TJP3, and SOCS2; DDR1, EPS8L2, GMIP, IKBKE, P2RX4, P4HB, PHKG2, PPP1R16A, RASSF7, SIRT6, TJP3, RNF183 and SOCS2;GMIP, IKBKE, P4HB, SOCS2 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2 and DDR1; GMIP, IKBKE, P4HB, SOCS2 and PHKG2; GMIP, IKBKE, P4HB, SOCS2 and SIRT6; GMIP, IKBKE, P4HB, SOCS2 and ACAA1; GMIP, IKBKE, P4HB, SOCS2 and EFEMP2; GMIP, IKBKE, P4HB, SOCS2 and EPS8L2; GMIP, IKBKE, P4HB, SOCS2 and P2RX4; GMIP, IKBKE, P4HB, SOCS2 and PPFIBP2; GMIP, IKBKE, P4HB, SOCS2 and PPP1R16A; GMIP, IKBKE, P4HB, SOCS2, ACAA1 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2, PHKG2 and FASTKD1; GMIP, IKBKE, P4HB, SOCS2, SIRT6 and FASTKD1; ACAA1, AP1M2, EPS8L2, IKBKE, P2RX4, P4HB, PPFIBP2, PPP1R16A, SIRT6, and EFEMP2; GMIP, IKBKE, P4HB, and EFEMP2; DDR1, FASTKD1, PHKG2, SIRT6, SOCS2, GMIP, IKBKE, P4HB, and EFEMP2; DDR1, FASTKD1, PHKG2, SIRT6, GMIP, IKBKE, P4HB, and EFEMP2; P4HB, EFEMP2, IKBKE, GMIP, and FASTKD1; GMIP, IKBKE, P4HB, EFEMP2 and FASTKD1; GMIP, IKBKE, P4HB, EFEMP2and DDR1; GMIP, IKBKE, P4HB, EFEMP2 and PHKG2; GMIP, IKBKE, P4HB, EFEMP2 and SIRT6; GMIP, IKBKE, P4HB, EFEMP2 and ACAA1; GMIP, IKBKE, P4HB, SOCS2 and EFEMP2; GMIP, IKBKE, P4HB, EFEMP2 and EPS8L2; GMIP, IKBKE, P4HB, EFEMP2 and P2RX4; GMIP, IKBKE, P4HB, EFEMP2 and PPFIBP2; GMIP, IKBKE, P4HB, EFEMP2 and PPP1R16A; GMIP, IKBKE, P4HB, EFEMP2, ACAA1 and FASTKD1; GMIP, IKBKE, P4HB, EFEMP2, PHKG2 and FASTKD1; or GMIP, IKBKE, P4HB, EFEMP2, SIRT6 and FASTKD1.



16. The *in vitro* diagnostic method of any one of claims 1 to 9 and 11 to 15, comprising providing a uterine fluid sample obtained from a patient with a pipelle device or syringe, wherein the patient has a risk factor or symptom of endometrial cancer;
  - contacting said sample with an agent capable of preserving, preventing, or lessening the degradation of RNA in said uterine fluid sample;
  - determining in said sample the expression level of mRNA corresponding to said biomarker P4HB and, optionally, one biomarker chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS and DCN, and one or more endogenous genes using quantitative PCR;
  - normalizing the expression level of said biomarker P4HB and, optionally, one biomarker chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS and DCN, with the one or more endogenous genes;
  - comparing the normalized level of said biomarker P4HB and, optionally, one biomarker chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS and DCN, to a control value wherein differential expression of said biomarker P4HB and, optionally, one biomarker chosen from ACAA1, AP1M2, CGN, DDR1, EPS8L2, FASTKD1, GMIP, IKBKE, P2RX4, PHKG2, PPFIBP2, PPP1R16A, RASSF7, RNF183, SIRT6, TJP3, EFEMP2, SOCS and DCN, indicates endometrial cancer or an increased likelihood of endometrial cancer.
17. The method of claim 16, wherein said one or more endogenous genes are chosen from POLR2A, B2M and PFN1.
18. Use of a kit comprising a nucleic acid being P4HB mRNA, cDNA, or a complement thereof, to diagnose endometrial cancer *in vitro*.

19. Use of a kit comprising a nucleic acid being a primer for P4HB to diagnose endometrial cancer *in vitro*.
20. Use of kit comprising a nucleic acid being a probe for P4HB to diagnose endometrial cancer *in vitro*.
21. The method of any one of claims 1 to 17, or the use of any one of claims 18 to 20, substantially as hereinbefore described with reference to the figures and/or examples.

FIG 1

## Gene Expression from Aspirates vs Primary Tumors

Calculated using RT-PCR with 64 Genes in 9 Samples

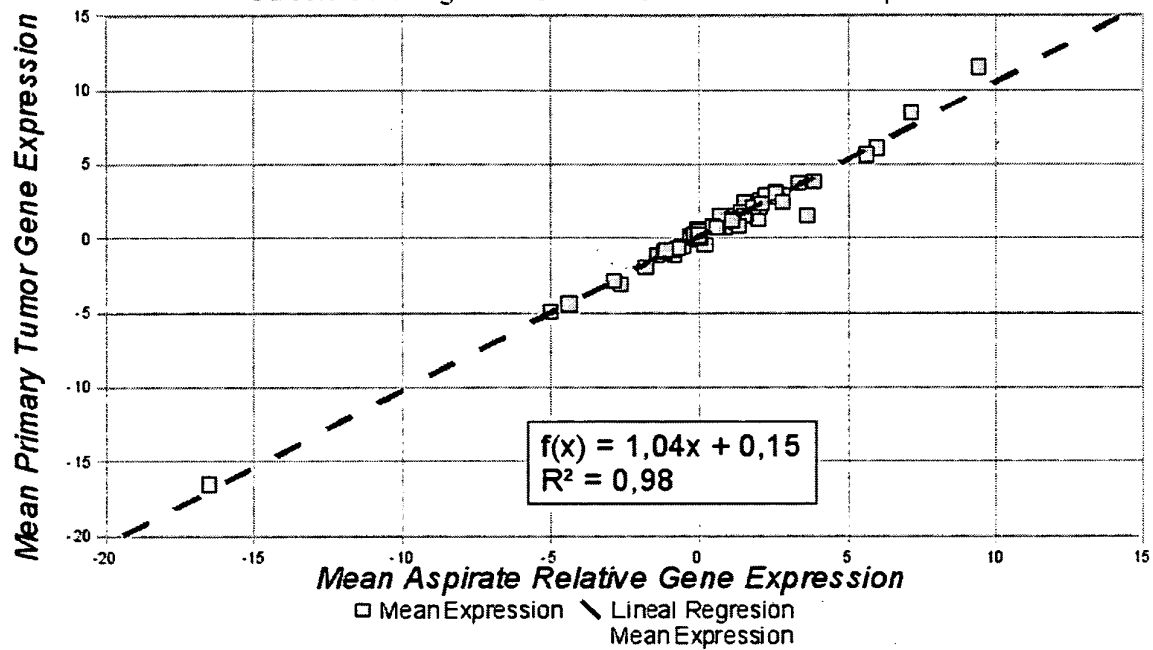


FIG 2A

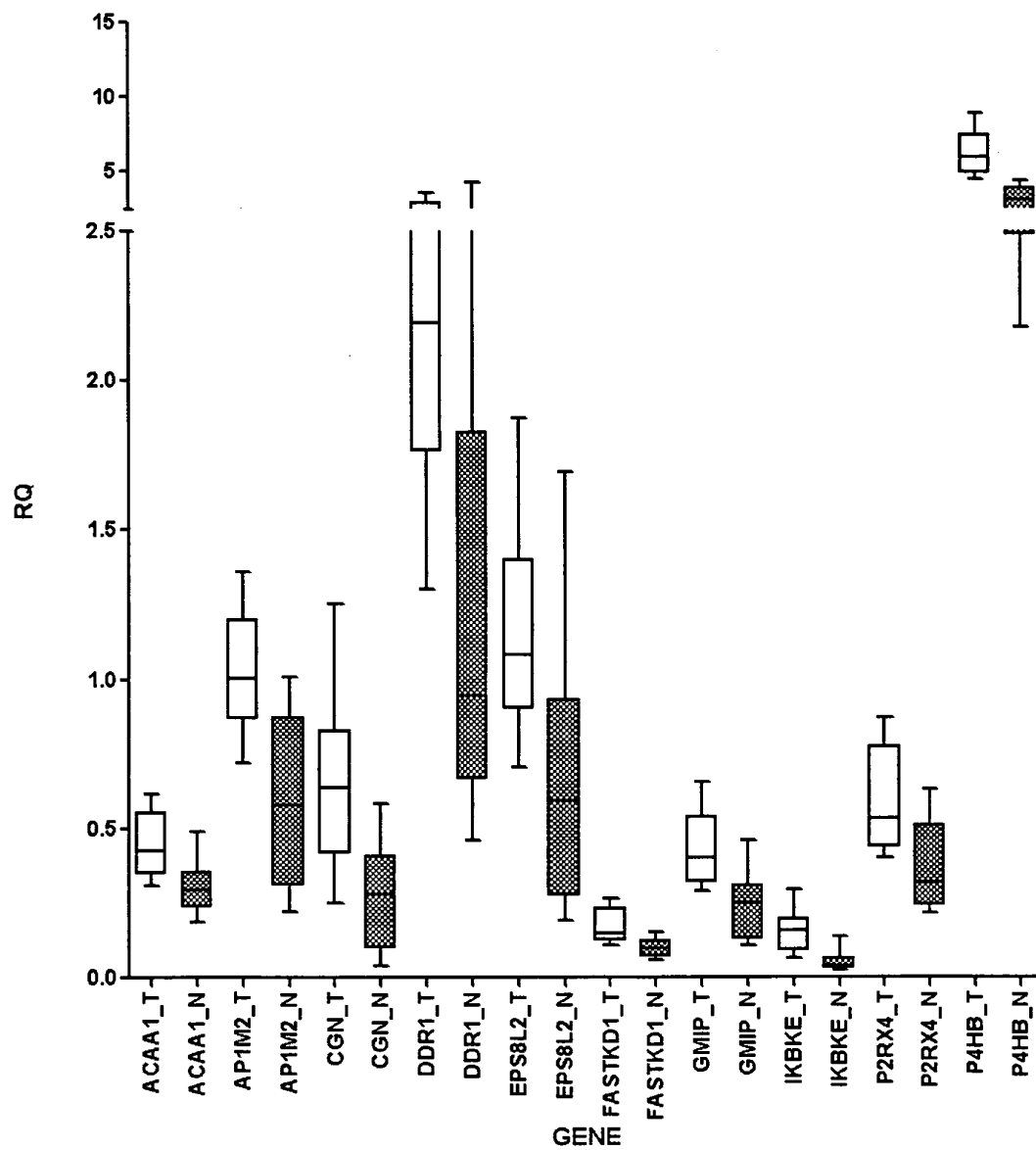


FIG. 2B

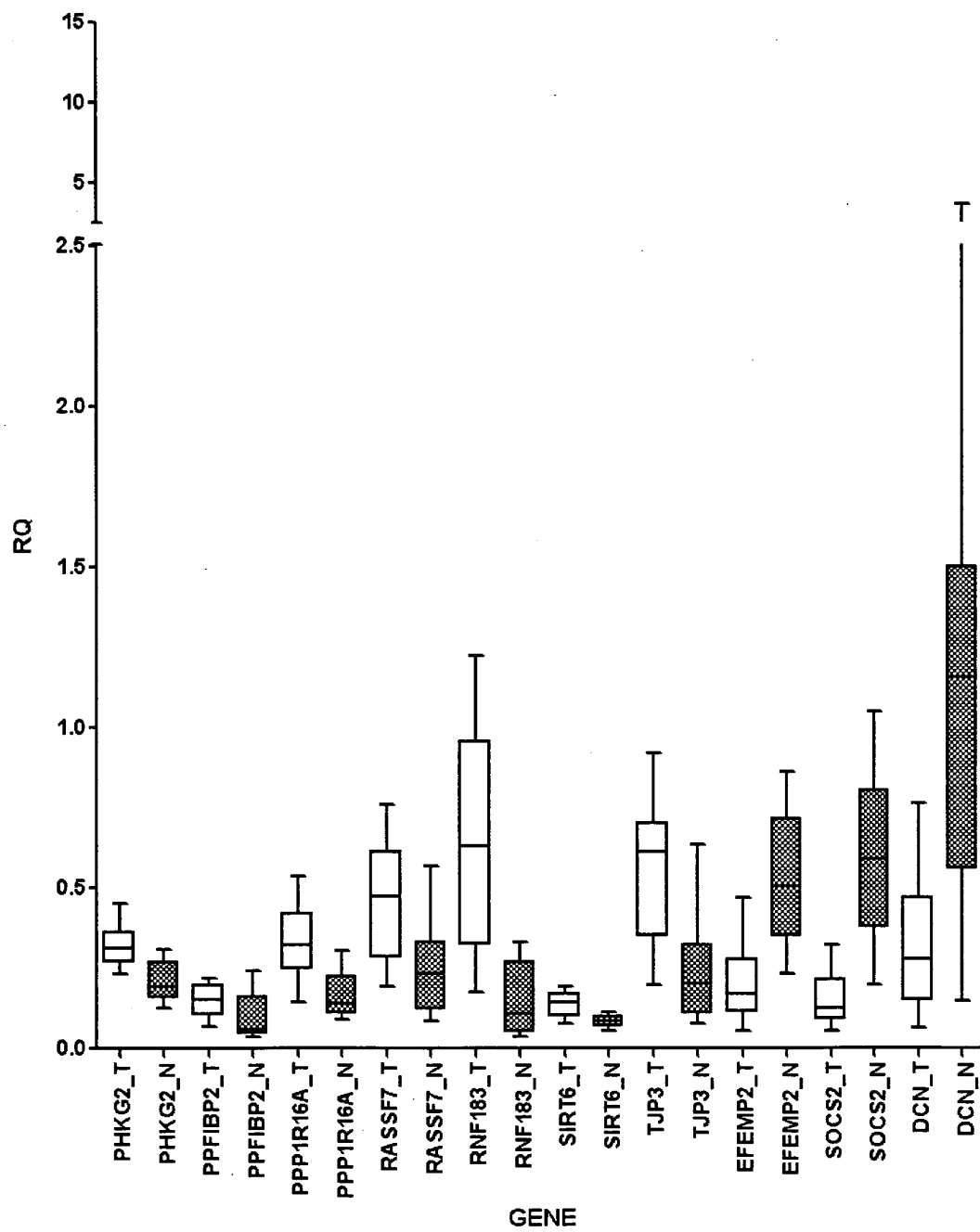


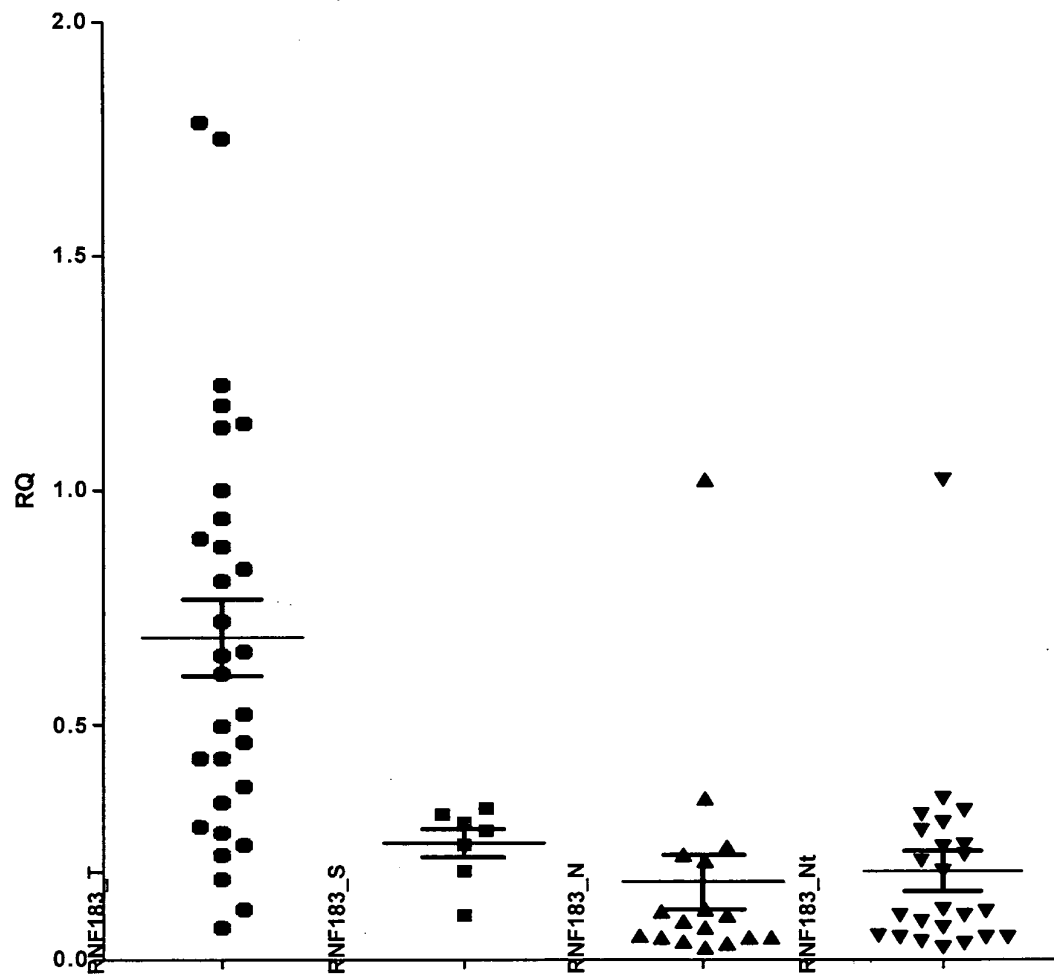
**FIG. 3 RNF183 data:**

FIG. 4 AP1M2

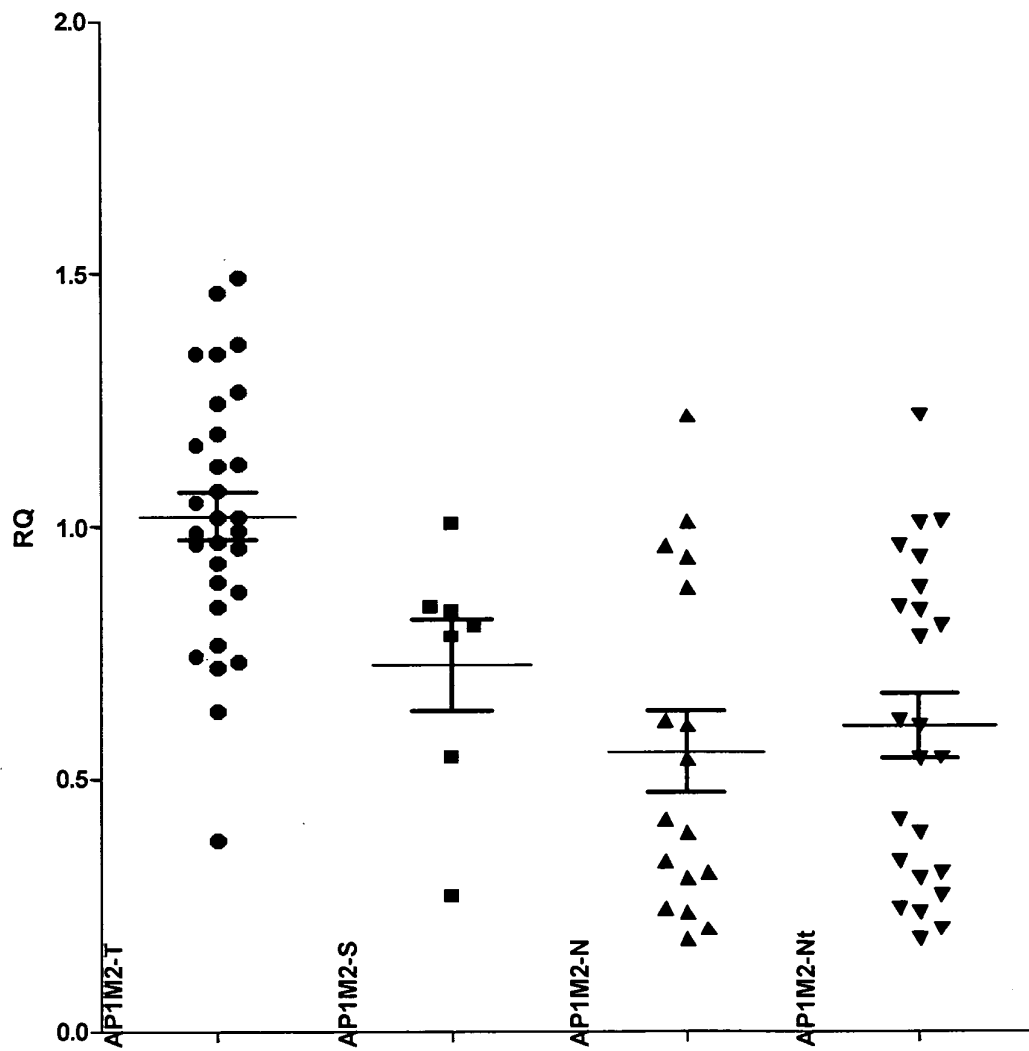


FIG. 5 CGN

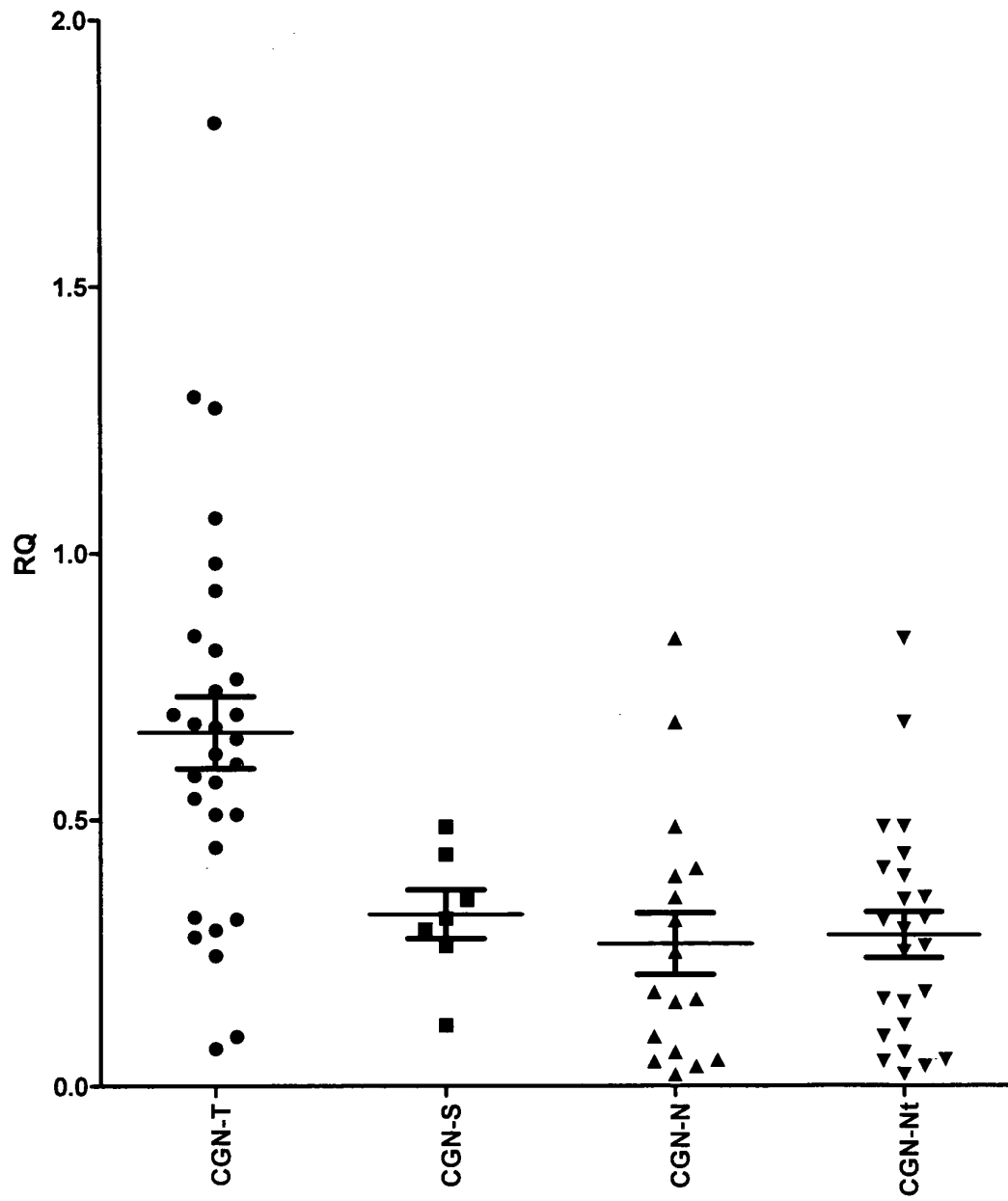




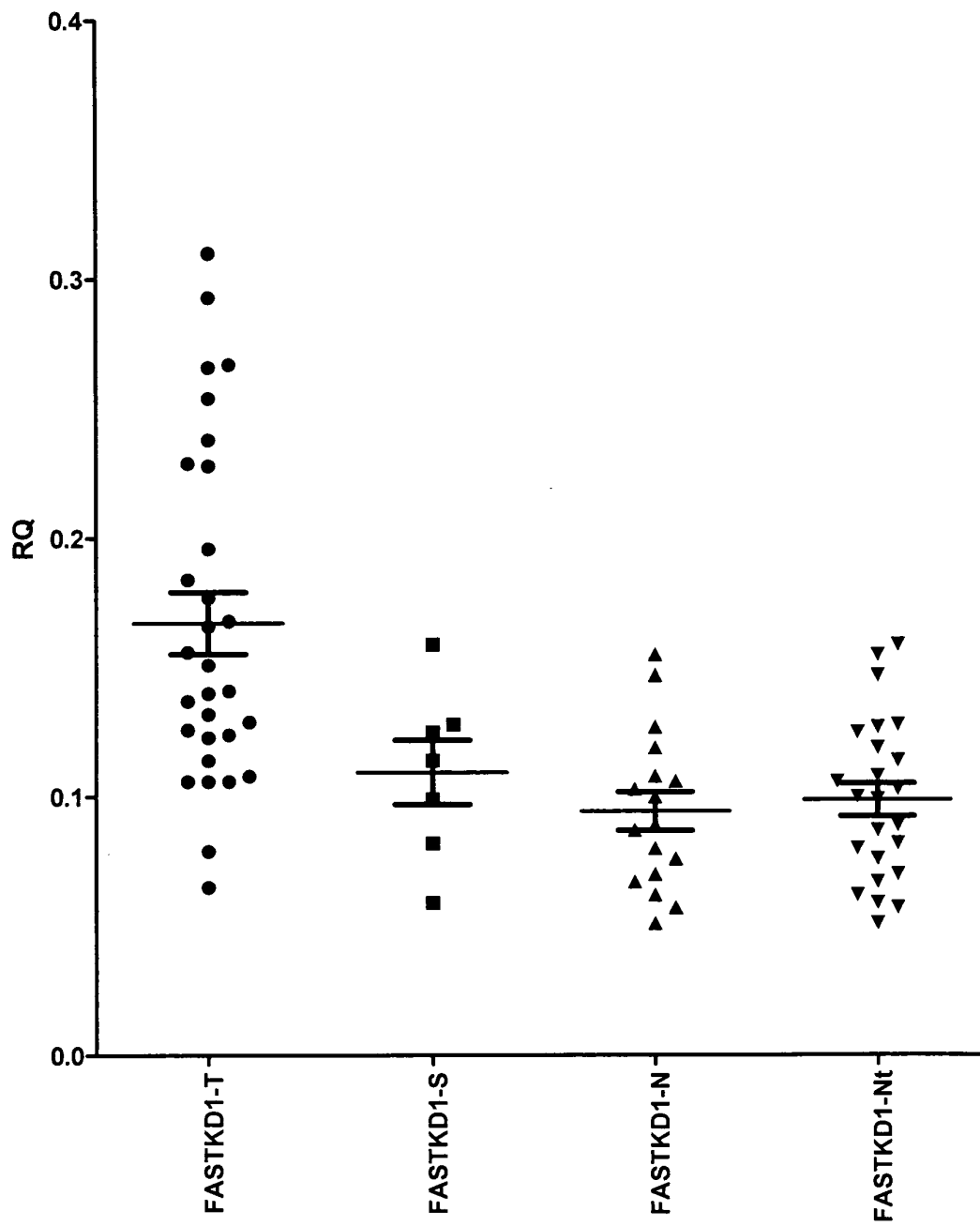
**FIG 6. FASTKD1**

FIG. 7 IKBKE

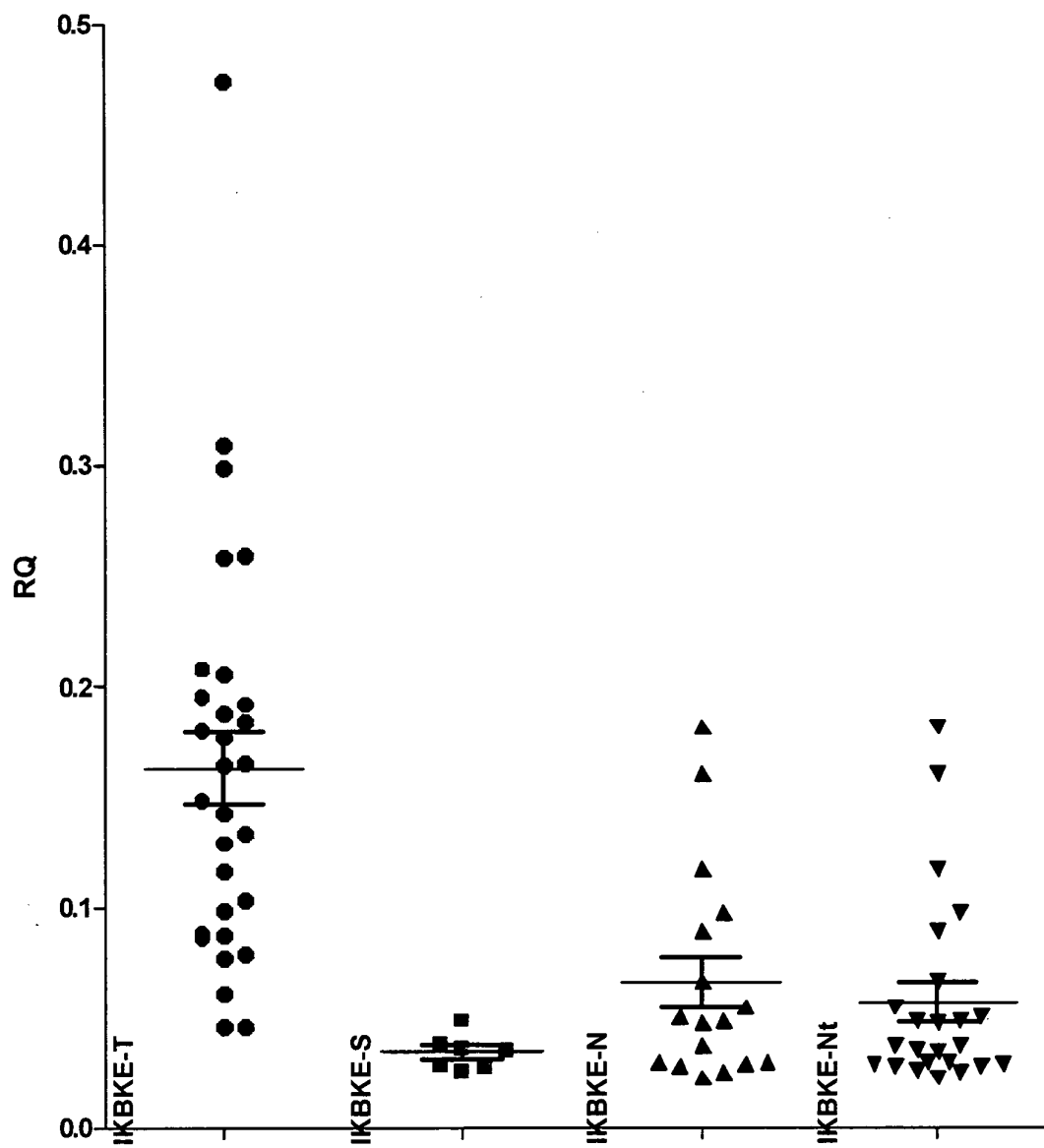


FIG 8. P4HB

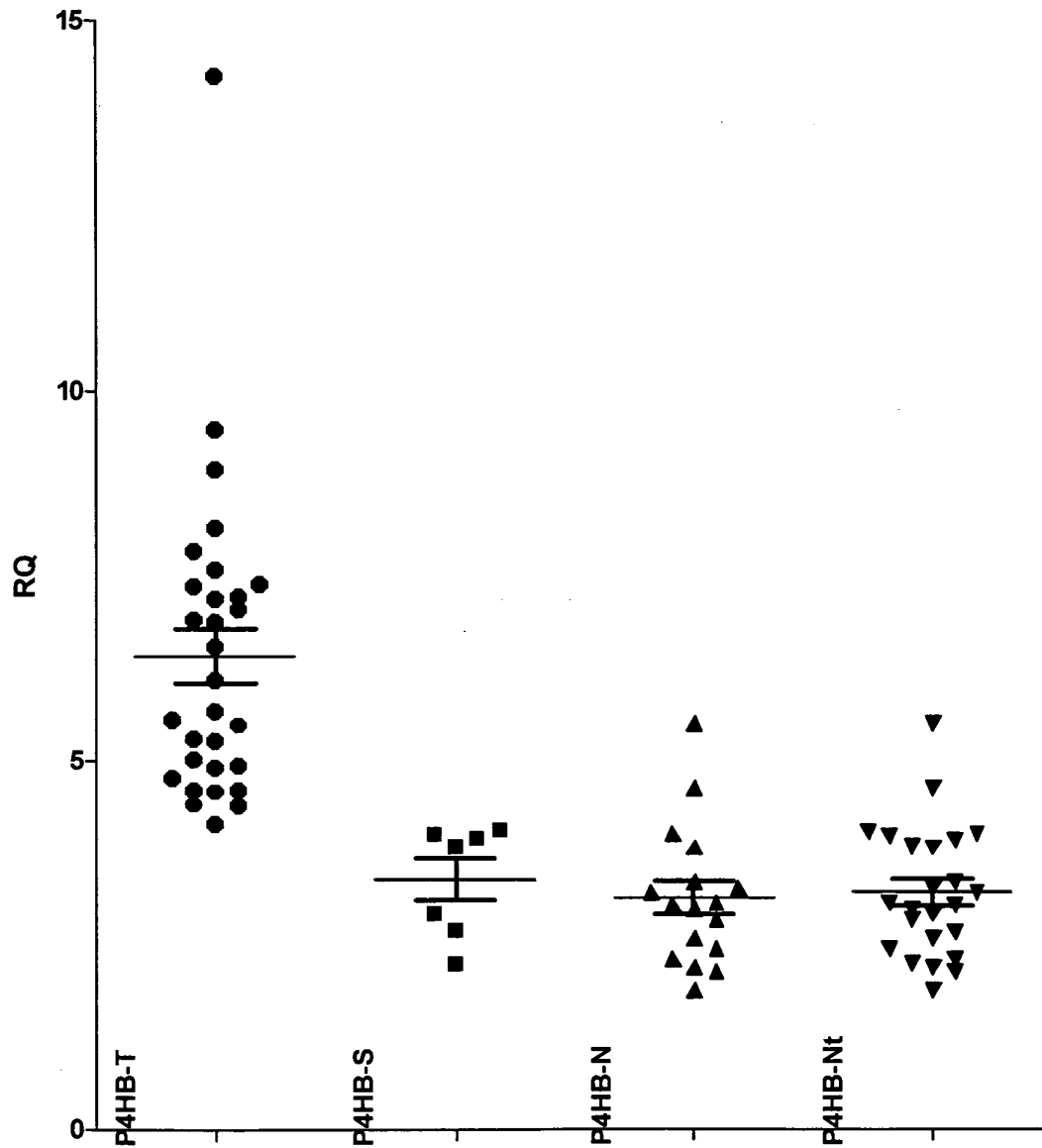


FIG. 9 SOCS2

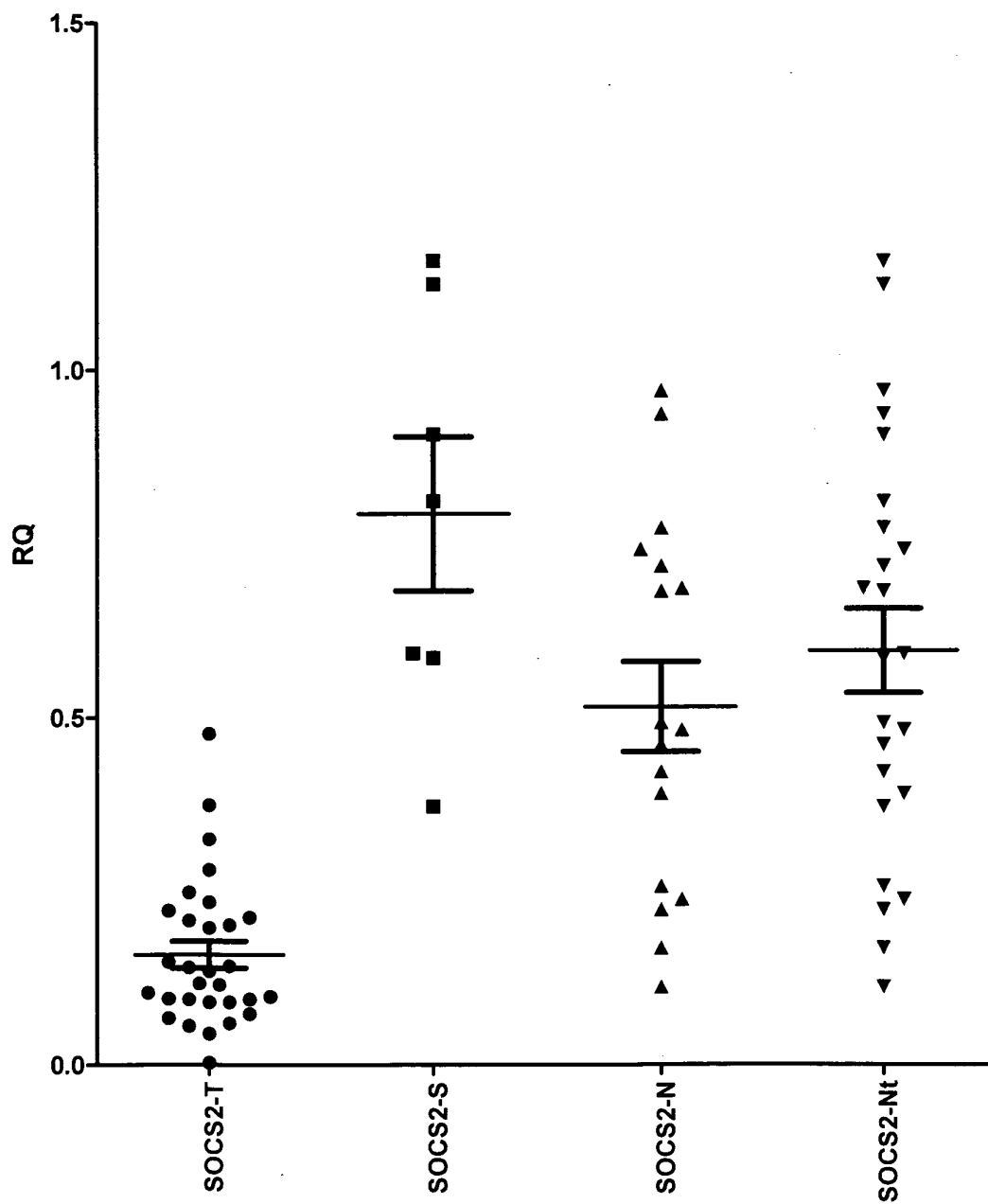


FIG. 10

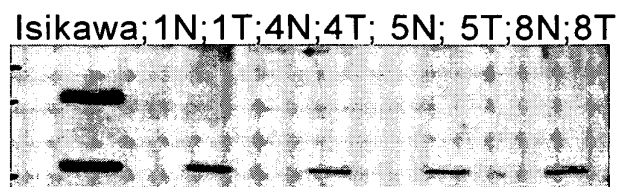


FIG. 11

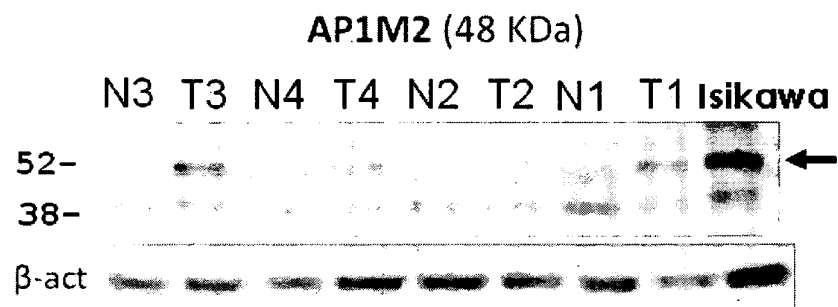


FIG. 12

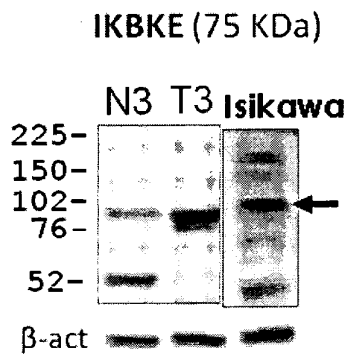


FIG. 13

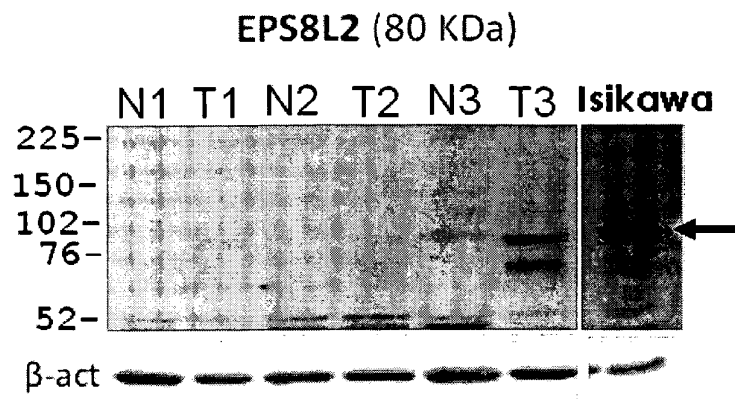


FIG. 14

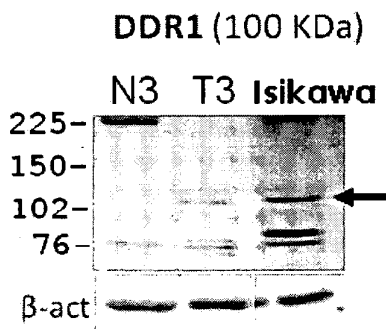


FIG. 15

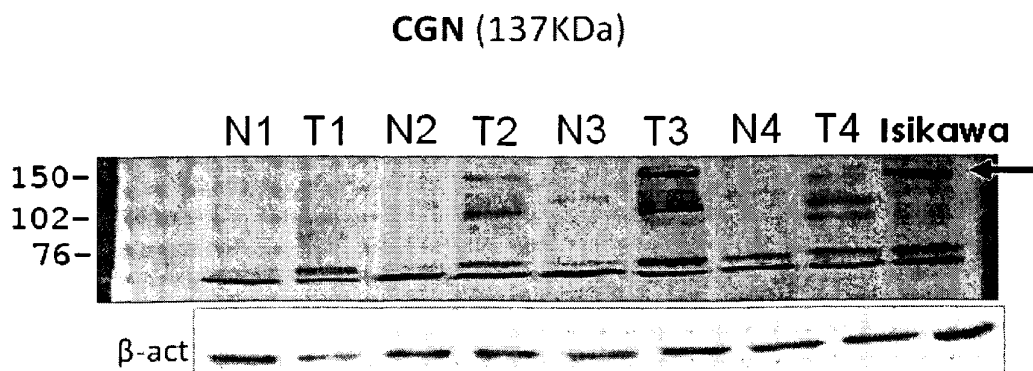


FIG. 16

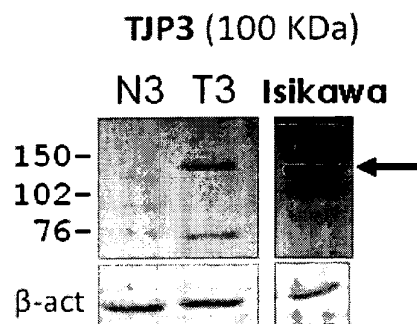


FIG. 17

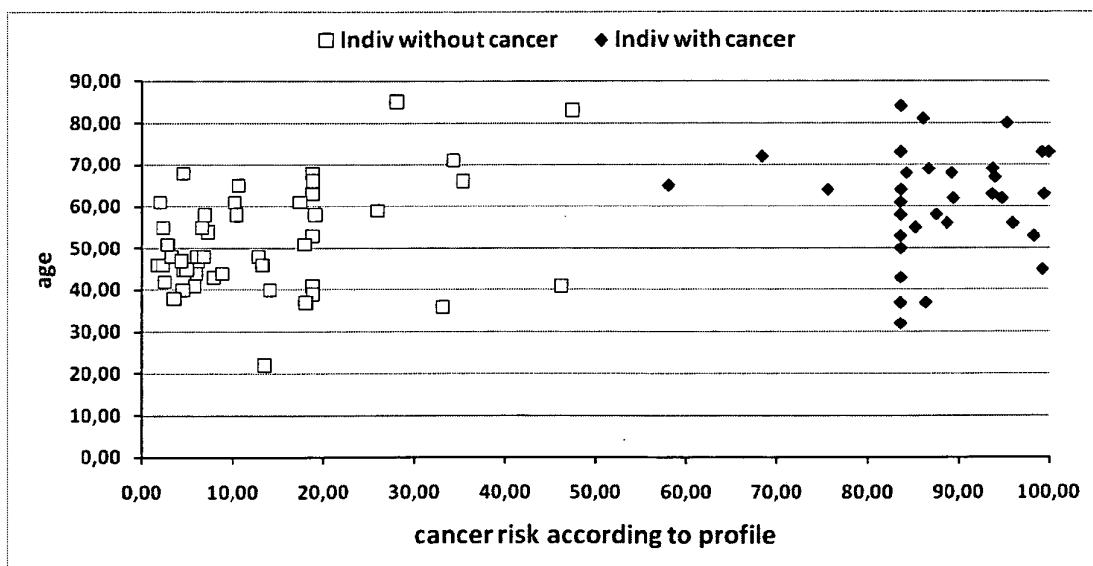


FIG. 18

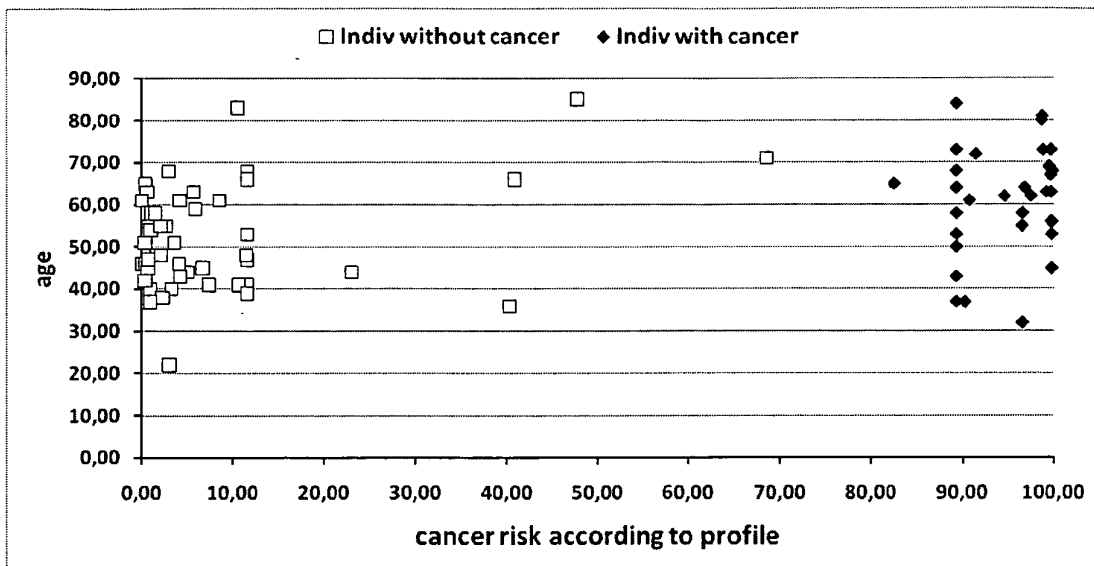
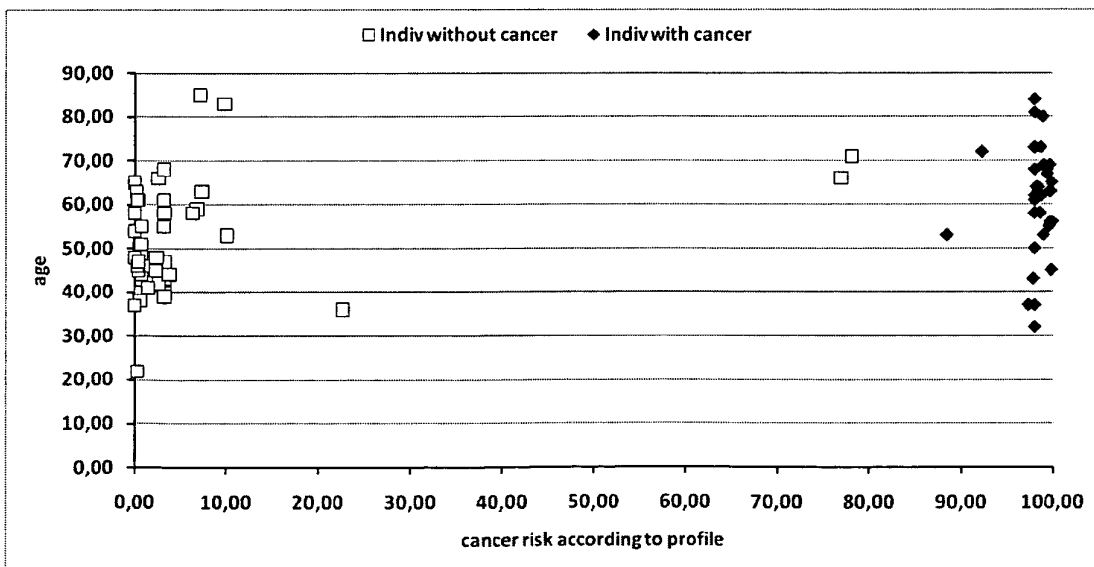


FIG. 19





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<150> EP 09 16 6398.9

<151> 2009-07-24

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35 40 45

Cys Arg Ala Gly Arg Gly Gly Phe Lys Asp Thr Thr Pro Asp Glu Leu  
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Leu Ser Ala Val Met Thr Ala Val Leu Lys Asp Val Asn Leu Arg Pro  
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Glu Gln Leu Gly Asp Ile Cys Val Gly Asn Val Leu Gln Pro Gly Ala  
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Thr Val Pro Leu Ser Thr Val Asn Arg Gln Cys Ser Ser Gly Leu Gln  
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Cys Leu Ile Pro Met Gly Ile Thr Ser Glu Asn Val Ala Glu Arg Phe  
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Pro Val Thr Thr Thr Val His Asp Asp Lys Gly Thr Lys Arg Ser Ile  
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340 345 350

Ala Tyr Cys Val Glu Lys Leu Arg Leu Pro Pro Glu Lys Val Asn Pro  
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Leu Gly Gly Ala Val Ala Leu Gly His Pro Leu Gly Cys Thr Gly Ala  
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Arg Gln Val Ile Thr Leu Leu Asn Glu Leu Lys Arg Arg Gly Lys Arg  
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<400> 41

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Phe Met Pro Leu Leu Val Gln Arg Glu Glu Glu Gly Ala Leu Ala Pro  
 35 40 45

Leu Leu Ser His Gly Gln Val His Phe Leu Trp Ile Lys His Ser Asn  
 50 55 60

Leu Tyr Leu Val Ala Thr Thr Ser Lys Asn Ala Asn Ala Ser Leu Val  
 65 70 75 80

Tyr Ser Phe Leu Tyr Lys Thr Ile Glu Val Phe Cys Glu Tyr Phe Lys  
85 90 95

Glu Leu Glu Glu Glu Ser Ile Arg Asp Asn Phe Val Ile Val Tyr Glu  
100 105 110

Leu Leu Asp Glu Leu Met Asp Phe Gly Phe Pro Gln Thr Thr Asp Ser  
115 120 125

Lys Ile Leu Gln Glu Tyr Ile Thr Gln Gln Ser Asn Lys Leu Glu Thr  
130 135 140

Gly Lys Ser Arg Val Pro Pro Thr Val Thr Asn Ala Val Ser Trp Arg  
145 150 155 160

Ser Glu Gly Ile Lys Tyr Lys Lys Asn Glu Val Phe Ile Asp Val Ile  
165 170 175

Glu Ser Val Asn Leu Leu Val Asn Ala Asn Gly Ser Val Leu Leu Ser  
180 185 190

Glu Ile Val Gly Thr Ile Lys Leu Lys Val Phe Leu Ser Gly Met Pro  
195 200 205

Glu Leu Arg Leu Gly Leu Asn Asp Arg Val Leu Phe Glu Leu Thr Gly  
210 215 220

Arg Ser Lys Asn Lys Ser Val Glu Leu Glu Asp Val Lys Phe His Gln  
225 230 235 240

Cys Val Arg Leu Ser Arg Phe Asp Asn Asp Arg Thr Ile Ser Phe Ile  
245 250 255

Pro Pro Asp Gly Asp Phe Glu Leu Met Ser Tyr Arg Leu Ser Thr Gln  
260 265 270

Val Lys Pro Leu Ile Trp Ile Glu Ser Val Ile Glu Lys Phe Ser His  
275 280 285

Ser Arg Val Glu Ile Met Val Lys Ala Lys Gly Gln Phe Lys Lys Gln  
290 295 300

Ser Val Ala Asn Gly Val Glu Ile Ser Val Pro Val Pro Ser Asp Ala  
305 310 315 320

Asp Ser Pro Arg Phe Lys Thr Ser Val Gly Ser Ala Lys Tyr Val Pro  
325 330 335

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340 345 350

Glu Tyr Leu Met Arg Ala His Phe Gly Leu Pro Ser Val Glu Lys Glu  
355 360 365

Glu Val Glu Gly Arg Pro Pro Ile Gly Val Lys Phe Glu Ile Pro Tyr  
370 375 380

Phe Thr Val Ser Gly Ile Gln Val Arg Tyr Met Lys Ile Ile Glu Lys  
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<400> 42  
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<210> 43  
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<220>  
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<400> 43  
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<210> 44  
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<220>  
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<400> 44  
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<210> 45  
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<212> DNA  
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<220>  
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<210> 46  
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<220>  
<221> Source  
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<400> 46  
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<210> 47  
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<210> 48  
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<210> 49  
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<212> DNA  
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<210> 54  
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<400> 55  
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<210> 56  
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<210> 57  
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<400> 57  
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<210> 58  
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<212> DNA  
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<400> 62  
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<210> 63  
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<210> 64  
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<220>  
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<212> DNA  
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|             |            |            |            |            |            |      |
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| agcaacagca  | tgctggagct | agccccgaaa | gtggcttccc | caggtagcac | cattgacact | 660  |
| gctccccgt   | cttcagtga  | ctcactcatc | aacaagtttg | acagtcaact | tggaggccag | 720  |
| gcccggggtc  | ggactggccg | ccgaacacgg | atgctacccc | ctgaacagcg | caaacggagc | 780  |
| aagagcctgg  | acagccgcct | cccacgggac | acctttgagg | aacgggagcg | ccagtccacc | 840  |
| aaccactgga  | cctctagcac | aaaatatgac | aaccatgtgg | gcacttcgaa | gcagccagcc | 900  |
| cagagccaga  | acctgagtcc | tctcagtggc | tttagccgtt | ctcgtcagac | tcaggactgg | 960  |
| gtccttcaga  | gttttgagga | gccgcggagg | agtgcacagg | acccaccat  | gctgcagttc | 1020 |
| aaatcaactc  | cagacctcct | tcgagaccag | caggaggcag | ccccaccagg | cagtgtggac | 1080 |
| catatgaagg  | ccaccatcta | tggcatcctg | agggagggaa | gctcagaaag | tgaaacctct | 1140 |
| gtgaggagga  | aggttagttt | ggtgctggag | aagatgcagc | ctctagtgat | ggtttcttct | 1200 |
| ggttctacta  | aggccgtggc | agggcagggg | gagcttacc  | gaaaagtgga | ggagctacag | 1260 |
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| gagcggcagc  | tggaggagaa | aacagaagag | tgcagccgac | tgcaggagct | gctggagagg | 1380 |
| aggaaggggg  | aggcccagca | gagcaacaag | gagctccaga | acatgaagcg | cctcttgagc | 1440 |
| caggggtgaag | atttacgaca | tgggctggag | accaggtga  | tggagctgca | gaacaagctg | 1500 |
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| cgggagcggg  | agttgacagc | cctgaagggg | gccctgaaag | aggaggtagc | ctcccgtgac | 1680 |
| caggaggtgg  | aacatgtccg | gcagcagtac | cagcgagaca | cagagcagct | ccgcaggagc | 1740 |
| atgcaagatg  | caaccagga  | ccatgcagtg | ctggaggccg | agaggcagaa | gatgtcagcc | 1800 |
| cttgtgcgag  | ggctgcagag | ggagctggag | gagacttcag | aggagacagg | gcattggcag | 1860 |
| agtatgttcc  | agaagaacaa | ggaggatctt | agagccacca | agcaggaact | cctgcagctg | 1920 |
| cgaatggaga  | aggaggagat | ggaagaggag | cttgagagaa | agatagaggt | cttgcagagg | 1980 |
| gaattagagc  | aggcccagc  | tagtgctgga | gatactcgcc | aggttgaggt | gctcaagaag | 2040 |
| gagctgctcc  | ggacacagga | ggagcttaag | gaactgcagg | cagaacggca | gagccaggag | 2100 |
| gtggctgggc  | gacaccggga | ccgggagttg | gagaagcagc | tggcggtcct | gagggtcgag | 2160 |
| gctgatcgag  | gtcgggagct | ggaagaacag | aacctccagc | tacaaaagac | cctccagcaa | 2220 |
| ctgcgacagg  | actgtgaaga | ggcttccaag | gctaagatgg | tggccgaggc | agaggcaaca | 2280 |
| gtgctggggc  | agcggcgggc | cgcagtggag | acgacgcttc | gggagacca  | ggaggaaaat | 2340 |
| gacgaattcc  | gccggcgcat | cctgggtttg | gagcagcagc | tgaaggagac | tcgaggtctg | 2400 |
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|                                                                    |      |
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| gagaaacagc agctggagga ggcctgaat gcgtcccagg aagaggaggg gagtctggca   | 2520 |
| gcagccaagc gggcactgga ggcacgccta gaggaggctc agcgggggct ggcccgcctg  | 2580 |
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| cgtgaggtgg aggagcagca tgaggtcaat gaacagctcc aggcccgat caagtctctg   | 3600 |
| gagaaggact cctggcgcaa agcttcccgc tcagctgctg agtcagctct caaaaacgaa  | 3660 |
| gggctgagct cagatgagga attcgacagt gtctacgac cctcgtccat tgcactctg    | 3720 |
| cttacggaga gcaacctaca gaccagctcc tgtagctcg tggtcctcaa ggactcagaa   | 3780 |
| accaggctcg aggcctatcc cagcaagtgc tgctctgctc tgcccaccct gggttctgca  | 3840 |
| ttcctatggg tgacccaatt attcagacct aagacagga ggggtcagag tgatggtgat   | 3900 |
| aaaaaaaaa aatcatcagc aataagctga tagatggact ttccactgta ggagtggaca   | 3960 |
| tttcaagcca actgagcctt ttctcaagt gccgacacct ccctcatctc tcttatagt    | 4020 |
| gaaggatggt cagcattagg ctgatgggga ctgagaagga taggaaggga tagaaattgc  | 4080 |
| catgtgtata aagctttatt ctttagccct taaccctaag gctcaggga ataccctatg   | 4140 |
| ttattgtgct ccctggattc ctgcaactca ttttccttc actctggagc agggtgaggg   | 4200 |
| gaatgttatg ggtaacagac atgcaggcat ggctctaccc atttctttgc acaagtatgg  | 4260 |
| ggcccatgtg gtagtcccca taccctcca gttcctatat tttgtcttc ttctttccc     | 4320 |
| ctctttgcca ttctacctt gcatttttcc tgtcagtgcc ttagccaagg caaggagata   | 4380 |

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 <213> Homo Sapiens

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20          25          30

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```

Gly Thr Leu Arg Arg Gly Gly Arg Arg Pro Ala Lys Asp Ala Arg Ala
35          40          45

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Ser Thr Tyr Gly Val Ala Val Arg Val Gln Gly Ile Ala Gly Gln Pro
50          55          60

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Phe Val Val Leu Asn Ser Gly Glu Lys Gly Gly Asp Ser Phe Gly Val
65          70          75          80

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```

Gln Ile Lys Gly Ala Asn Asp Gln Gly Ala Ser Gly Ala Leu Ser Ser
85          90          95

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```

Asp Leu Glu Leu Pro Glu Asn Pro Tyr Ser Gln Val Lys Gly Phe Pro
100          105          110

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115 120 125

Asn Gly Lys Leu Leu Arg Ser His Ser Gln Ala Ser Leu Ala Gly Pro  
130 135 140

Gly Pro Val Asp Pro Ser Asn Arg Ser Asn Ser Met Leu Glu Leu Ala  
145 150 155 160

Pro Lys Val Ala Ser Pro Gly Ser Thr Ile Asp Thr Ala Pro Leu Ser  
165 170 175

Ser Val Asp Ser Leu Ile Asn Lys Phe Asp Ser Gln Leu Gly Gly Gln  
180 185 190

Ala Arg Gly Arg Thr Gly Arg Arg Thr Arg Met Leu Pro Pro Glu Gln  
195 200 205

Arg Lys Arg Ser Lys Ser Leu Asp Ser Arg Leu Pro Arg Asp Thr Phe  
210 215 220

Glu Glu Arg Glu Arg Gln Ser Thr Asn His Trp Thr Ser Ser Thr Lys  
225 230 235 240

Tyr Asp Asn His Val Gly Thr Ser Lys Gln Pro Ala Gln Ser Gln Asn  
245 250 255

Leu Ser Pro Leu Ser Gly Phe Ser Arg Ser Arg Gln Thr Gln Asp Trp  
260 265 270

Val Leu Gln Ser Phe Glu Glu Pro Arg Arg Ser Ala Gln Asp Pro Thr  
275 280 285

Met Leu Gln Phe Lys Ser Thr Pro Asp Leu Leu Arg Asp Gln Gln Glu  
290 295 300

Ala Ala Pro Pro Gly Ser Val Asp His Met Lys Ala Thr Ile Tyr Gly  
305 310 315 320

Ile Leu Arg Glu Gly Ser Ser Glu Ser Glu Thr Ser Val Arg Arg Lys  
325 330 335

Val Ser Leu Val Leu Glu Lys Met Gln Pro Leu Val Met Val Ser Ser  
340 345 350

Gly Ser Thr Lys Ala Val Ala Gly Gln Gly Glu Leu Thr Arg Lys Val  
355 360 365



Glu Glu Leu Gln Arg Lys Leu Asp Glu Glu Val Lys Lys Arg Gln Lys  
370 375 380

Leu Glu Pro Ser Gln Val Gly Leu Glu Arg Gln Leu Glu Glu Lys Thr  
385 390 395 400

Glu Glu Cys Ser Arg Leu Gln Glu Leu Leu Glu Arg Arg Lys Gly Glu  
405 410 415

Ala Gln Gln Ser Asn Lys Glu Leu Gln Asn Met Lys Arg Leu Leu Asp  
420 425 430

Gln Gly Glu Asp Leu Arg His Gly Leu Glu Thr Gln Val Met Glu Leu  
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Gln Asn Lys Leu Lys His Val Gln Gly Pro Glu Pro Ala Lys Glu Val  
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Leu Thr Ala Leu Lys Gly Ala Leu Lys Glu Glu Val Ala Ser Arg Asp  
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Gln Glu Val Glu His Val Arg Gln Gln Tyr Gln Arg Asp Thr Glu Gln  
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Ala Glu Arg Gln Lys Met Ser Ala Leu Val Arg Gly Leu Gln Arg Glu  
545 550 555 560

Leu Glu Glu Thr Ser Glu Glu Thr Gly His Trp Gln Ser Met Phe Gln  
565 570 575

Lys Asn Lys Glu Asp Leu Arg Ala Thr Lys Gln Glu Leu Leu Gln Leu  
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Arg Met Glu Lys Glu Glu Met Glu Glu Glu Leu Gly Glu Lys Ile Glu  
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Val Leu Gln Arg Glu Leu Glu Gln Ala Arg Ala Ser Ala Gly Asp Thr  
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Arg Gln Val Glu Val Leu Lys Lys Glu Leu Leu Arg Thr Gln Glu Glu  
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Leu Lys Glu Leu Gln Ala Glu Arg Gln Ser Gln Glu Val Ala Gly Arg  
645 650 655

His Arg Asp Arg Glu Leu Glu Lys Gln Leu Ala Val Leu Arg Val Glu  
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Ala Asp Arg Gly Arg Glu Leu Glu Glu Gln Asn Leu Gln Leu Gln Lys  
675 680 685

Thr Leu Gln Gln Leu Arg Gln Asp Cys Glu Glu Ala Ser Lys Ala Lys  
690 695 700

Met Val Ala Glu Ala Glu Ala Thr Val Leu Gly Gln Arg Arg Ala Ala  
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Val Glu Thr Thr Leu Arg Glu Thr Gln Glu Glu Asn Asp Glu Phe Arg  
725 730 735

Arg Arg Ile Leu Gly Leu Glu Gln Gln Leu Lys Glu Thr Arg Gly Leu  
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Val Asp Gly Gly Glu Ala Val Glu Ala Arg Leu Arg Asp Lys Leu Gln  
755 760 765

Arg Leu Glu Ala Glu Lys Gln Gln Leu Glu Glu Ala Leu Asn Ala Ser  
770 775 780

Gln Glu Glu Glu Gly Ser Leu Ala Ala Ala Lys Arg Ala Leu Glu Ala  
785 790 795 800

Arg Leu Glu Glu Ala Gln Arg Gly Leu Ala Arg Leu Gly Gln Glu Gln  
805 810 815

Gln Thr Leu Asn Arg Ala Leu Glu Glu Glu Gly Lys Gln Arg Glu Val  
820 825 830

Leu Arg Arg Gly Lys Ala Glu Leu Glu Glu Gln Lys Arg Leu Leu Asp  
835 840 845

Arg Thr Val Asp Arg Leu Asn Lys Glu Leu Glu Lys Ile Gly Glu Asp  
850 855 860

Ser Lys Gln Ala Leu Gln Gln Leu Gln Ala Gln Leu Glu Asp Tyr Lys

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| 865                                                             | 870  | 875  | 880  |
| Glu Lys Ala Arg Arg Glu Val Ala Asp Ala Gln Arg Gln Ala Lys Asp | 885  | 890  | 895  |
| Trp Ala Ser Glu Ala Glu Lys Thr Ser Gly Gly Leu Ser Arg Leu Gln | 900  | 905  | 910  |
| Asp Glu Ile Gln Arg Leu Arg Gln Ala Leu Gln Ala Ser Gln Ala Glu | 915  | 920  | 925  |
| Arg Asp Thr Ala Arg Leu Asp Lys Glu Leu Leu Ala Gln Arg Leu Gln | 930  | 935  | 940  |
| Gly Leu Glu Gln Glu Ala Glu Asn Lys Lys Arg Ser Gln Asp Asp Arg | 945  | 950  | 955  |
| Ala Arg Gln Leu Lys Gly Leu Glu Glu Lys Val Ser Arg Leu Glu Thr | 965  | 970  | 975  |
| Glu Leu Asp Glu Glu Lys Asn Thr Val Glu Leu Leu Thr Asp Arg Val | 980  | 985  | 990  |
| Asn Arg Gly Arg Asp Gln Val Asp Gln Leu Arg Thr Glu Leu Met Gln | 995  | 1000 | 1005 |
| Glu Arg Ser Ala Arg Gln Asp Leu Glu Cys Asp Lys Ile Ser Leu     | 1010 | 1015 | 1020 |
| Glu Arg Gln Asn Lys Asp Leu Lys Thr Arg Leu Ala Ser Ser Glu     | 1025 | 1030 | 1035 |
| Gly Phe Gln Lys Pro Ser Ala Ser Leu Ser Gln Leu Glu Ser Gln     | 1040 | 1045 | 1050 |
| Asn Gln Leu Leu Gln Glu Arg Leu Gln Ala Glu Glu Arg Glu Lys     | 1055 | 1060 | 1065 |
| Thr Val Leu Gln Ser Thr Asn Arg Lys Leu Glu Arg Lys Val Lys     | 1070 | 1075 | 1080 |
| Glu Leu Ser Ile Gln Ile Glu Asp Glu Arg Gln His Val Asn Asp     | 1085 | 1090 | 1095 |
| Gln Lys Asp Gln Leu Ser Leu Arg Val Lys Ala Leu Lys Arg Gln     | 1100 | 1105 | 1110 |

Val Asp Glu Ala Glu Glu Glu Ile Glu Arg Leu Asp Gly Leu Arg  
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Lys Lys Ala Gln Arg Glu Val Glu Glu Gln His Glu Val Asn Glu  
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Gln Leu Gln Ala Arg Ile Lys Ser Leu Glu Lys Asp Ser Trp Arg  
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Lys Ala Ser Arg Ser Ala Ala Glu Ser Ala Leu Lys Asn Glu Gly  
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<210> 68  
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| ccattatgcc gaggctgaca ttgttaccct gcagggcgct accgggggca acacctatcc  | 1980 |
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Val Ala Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly Leu Gly Lys  
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Ala Thr Leu Asn Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu  
725 730 735

Val Gly Glu Asn Phe Thr Ile Lys Ile Ala Asp Phe Gly Met Ser Arg  
740 745 750

Asn Leu Tyr Ala Gly Asp Tyr Tyr Arg Val Gln Gly Arg Ala Val Leu  
755 760 765

Pro Ile Arg Trp Met Ala Trp Glu Cys Ile Leu Met Gly Lys Phe Thr  
770 775 780

Thr Ala Ser Asp Val Trp Ala Phe Gly Val Thr Leu Trp Glu Val Leu

785 790 795 800

Met Leu Cys Arg Ala Gln Pro Phe Gly Gln Leu Thr Asp Glu Gln Val  
805 810 815

Ile Glu Asn Ala Gly Glu Phe Phe Arg Asp Gln Gly Arg Gln Val Tyr  
820 825 830

Leu Ser Arg Pro Pro Ala Cys Pro Gln Gly Leu Tyr Glu Leu Met Leu  
835 840 845

Arg Cys Trp Ser Arg Glu Ser Glu Gln Arg Pro Pro Phe Ser Gln Leu  
850 855 860

His Arg Phe Leu Ala Glu Asp Ala Leu Asn Thr Val  
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<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 94  
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<210> 115  
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<400> 115  
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<210> 116  
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<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding DDR1 protein"

<400> 116  
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<210> 117  
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<213> Artificial Sequence

<220>  
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<210> 118  
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<210> 119  
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<210> 124

<211> 60

<212> DNA

<213> Artificial Sequence

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<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding DDR1 protein"

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<211> 3156

<212> DNA

<213> Homo Sapiens

<400> 125

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gagcgtccca cccgcccgcg ggagacctgg cgccccggcc gaggcgcgaa cagacggacg

120

caccggcgag cgccgagggg acaggccgag cgcgggggcg cggaggcagg tgtgggacag

180

gcaactggcct cagaccgggg ccacactgag gtctgccctt ctcccgctgg ccgccaccca

240

agacaccatg agccagtccg gggccgtgag ctgctgcccg ggtgccacca atggcagcct

300

gggcccgtcc gacgggtgtg ccaagatgag cccaaggac ctgtttgagc agaggaagaa

360

gtattccaac tccaacgtca tcatgcacga gacctcgag taccacgtcc agcacctggc

420

cacattcatc atggacaaga gcgaagccat cacgtctgtg gacgacgcca tccggaagct

480

ggtgcagctg agctccaagg agaagatctg gaccaggag atgctgctgc aggtgaacga

540

ccagtcgctg cggtgctg acatcgagtc acaggaggag ctggaagact tcccgtgccc

600

cacggtgcag cgcagccaga cggtcctcaa ccagctgcgc taccgctctg tgctgctgct

660

cgtgtgccag gactcggagc agagcaagcc ggatgtccac ttcttccact gcgatgaggt

720

ggaggcagag ctggtgcacg aggacatcga gagcgcgttg gccgactgcc ggctgggcaa

780

gaagatgcgg ccgcagaccc tgaagggaca ccaggagaag attcggcagc ggcagtcct

840

cctgcctcct ccccagggcc cggcgcccat ccccttcag caccgcggcg gggattcccc

900

|                                                                   |      |
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| ggagtcgcag gaggagccgc gggccgtgct ggctcagaag atagagaagg agacgcaa   | 1020 |
| cctcaactgc gccctggacg acatcgagtg gtttgtggcc cggctgcaga aggcagccga | 1080 |
| ggctttcaag cagctgaacc agcggaaaaa ggggaagaag aagggaaga aggcgccagc  | 1140 |
| agagggcgtc ctacactgc gggcacggcc cccctctgag ggcgagttca tcgactgctt  | 1200 |
| ccagaaaatc aagctggcga ttaacttgct ggcaaagctg cagaagcaca tccagaaccc | 1260 |
| cagcgccgcg gagctcgtgc acttcctctt cgggcctctg gacctgatcg tcaacacctg | 1320 |
| cagtggccca gacatcgcac gctccgtctc ctgccactg ctctcccgag atgccgtgga  | 1380 |
| cttctcgcg ggcacactgg tccctaagga gatgtcgtg tgggagtcac tgggagagag   | 1440 |
| ctggatgcgg ccccgttccg agtggccgcg ggagccacag gtgcccctct acgtgccaa  | 1500 |
| gttccacagc ggctgggagc ctctgtgga tgtgtgcag gaggccccct gggaggtgga   | 1560 |
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| ctcccagaag cacagccccca cttcagagcc ccccccccg ggggatgcc taccaccagt  | 1680 |
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| cctagagggt ctggaggacg gccggcagtg gtggaagctg cgcagccgca gcggccaggc | 1860 |
| ggggtacgtg cctgcaaca tcctaggcga ggcgcgaccg gaggacgccg gcgcccgtt   | 1920 |
| cgagcaggcc ggtcagaagt actggggccc cgccagcccg acccacaagc taccccaag  | 1980 |
| cttcccgggg aacaaagacg agctcatgca gcacatggac gaggtaacg acgagctcat  | 2040 |
| ccggaaaatc agcaacatca gggcgcagcc acagaggcac ttccgcgtgg agcgcagcca | 2100 |
| gcccgtgagc cagccgctca cctacgagtc gggtcggac gaggtcgcg cctggctgga   | 2160 |
| agccaaggcc ttcagccgc ggatcgtgga gaacctgggc atcctgaccg ggccgcagct  | 2220 |
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| cagccagctc accatgcaga aggccttcct ggagaagcag caaagtgggt cggagctgga | 2340 |
| agaactcatg aacaagtttc attccatgaa tcagaggagg ggggaggaca gctaggccca | 2400 |
| gctgccttgg gctggggcct gcggagggga agcccacca caatgcatgg agtattattt  | 2460 |
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| cccacaccaa gactaatctc agccaaacct gctgcttggg ggtgccagcc ccttgtccac | 2640 |
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gttctgctcc ctgagggggg cccgggaggg gctccagcag gaggccgtgg gtgccattcg 2880  
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Phe Glu Gln Arg Lys Lys Tyr Ser Asn Ser Asn Val Ile Met His Glu  
 35 40 45

Thr Ser Gln Tyr His Val Gln His Leu Ala Thr Phe Ile Met Asp Lys  
 50 55 60

Ser Glu Ala Ile Thr Ser Val Asp Asp Ala Ile Arg Lys Leu Val Gln  
 65 70 75 80

Leu Ser Ser Lys Glu Lys Ile Trp Thr Gln Glu Met Leu Leu Gln Val  
 85 90 95

Asn Asp Gln Ser Leu Arg Leu Leu Asp Ile Glu Ser Gln Glu Glu Leu  
 100 105 110

Glu Asp Phe Pro Leu Pro Thr Val Gln Arg Ser Gln Thr Val Leu Asn  
 115 120 125

Gln Leu Arg Tyr Pro Ser Val Leu Leu Leu Val Cys Gln Asp Ser Glu  
 130 135 140

Gln Ser Lys Pro Asp Val His Phe Phe His Cys Asp Glu Val Glu Ala  
 145 150 155 160

Glu Leu Val His Glu Asp Ile Glu Ser Ala Leu Ala Asp Cys Arg Leu  
 165 170 175

Gly Lys Lys Met Arg Pro Gln Thr Leu Lys Gly His Gln Glu Lys Ile  
180 185 190

Arg Gln Arg Gln Ser Ile Leu Pro Pro Pro Gln Gly Pro Ala Pro Ile  
195 200 205

Pro Phe Gln His Arg Gly Gly Asp Ser Pro Glu Ala Lys Asn Arg Val  
210 215 220

Gly Pro Gln Val Pro Leu Ser Glu Pro Gly Phe Arg Arg Arg Glu Ser  
225 230 235 240

Gln Glu Glu Pro Arg Ala Val Leu Ala Gln Lys Ile Glu Lys Glu Thr  
245 250 255

Gln Ile Leu Asn Cys Ala Leu Asp Asp Ile Glu Trp Phe Val Ala Arg  
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Leu Gln Lys Ala Ala Glu Ala Phe Lys Gln Leu Asn Gln Arg Lys Lys  
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Gly Lys Lys Lys Gly Lys Lys Ala Pro Ala Glu Gly Val Leu Thr Leu  
290 295 300

Arg Ala Arg Pro Pro Ser Glu Gly Glu Phe Ile Asp Cys Phe Gln Lys  
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Ile Lys Leu Ala Ile Asn Leu Leu Ala Lys Leu Gln Lys His Ile Gln  
325 330 335

Asn Pro Ser Ala Ala Glu Leu Val His Phe Leu Phe Gly Pro Leu Asp  
340 345 350

Leu Ile Val Asn Thr Cys Ser Gly Pro Asp Ile Ala Arg Ser Val Ser  
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Cys Pro Leu Leu Ser Arg Asp Ala Val Asp Phe Leu Arg Gly His Leu  
370 375 380

Val Pro Lys Glu Met Ser Leu Trp Glu Ser Leu Gly Glu Ser Trp Met  
385 390 395 400

Arg Pro Arg Ser Glu Trp Pro Arg Glu Pro Gln Val Pro Leu Tyr Val  
405 410 415

Pro Lys Phe His Ser Gly Trp Glu Pro Pro Val Asp Val Leu Gln Glu

|                                                                 |     |         |
|-----------------------------------------------------------------|-----|---------|
| 420                                                             | 425 | 430     |
| Ala Pro Trp Glu Val Glu Gly Leu Ala Ser Ala Pro Ile Glu Glu Val |     |         |
| 435                                                             | 440 | 445     |
| Ser Pro Val Ser Arg Gln Ser Ile Arg Asn Ser Gln Lys His Ser Pro |     |         |
| 450                                                             | 455 | 460     |
| Thr Ser Glu Pro Thr Pro Pro Gly Asp Ala Leu Pro Pro Val Ser Ser |     |         |
| 465                                                             | 470 | 475 480 |
| Pro His Thr His Arg Gly Tyr Gln Pro Thr Pro Ala Met Ala Lys Tyr |     |         |
|                                                                 | 485 | 490 495 |
| Val Lys Ile Leu Tyr Asp Phe Thr Ala Arg Asn Ala Asn Glu Leu Ser |     |         |
|                                                                 | 500 | 505 510 |
| Val Leu Lys Asp Glu Val Leu Glu Val Leu Glu Asp Gly Arg Gln Trp |     |         |
|                                                                 | 515 | 520 525 |
| Trp Lys Leu Arg Ser Arg Ser Gly Gln Ala Gly Tyr Val Pro Cys Asn |     |         |
|                                                                 | 530 | 535 540 |
| Ile Leu Gly Glu Ala Arg Pro Glu Asp Ala Gly Ala Pro Phe Glu Gln |     |         |
| 545                                                             | 550 | 555 560 |
| Ala Gly Gln Lys Tyr Trp Gly Pro Ala Ser Pro Thr His Lys Leu Pro |     |         |
|                                                                 | 565 | 570 575 |
| Pro Ser Phe Pro Gly Asn Lys Asp Glu Leu Met Gln His Met Asp Glu |     |         |
|                                                                 | 580 | 585 590 |
| Val Asn Asp Glu Leu Ile Arg Lys Ile Ser Asn Ile Arg Ala Gln Pro |     |         |
|                                                                 | 595 | 600 605 |
| Gln Arg His Phe Arg Val Glu Arg Ser Gln Pro Val Ser Gln Pro Leu |     |         |
|                                                                 | 610 | 615 620 |
| Thr Tyr Glu Ser Gly Pro Asp Glu Val Arg Ala Trp Leu Glu Ala Lys |     |         |
| 625                                                             | 630 | 635 640 |
| Ala Phe Ser Pro Arg Ile Val Glu Asn Leu Gly Ile Leu Thr Gly Pro |     |         |
|                                                                 | 645 | 650 655 |
| Gln Leu Phe Ser Leu Asn Lys Glu Glu Leu Lys Lys Val Cys Gly Glu |     |         |
|                                                                 | 660 | 665 670 |

Glu Gly Val Arg Val Tyr Ser Gln Leu Thr Met Gln Lys Ala Phe Leu  
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Glu Lys Gln Gln Ser Gly Ser Glu Leu Glu Glu Leu Met Asn Lys Phe  
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His Ser Met Asn Gln Arg Arg Gly Glu Asp Ser  
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<400> 130  
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<400> 131  
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<210> 132  
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 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding EPS8L2 protein"

<400> 139  
gaggccaaga atcgcggtggg c 21

<210> 140  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding EPS8L2 protein"

<400> 140  
gtccagggcg cagttgagg 19

<210> 141  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding EPS8L2 protein"

<400> 141  
cgactgcttc cagaaaatc 19

<210> 142  
<211> 19  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding EPS8L2 protein"

<400> 142  
cgaagaggaa gtgcacgag 19

<210> 143  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding EPS8L2 protein"

<400> 143  
gatgtcgctg tgggagtcac 20

<210> 144  
<211> 18

<212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 144  
 gaggggcacc tgtggctc 18  
  
 <210> 145  
 <211> 18  
 <212> DNA  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 145  
 ggtggagggg ctggcgctc 18  
  
 <210> 146  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 146  
 ggctctgaag tggggctgtg 20  
  
 <210> 147  
 <211> 60  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 EPS8L2 protein"  
  
 <400> 147  
 gcttcccggg gaacaaagac gagctcatgc agcacatgga cgagggtcaac gacgagctca 60  
  
 <210> 148  
 <211> 48  
 <212> DNA  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a



nucleotide molecule having a nucleic acid sequence encoding  
EPS8L2 protein"

<400> 148  
gcagagctgg tgcacgagga catcgagagc gcgttgccg actgccgg 48

<210> 149  
<211> 51  
<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a  
nucleotide molecule having a nucleic acid sequence encoding  
EPS8L2 protein"

<400> 149  
gccgtcggga gtcgcaggag gagccgcggg ccgtgctggc tcagaagata g 51

<210> 150  
<211> 43  
<212> DNA  
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<220>  
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nucleotide molecule having a nucleic acid sequence encoding  
EPS8L2 protein"

<400> 150  
gctcgtgtgc caggactcgg agcagagcaa gccgatgtc cac 43

<210> 151  
<211> 48  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a  
nucleotide molecule having a nucleic acid sequence encoding  
EPS8L2 protein"

<400> 151  
gtacagccag ctcacatgc agaaggcctt cctggagaag cagcaaag 48

<210> 152  
<211> 2767  
<212> DNA  
<213> Homo Sapiens

<400> 152  
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accaggaata accctgactt ctgagctttc ataaccacag gatcctccag aaaatttgcg 120  
gcgcgctgag ggaaaacctt gctgaagctg tacattggaa tgcgtttaca gtcattgtaa 180

|                                                                     |      |
|---------------------------------------------------------------------|------|
| tggaagcaaa atacatgaag gaaaaactgt tatttgtatc cctgcttatt gcacctgacg   | 240  |
| actagttgca gatggttttg tttacctaag aaaacttgtg atataaatga aaaaaacacc   | 300  |
| tgttttccta gagtcattgg ttacaaatat gcttcgtcta agagctatth gtccattctc   | 360  |
| ctggagagtg tttcaatttc gacccatcag ttgtgaacca ctaattattc agatgaataa   | 420  |
| gtgtacagat gaggagcaaa tgtttggttt tattgaaaga aacaaagcca tactttcaga   | 480  |
| aaagcaagtg ggatgtgcat ttgatatgct ttggaagctt caaaagcaga agaccagcct   | 540  |
| gttaaaaaat gctgagtatg tcagagacca tcctcaatth cttactcttc ataatttagc   | 600  |
| tacaaataaa ttcaaattaa tgaatgacga taccctgggtg aatgtgttat acgtcacaca  | 660  |
| acagtttgct ggtgaggccc atgacccgct agttgaagca ctagttacag aagcatggag   | 720  |
| aaggctagaa aggtttgata ttaaactgct ctcagaatth tcctcttgcc tagcagatca   | 780  |
| gcatttgtat tttagtccat taatgggaaa aatagctgat attgttcata ggaacttgga   | 840  |
| aaccacacag gacttaagtt ccttgtctgt cttgatggtc aacatatctt ctttaatatc   | 900  |
| acgacattth caacaacaac tggatgaacaa aacagaactt ctttttgaca ccatagattc  | 960  |
| ttctgaggtc aacgttgcaa aaagcatagc aaagtttctt cgaaatgtta gatatcgtha   | 1020 |
| tcaaccacta ttagaaaagat gtaataacgt atthtttaagt aatgtggacc accttgattt | 1080 |
| ggattccatc agtaaaatac ttagtgtata caaatttcta caatttaata gttttgaatt   | 1140 |
| tattataatg gctaaaaaga agctaactga aatgattcct ctgtgtaatc atcctgctag   | 1200 |
| ctttgtaaaa ttgtttgtag cattgggacc cattgcagga cctgaagaaa agaaacaact   | 1260 |
| taaatcaact atgttattga tgtcagagga cctaactggc gagcaagccc tggcagtggt   | 1320 |
| gggagcaatg ggagatatgg aaagcagaaa ctcatgtctg attaaaagag ttacttcagt   | 1380 |
| tctgcataaa catttggtatg gctataaacc attagagttg ttgaagataa ctcaagaatt  | 1440 |
| aacttttctg cattttccaaa ggaaggagtt ttttgcgaaa cttagagaat tactgcttag  | 1500 |
| ttatttgaaa aatagtttca taccaactga ggtgtctgtt ctggtccgtg ctatttccct   | 1560 |
| gctcccttct cctcacttgg acgaagtggg gatatcccga attgaagccg ttttaccaca   | 1620 |
| gtgtgaccta aataacctga gtagttttgc cacatctgtt ttaagatgga ttcagcatga   | 1680 |
| tcacatgtat ttggataata tgactgcgaa acaactgaaa ctacttcaaa aattagatca   | 1740 |
| ctatggctgt cagagactac aacacagcaa cagtttggat ctgttacgga aggaacttaa   | 1800 |
| atctctcaaa ggaaacacgt ttcttgagtc acttcttgaa gaaatgattg ctactttaca   | 1860 |
| gcatttcatg gatgatatta attacataaa tgttggggag attgcatctt ttatttctag   | 1920 |
| tactgattac ctcagtactt tgctactaga taggatagcc tcagtggctg ttcagcagat   | 1980 |
| tgaaaagatc catcctthta caatccctgc tattattcgt ccattcagcg tattgaacta   | 2040 |

|                                                                      |      |
|----------------------------------------------------------------------|------|
| tgatccacct caaagggatg aatTTTTTggg aacttgcgtg caacatctta attcttactt   | 2100 |
| aggtatatattg gatcctTTTta tattagtgtt tcttggTTTt tctttggcca cacttgaata | 2160 |
| ttttccagaa gatctgctaa aggcaatttt taacatcaaa ttcttagcta gattggattc    | 2220 |
| tcaacttgaa agtattggtg gcatggatgg aacacaacag cagattTTTta aaatgttagc   | 2280 |
| agaggtacta ggaggaatca attgtgtaaa agcctcggtt cttacgcctt attaccacaa    | 2340 |
| agtagatttt gagtgtatct tggataaaaag aaaaaaacct cttccgtatg gaagccataa   | 2400 |
| tatagcattg ggacaactac cagaaatgcc ctgggaatca aatatcgaaa tagttggatc    | 2460 |
| aaggctgcca ccaggggctg aaaggattgc tttggaattt ttggattcaa aagcactttg    | 2520 |
| tagaaatata cctcacatga aaggaaaaatc tgctatgaaa aaacgacatt tggaaattct   | 2580 |
| ggggtatcgt gtaattcaga tttcccagtt tgaatggaac tctatggcac tgtcaacaaa    | 2640 |
| ggatgctcgg atggactacc tgagagaatg tatatttggga gaagtcaagt catgtttgta   | 2700 |
| gtttttattt aaaatgaatg ttatcgtgtg ttacatttgg acctatttta ataaagtggc    | 2760 |
| ctgtctc                                                              | 2767 |

<210> 153  
 <211> 804  
 <212> PRT  
 <213> Homo Sapiens

<400> 153

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Lys | Lys | Thr | Pro | Val | Phe | Leu | Glu | Ser | Leu | Val | Thr | Asn | Met | Leu |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Leu | Arg | Ala | Ile | Cys | Pro | Phe | Ser | Trp | Arg | Val | Phe | Gln | Phe | Arg |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Ile | Ser | Cys | Glu | Pro | Leu | Ile | Ile | Gln | Met | Asn | Lys | Cys | Thr | Asp |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Glu | Gln | Met | Phe | Gly | Phe | Ile | Glu | Arg | Asn | Lys | Ala | Ile | Leu | Ser |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Lys | Gln | Val | Gly | Cys | Ala | Phe | Asp | Met | Leu | Trp | Lys | Leu | Gln | Lys |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Lys | Thr | Ser | Leu | Leu | Lys | Asn | Ala | Glu | Tyr | Val | Arg | Asp | His | Pro |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Phe | Leu | Thr | Leu | His | Asn | Leu | Ala | Thr | Asn | Lys | Phe | Lys | Leu | Met |
|     |     |     |     | 100 |     |     |     | 105 |     |     |     |     | 110 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asn | Asp | Asp | Thr | Leu | Val | Asn | Val | Leu | Tyr | Val | Thr | Gln | Gln | Phe | Ala |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

| 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Glu | Ala | His | Asp | Pro | Leu | Val | Glu | Ala | Leu | Val | Thr | Glu | Ala | Trp |
| 130 |     |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Arg | Arg | Leu | Glu | Arg | Phe | Asp | Ile | Lys | Leu | Leu | Ser | Glu | Phe | Ser | Ser |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Cys | Leu | Ala | Asp | Gln | His | Leu | Tyr | Phe | Ser | Pro | Leu | Met | Gly | Lys | Ile |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Ala | Asp | Ile | Val | His | Arg | Asn | Leu | Glu | Thr | Thr | Gln | Asp | Leu | Ser | Ser |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Leu | Ser | Val | Leu | Met | Val | Asn | Ile | Ser | Ser | Leu | Ile | Ser | Arg | His | Phe |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     |     | 205 |     |     |
| Gln | Gln | Gln | Leu | Val | Asn | Lys | Thr | Glu | Leu | Leu | Phe | Asp | Thr | Ile | Asp |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Ser | Ser | Glu | Val | Asn | Val | Ala | Lys | Ser | Ile | Ala | Lys | Phe | Leu | Arg | Asn |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Val | Arg | Tyr | Arg | Tyr | Gln | Pro | Leu | Leu | Glu | Arg | Cys | Asn | Asn | Val | Phe |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Leu | Ser | Asn | Val | Asp | His | Leu | Asp | Leu | Asp | Ser | Ile | Ser | Lys | Ile | Leu |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Ser | Val | Tyr | Lys | Phe | Leu | Gln | Phe | Asn | Ser | Phe | Glu | Phe | Ile | Ile | Met |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Ala | Lys | Lys | Lys | Leu | Thr | Glu | Met | Ile | Pro | Leu | Cys | Asn | His | Pro | Ala |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| Ser | Phe | Val | Lys | Leu | Phe | Val | Ala | Leu | Gly | Pro | Ile | Ala | Gly | Pro | Glu |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| Glu | Lys | Lys | Gln | Leu | Lys | Ser | Thr | Met | Leu | Leu | Met | Ser | Glu | Asp | Leu |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| Thr | Gly | Glu | Gln | Ala | Leu | Ala | Val | Leu | Gly | Ala | Met | Gly | Asp | Met | Glu |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| Ser | Arg | Asn | Ser | Cys | Leu | Ile | Lys | Arg | Val | Thr | Ser | Val | Leu | His | Lys |
|     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |

His Leu Asp Gly Tyr Lys Pro Leu Glu Leu Leu Lys Ile Thr Gln Glu  
370 375 380

Leu Thr Phe Leu His Phe Gln Arg Lys Glu Phe Phe Ala Lys Leu Arg  
385 390 395 400

Glu Leu Leu Leu Ser Tyr Leu Lys Asn Ser Phe Ile Pro Thr Glu Val  
405 410 415

Ser Val Leu Val Arg Ala Ile Ser Leu Leu Pro Ser Pro His Leu Asp  
420 425 430

Glu Val Gly Ile Ser Arg Ile Glu Ala Val Leu Pro Gln Cys Asp Leu  
435 440 445

Asn Asn Leu Ser Ser Phe Ala Thr Ser Val Leu Arg Trp Ile Gln His  
450 455 460

Asp His Met Tyr Leu Asp Asn Met Thr Ala Lys Gln Leu Lys Leu Leu  
465 470 475 480

Gln Lys Leu Asp His Tyr Gly Arg Gln Arg Leu Gln His Ser Asn Ser  
485 490 495

Leu Asp Leu Leu Arg Lys Glu Leu Lys Ser Leu Lys Gly Asn Thr Phe  
500 505 510

Pro Glu Ser Leu Leu Glu Glu Met Ile Ala Thr Leu Gln His Phe Met  
515 520 525

Asp Asp Ile Asn Tyr Ile Asn Val Gly Glu Ile Ala Ser Phe Ile Ser  
530 535 540

Ser Thr Asp Tyr Leu Ser Thr Leu Leu Leu Asp Arg Ile Ala Ser Val  
545 550 555 560

Ala Val Gln Gln Ile Glu Lys Ile His Pro Phe Thr Ile Pro Ala Ile  
565 570 575

Ile Arg Pro Phe Ser Val Leu Asn Tyr Asp Pro Pro Gln Arg Asp Glu  
580 585 590

Phe Leu Gly Thr Cys Val Gln His Leu Asn Ser Tyr Leu Gly Ile Leu  
595 600 605

Asp Pro Phe Ile Leu Val Phe Leu Gly Phe Ser Leu Ala Thr Leu Glu  
610 615 620

Tyr Phe Pro Glu Asp Leu Leu Lys Ala Ile Phe Asn Ile Lys Phe Leu  
625 630 635 640

Ala Arg Leu Asp Ser Gln Leu Glu Ser Ile Gly Gly Met Asp Gly Thr  
645 650 655

Gln Gln Gln Ile Phe Lys Met Leu Ala Glu Val Leu Gly Gly Ile Asn  
660 665 670

Cys Val Lys Ala Ser Val Leu Thr Pro Tyr Tyr His Lys Val Asp Phe  
675 680 685

Glu Cys Ile Leu Asp Lys Arg Lys Lys Pro Leu Pro Tyr Gly Ser His  
690 695 700

Asn Ile Ala Leu Gly Gln Leu Pro Glu Met Pro Trp Glu Ser Asn Ile  
705 710 715 720

Glu Ile Val Gly Ser Arg Leu Pro Pro Gly Ala Glu Arg Ile Ala Leu  
725 730 735

Glu Phe Leu Asp Ser Lys Ala Leu Cys Arg Asn Ile Pro His Met Lys  
740 745 750

Gly Lys Ser Ala Met Lys Lys Arg His Leu Glu Ile Leu Gly Tyr Arg  
755 760 765

Val Ile Gln Ile Ser Gln Phe Glu Trp Asn Ser Met Ala Leu Ser Thr  
770 775 780

Lys Asp Ala Arg Met Asp Tyr Leu Arg Glu Cys Ile Phe Gly Glu Val  
785 790 795 800

Lys Ser Cys Leu

<210> 154  
<211> 20  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 154  
tgaatgacga taccctggtg

20

<210> 155  
 <211> 20  
 <212> DNA  
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 <220>  
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 amplifying the nucleotide sequence encoding FASTKD1 protein"  
  
 <400> 155  
 agccttctcc atgcttctgt 20  
  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 156  
 ccatgacccg ctagttgaag 20  
  
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 <400> 157  
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 <400> 158  
 ttctcttgc ctagcagatc a 21  
  
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<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 159  
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<210> 160  
 <211> 22  
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<220>  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 160  
 tcctctgtgt aatcatcctg ct 22

<210> 161  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding FASTKD1 protein"

<400> 161  
 ctcgccagtt aggtcctctg 20

<210> 162  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding FASTKD1 protein"

<400> 162  
 ggagcaatgg gagatatgga 20

<210> 163  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding FASTKD1 protein"

<400> 163  
 ttcccttggga aatgcagaaa a 21



<210> 164  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding FASTKD1 protein"  
  
 <400> 164  
 tgcatttcca aaggaaggag 20  
  
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 <220>  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 165  
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 <210> 166  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 166  
 aaatgttggg gagattgcat 20  
  
 <210> 167  
 <211> 20  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 167  
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 <221> Source

<223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding FASTKD1 protein"

<400> 168  
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<210> 169  
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<220>  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding FASTKD1 protein"

<400> 169  
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| tctgtgtcct | cgagcccagc  | gtctcagcac | agcacatgc  | ccacacgacg  | gcaagcagcc  | 1500 |
| ccctgaccct | cttcagcaca  | gccatcccta | aggggctggc | cttcaggga   | cctgctctgg  | 1560 |
| acgtcccaaa | gttcgtcccc  | aaagtggacc | tgcaggcgga | ttacaacact  | gccaagggcg  | 1620 |
| tggtggggcg | cggctaccag  | gccctgcggc | tggcacgggc | cctgctggat  | gggcaggagc  | 1680 |
| taatgtttcg | ggggctgcac  | tgggtcatgg | aggtgctcca | ggccacatgc  | agacggactc  | 1740 |
| tggaagtggc | aaggacatcc  | ctcctctacc | tcagcagcag | cctgggaact  | gagaggttca  | 1800 |
| gcagcgtggc | tggaacgcct  | gagatccagg | aactgaaggc | ggctgcagaa  | ctgagggtcca | 1860 |
| ggctgcggac | tctagcggag  | gtcctctcca | gatgctccca | aaatatcacg  | gagaccaggg  | 1920 |
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| gaagcatcca | gcagattcag  | tgctgtttgg | acaagatgaa | cttcattctac | aaacagttca  | 2040 |
| agaagtctag | gatgaggcca  | gggcttggct | acaacgagga | gcagattcac  | aagctggata  | 2100 |
| aggtgaattt | cagtcattta  | gcaaaaagac | tcttcagagt | gttcaggag   | gagtgcgtgc  | 2160 |
| agaagtatca | agcgtcctta  | gtcacacacg | gcaagaggat | gaggggtggg  | cacgagacca  | 2220 |
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| tggacaacaa | ccgcatcatc  | gaacgggtaa | atagagtccc | agcacctcct  | gatgtctgag  | 2520 |
| ctccatgggg | cacatgaggc  | atcctgaagc | attagaatga | ttccaacact  | gctcttctgc  | 2580 |
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3263

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35 40 45

Arg Glu Val Gln Val Arg Glu Phe Glu Val Leu Arg Lys Leu Asn His  
50 55 60

Gln Asn Ile Val Lys Leu Phe Ala Val Glu Glu Thr Gly Gly Ser Arg  
65 70 75 80

Gln Lys Val Leu Val Met Glu Tyr Cys Ser Ser Gly Ser Leu Leu Ser  
85 90 95

Val Leu Glu Ser Pro Glu Asn Ala Phe Gly Leu Pro Glu Asp Glu Phe  
100 105 110

Leu Val Val Leu Arg Cys Val Val Ala Gly Met Asn His Leu Arg Glu  
115 120 125

Asn Gly Ile Val His Arg Asp Ile Lys Pro Gly Asn Ile Met Arg Leu  
130 135 140

Val Gly Glu Glu Gly Gln Ser Ile Tyr Lys Leu Thr Asp Phe Gly Ala  
145 150 155 160

Ala Arg Glu Leu Asp Asp Asp Glu Lys Phe Val Ser Val Tyr Gly Thr  
165 170 175

Glu Glu Tyr Leu His Pro Asp Met Tyr Glu Arg Ala Val Leu Arg Lys  
180 185 190

Pro Gln Gln Lys Ala Phe Gly Val Thr Val Asp Leu Trp Ser Ile Gly  
195 200 205

Val Thr Leu Tyr His Ala Ala Thr Gly Ser Leu Pro Phe Ile Pro Phe  
210 215 220

Gly Gly Pro Arg Arg Asn Lys Glu Ile Met Tyr Arg Ile Thr Thr Glu  
225 230 235 240

Lys Pro Ala Gly Ala Ile Ala Gly Ala Gln Arg Arg Glu Asn Gly Pro  
245 250 255

Leu Glu Trp Ser Tyr Thr Leu Pro Ile Thr Cys Gln Leu Ser Leu Gly  
260 265 270

Leu Gln Ser Gln Leu Val Pro Ile Leu Ala Asn Ile Leu Glu Val Glu  
275 280 285

Gln Ala Lys Cys Trp Gly Phe Asp Gln Phe Phe Ala Glu Thr Ser Asp  
290 295 300

Ile Leu Gln Arg Val Val Val His Val Phe Ser Leu Ser Gln Ala Val  
305 310 315 320

Leu His His Ile Tyr Ile His Ala His Asn Thr Ile Ala Ile Phe Gln  
325 330 335

Glu Ala Val His Lys Gln Thr Ser Val Ala Pro Arg His Gln Glu Tyr  
340 345 350

Leu Phe Glu Gly His Leu Cys Val Leu Glu Pro Ser Val Ser Ala Gln  
355 360 365

His Ile Ala His Thr Thr Ala Ser Ser Pro Leu Thr Leu Phe Ser Thr  
370 375 380

Ala Ile Pro Lys Gly Leu Ala Phe Arg Asp Pro Ala Leu Asp Val Pro  
385 390 395 400

Lys Phe Val Pro Lys Val Asp Leu Gln Ala Asp Tyr Asn Thr Ala Lys  
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Gly Val Leu Gly Ala Gly Tyr Gln Ala Leu Arg Leu Ala Arg Ala Leu  
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Leu Asp Gly Gln Glu Leu Met Phe Arg Gly Leu His Trp Val Met Glu  
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Val Leu Gln Ala Thr Cys Arg Arg Thr Leu Glu Val Ala Arg Thr Ser  
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Leu Leu Tyr Leu Ser Ser Ser Leu Gly Thr Glu Arg Phe Ser Ser Val  
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Ala Gly Thr Pro Glu Ile Gln Glu Leu Lys Ala Ala Ala Glu Leu Arg  
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Ser Arg Leu Arg Thr Leu Ala Glu Val Leu Ser Arg Cys Ser Gln Asn  
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Ile Thr Glu Thr Gln Glu Ser Leu Ser Ser Leu Asn Arg Glu Leu Val  
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Lys Ser Arg Asp Gln Val His Glu Asp Arg Ser Ile Gln Gln Ile Gln  
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Cys Cys Leu Asp Lys Met Asn Phe Ile Tyr Lys Gln Phe Lys Lys Ser  
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Arg Met Arg Pro Gly Leu Gly Tyr Asn Glu Glu Gln Ile His Lys Leu  
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Asp Lys Val Asn Phe Ser His Leu Ala Lys Arg Leu Leu Gln Val Phe  
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Gln Glu Glu Cys Val Gln Lys Tyr Gln Ala Ser Leu Val Thr His Gly  
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Ser Pro Thr Arg Lys Asp Leu Leu Leu His Met Gln Glu Leu Cys Glu  
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 <210> 215  
 <211> 35  
 <212> DNA



<213> Artificial Sequence  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding IKBKE protein"  
 <400> 215  
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 <210> 216  
 <211> 40  
 <212> DNA  
 <213> Artificial Sequence  
 <220>  
 <221> Source  
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 <400> 216  
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 <210> 217  
 <211> 43  
 <212> DNA  
 <213> Artificial Sequence  
 <220>  
 <221> Source  
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 <400> 217  
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 <210> 218  
 <211> 1578  
 <212> DNA  
 <213> Homo Sapiens  
 <400> 218  
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 tgctgcccc ctcaggcccc cgctccttc aggatgacgc tggacgtggg gccggaggat 120  
 gagctgccc actgggcccgc cgccaaagag tttaccaga agtacgacc taaggacgtc 180  
 atcggcagag gagtgaagtc tgtggtccgc cgttgtgttc atcgagctac tggccacgag 240  
 tttgcggtga agattatgga agtgacagct gagcggctga gtcctgagca gctggaggag 300  
 gtgcgggaag ccacacggcg agagacacac atccttcgcc aggtcgccgg ccacccccac 360  
 atcatcacc tcacgattc ctacgagtct tctagcttca tgctcctggt gtttgacctg 420  
 atgcggaagg gagagctgtt tgactatctc acagagaagg tggccctctc tgaaaaggaa 480

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accagggtcca tcatgcggtc tctgctggaa gcagtgcgct ttctccatgc caacaacatt      540
gtgcatcgag atctgaagcc cgagaatatt ctcctagatg acaatatgca gatccgactt      600
tcagatttcg ggttctcctg ccacttggaa cctggcgaga agcttcgaga gttgtgtggg      660
accccaggggt atctagcgcc agagatcctt aaatgctcca tggatgaaac ccaccagggc      720
tatggcaagg aggtcgacct ctgggcctgt ggggtgatct tgttcacact cctggctggc      780
tcgccacctt tctggcaccg gcggcagatc ctgatgttac gcatgatcat ggagggccag      840
taccagttca gttccccga gtgggatgac cgttcagca ctgtcaaaga cctgatctcc      900
aggctgctgc aggtggatcc tgaggcacgc ctgacagctg agcaggccct acagcacccc      960
ttctttgagc gttgtgaagg cagccaaccc tggaacctca cccccgccca gcggttcgg      1020
gtggcagtgt ggacagtgtt ggctgctgga cgagtggccc taagcaccca tcgtgtacgg      1080
ccactgacca agaatgcact gttgagggac ccttatgcgc tgcggtcagt gcggcacctc      1140
atcgacaact gtgccttccg gctctacggg cactgggtaa agaaagggga gcagcagaac      1200
cgggcggctc tctttcagca ccggccccct gggccttttc ccatcatggg cctgaagag      1260
gagggagact ctgctgctat aactgaggat gaggccgtgc ttgtgctggg ctaggacctc      1320
aaccocaggg attcccagga agcagaactc tccagaagaa gggttttgat cattccagct      1380
cctctgggct ctggcctctg gcctcaggcc cactaatgat cctgctaccc tcttgaagac      1440
cagcccggta cctctctccc cactggccag gactctgaga tcagagctgg ggtggaaggg      1500
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<210> 219
<211> 406
<212> PRT
<213> Homo Sapiens

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<400> 219

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Met Thr Leu Asp Val Gly Pro Glu Asp Glu Leu Pro Asp Trp Ala Ala
1           5           10          15

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Ala Lys Glu Phe Tyr Gln Lys Tyr Asp Pro Lys Asp Val Ile Gly Arg
20           25          30

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```

Gly Val Ser Ser Val Val Arg Arg Cys Val His Arg Ala Thr Gly His
35           40          45

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Glu Phe Ala Val Lys Ile Met Glu Val Thr Ala Glu Arg Leu Ser Pro
50           55          60

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Glu Gln Leu Glu Glu Val Arg Glu Ala Thr Arg Arg Glu Thr His Ile  
65 70 75 80

Leu Arg Gln Val Ala Gly His Pro His Ile Ile Thr Leu Ile Asp Ser  
85 90 95

Tyr Glu Ser Ser Ser Phe Met Phe Leu Val Phe Asp Leu Met Arg Lys  
100 105 110

Gly Glu Leu Phe Asp Tyr Leu Thr Glu Lys Val Ala Leu Ser Glu Lys  
115 120 125

Glu Thr Arg Ser Ile Met Arg Ser Leu Leu Glu Ala Val Ser Phe Leu  
130 135 140

His Ala Asn Asn Ile Val His Arg Asp Leu Lys Pro Glu Asn Ile Leu  
145 150 155 160

Leu Asp Asp Asn Met Gln Ile Arg Leu Ser Asp Phe Gly Phe Ser Cys  
165 170 175

His Leu Glu Pro Gly Glu Lys Leu Arg Glu Leu Cys Gly Thr Pro Gly  
180 185 190

Tyr Leu Ala Pro Glu Ile Leu Lys Cys Ser Met Asp Glu Thr His Pro  
195 200 205

Gly Tyr Gly Lys Glu Val Asp Leu Trp Ala Cys Gly Val Ile Leu Phe  
210 215 220

Thr Leu Leu Ala Gly Ser Pro Pro Phe Trp His Arg Arg Gln Ile Leu  
225 230 235 240

Met Leu Arg Met Ile Met Glu Gly Gln Tyr Gln Phe Ser Ser Pro Glu  
245 250 255

Trp Asp Asp Arg Ser Ser Thr Val Lys Asp Leu Ile Ser Arg Leu Leu  
260 265 270

Gln Val Asp Pro Glu Ala Arg Leu Thr Ala Glu Gln Ala Leu Gln His  
275 280 285

Pro Phe Phe Glu Arg Cys Glu Gly Ser Gln Pro Trp Asn Leu Thr Pro  
290 295 300

Arg Gln Arg Phe Arg Val Ala Val Trp Thr Val Leu Ala Ala Gly Arg  
305 310 315 320

Val Ala Leu Ser Thr His Arg Val Arg Pro Leu Thr Lys Asn Ala Leu  
325 330 335

Leu Arg Asp Pro Tyr Ala Leu Arg Ser Val Arg His Leu Ile Asp Asn  
340 345 350

Cys Ala Phe Arg Leu Tyr Gly His Trp Val Lys Lys Gly Glu Gln Gln  
355 360 365

Asn Arg Ala Ala Leu Phe Gln His Arg Pro Pro Gly Pro Phe Pro Ile  
370 375 380

Met Gly Pro Glu Glu Glu Gly Asp Ser Ala Ala Ile Thr Glu Asp Glu  
385 390 395 400

Ala Val Leu Val Leu Gly  
405

<210> 220  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 220  
ccgccaaaga gttttaccag 20

<210> 221  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 221  
tccataatct tcaccgcaaa 20

<210> 222  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 222  
ggcgagagac acacatcctt 20

<210> 223  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 223  
caaacaccag gaacatgaag c 21

<210> 224  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 224  
gcttcattgtt cctggtgttt g 21

<210> 225  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 225  
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<210> 226  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 226  
ggaagggaga gctgtttgac t 21

<210> 227  
<211> 20  
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<213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Reverse primer for amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 227

tggtgttggc atggagaaag

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<210> 228

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Forward primer for amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 228

tcagatttcg gggtctcctg

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<210> 229

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Reverse primer for amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 229

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20

<210> 230

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Forward primer for amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 230

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20

<210> 231

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Reverse primer for amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 231  
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<210> 232  
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<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 232  
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<210> 233  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 233  
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<210> 234  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 234  
accccttctt tgagcgttgt 20

<210> 235  
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<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding PHKG2 protein"

<400> 235  
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<210> 236  
<211> 20  
<212> DNA

<213> Artificial Sequence  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PHKG2 protein"  
 <400> 236  
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 <210> 237  
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 <400> 237  
 catcacccctc atcgattcct 20  
 <210> 238  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PHKG2 protein"  
 <400> 238  
 ggaagggaga gctgtttgac t 21  
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 <400> 239  
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<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PHKG2 protein"

<400> 240  
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<210> 241  
<211> 20  
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<213> Artificial Sequence

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<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PHKG2 protein"

<400> 241  
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<210> 242  
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<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
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<400> 242  
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<210> 243  
<211> 20  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PHKG2 protein"

<400> 243  
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<210> 244  
<211> 60  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PHKG2 protein"

protein"

<400> 244  
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<210> 245  
<211> 2578  
<212> DNA  
<213> Homo Sapiens

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gggaccggcg cgcgctctcg tcgccccgc tgtcccggcg gcgccaaccg aagcgccccg 180  
cctgatccgt gtccgacatg ctgcgcgcgc ctctgctgtg cctggccgtg gccgccctgg 240  
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ccgagatcag gttggccaag gtggacgcca cggaggagtc tgacctggcc cagcagtacg 480  
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 cctcaccct acacaccgtc cgttcacccc cgtctcttcc ttctgctttt cggtttttgg 1920  
 aaagggatcc atctccaggc agcccaccct ggtggggctt gtttctgaa accatgatgt 1980  
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 gtggggaggt ggccaaggat gctggagctg aatcagacgc tgacagttct tcaggcattt 2520  
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<210> 246  
 <211> 508  
 <212> PRT  
 <213> Homo Sapiens

<400> 246

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 1 5 10 15

Ala Asp Ala Pro Glu Glu Glu Asp His Val Leu Val Leu Arg Lys Ser  
 20 25 30

Asn Phe Ala Glu Ala Leu Ala Ala His Lys Tyr Leu Leu Val Glu Phe  
 35 40 45

Tyr Ala Pro Trp Cys Gly His Cys Lys Ala Leu Ala Pro Glu Tyr Ala  
 50 55 60

Lys Ala Ala Gly Lys Leu Lys Ala Glu Gly Ser Glu Ile Arg Leu Ala  
 65 70 75 80

Lys Val Asp Ala Thr Glu Glu Ser Asp Leu Ala Gln Gln Tyr Gly Val  
85 90 95

Arg Gly Tyr Pro Thr Ile Lys Phe Phe Arg Asn Gly Asp Thr Ala Ser  
100 105 110

Pro Lys Glu Tyr Thr Ala Gly Arg Glu Ala Asp Asp Ile Val Asn Trp  
115 120 125

Leu Lys Lys Arg Thr Gly Pro Ala Ala Thr Thr Leu Pro Asp Gly Ala  
130 135 140

Ala Ala Glu Ser Leu Val Glu Ser Ser Glu Val Ala Val Ile Gly Phe  
145 150 155 160

Phe Lys Asp Val Glu Ser Asp Ser Ala Lys Gln Phe Leu Gln Ala Ala  
165 170 175

Glu Ala Ile Asp Asp Ile Pro Phe Gly Ile Thr Ser Asn Ser Asp Val  
180 185 190

Phe Ser Lys Tyr Gln Leu Asp Lys Asp Gly Val Val Leu Phe Lys Lys  
195 200 205

Phe Asp Glu Gly Arg Asn Asn Phe Glu Gly Glu Val Thr Lys Glu Asn  
210 215 220

Leu Leu Asp Phe Ile Lys His Asn Gln Leu Pro Leu Val Ile Glu Phe  
225 230 235 240

Thr Glu Gln Thr Ala Pro Lys Ile Phe Gly Gly Glu Ile Lys Thr His  
245 250 255

Ile Leu Leu Phe Leu Pro Lys Ser Val Ser Asp Tyr Asp Gly Lys Leu  
260 265 270

Ser Asn Phe Lys Thr Ala Ala Glu Ser Phe Lys Gly Lys Ile Leu Phe  
275 280 285

Ile Phe Ile Asp Ser Asp His Thr Asp Asn Gln Arg Ile Leu Glu Phe  
290 295 300

Phe Gly Leu Lys Lys Glu Glu Cys Pro Ala Val Arg Leu Ile Thr Leu  
305 310 315 320

Glu Glu Glu Met Thr Lys Tyr Lys Pro Glu Ser Glu Glu Leu Thr Ala  
325 330 335

Glu Arg Ile Thr Glu Phe Cys His Arg Phe Leu Glu Gly Lys Ile Lys  
 340 345 350

Pro His Leu Met Ser Gln Glu Leu Pro Glu Asp Trp Asp Lys Gln Pro  
 355 360 365

Val Lys Val Leu Val Gly Lys Asn Phe Glu Asp Val Ala Phe Asp Glu  
 370 375 380

Lys Lys Asn Val Phe Val Glu Phe Tyr Ala Pro Trp Cys Gly His Cys  
 385 390 395 400

Lys Gln Leu Ala Pro Ile Trp Asp Lys Leu Gly Glu Thr Tyr Lys Asp  
 405 410 415

His Glu Asn Ile Val Ile Ala Lys Met Asp Ser Thr Ala Asn Glu Val  
 420 425 430

Glu Ala Val Lys Val His Ser Phe Pro Thr Leu Lys Phe Phe Pro Ala  
 435 440 445

Ser Ala Asp Arg Thr Val Ile Asp Tyr Asn Gly Glu Arg Thr Leu Asp  
 450 455 460

Gly Phe Lys Lys Phe Leu Glu Ser Gly Gly Gln Asp Gly Ala Gly Asp  
 465 470 475 480

Asp Asp Asp Leu Glu Asp Leu Glu Glu Ala Glu Glu Pro Asp Met Glu  
 485 490 495

Glu Asp Asp Asp Gln Lys Ala Val Lys Asp Glu Leu  
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<210> 247  
 <211> 19  
 <212> DNA  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 247  
 gctgcggaaa agcaacttc

19

<210> 248  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence

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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 gcagagtcct tgggtggagtc 20  
  
 <210> 252  
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 <213> Artificial Sequence  
  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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<210> 253  
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<212> DNA  
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<210> 254  
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<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding P4HB protein"

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<210> 255  
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<220>  
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<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding P4HB protein"

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<210> 256  
<211> 20  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding P4HB protein"

<400> 256  
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<210> 257  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 258  
 gtcgctgtcg atgaagatga 20  
  
 <210> 259  
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 <400> 259  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 261



agcctgtcaa ggtgcttggt 20

<210> 262  
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<220>  
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<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 262  
caaatgggag ccaactgttt 20

<210> 263  
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<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 263  
acagcttccc cacactcaag 20

<210> 264  
<211> 19  
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<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 264  
caccgctctc caggaattt 19

<210> 265  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
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<400> 265  
gcacgctgga tggttttaag 20

<210> 266  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
 <221> Source  
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 <210> 267  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 <400> 267  
 cacaagtacc tgctggtgga 20  
  
 <210> 268  
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 <213> Artificial Sequence  
  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 <400> 268  
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 <210> 269  
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 <400> 269  
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 <210> 270  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a

nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 270  
ctcgacaaag atggggttgt 20

<210> 271  
<211> 20  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 271  
tcacatcctg ctgttcttgc 20

<210> 272  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 272  
ctatgacggc aaactgagca 20

<210> 273  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 273  
aaaatcaagc cccacctgat 20

<210> 274  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 274  
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<210> 275  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 275  
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<210> 276  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 276  
atgacgatct cgaggacctg 20

<210> 277  
<211> 60  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P4HB protein"

<400> 277  
ggcatttcta tttcacaatc gaattgaaca cattggccaa ataaagttga aattttcccc 60

<210> 278  
<211> 2026  
<212> DNA  
<213> Homo Sapiens

<400> 278  
aagtgtctggg atgacaggtg tgagccaccg cccccggccc ctgcccgcc ttttgaagga 60  
gcctttogtc ctcaagggcg aggccactcc cccccgcga gttccatgcc ccctagaggg 120  
tcatcgttcc cgacggggag gtggcgccct cccccgggcc ccgggccccg accgcccgtg 180  
ctgcctcctt ccgggccctc ctccgcgatg acggcgccgc cagcaggcca ggcggactgg 240

|                                                                     |      |
|---------------------------------------------------------------------|------|
| gcggggctcc gagcggggac tgggacccag accgactagg ggactgggag cgggcggcgc   | 300  |
| ggccatggcg ggctgctgcg ccgcgctggc ggcccttcctg ttcgagtacg acacgccgcg  | 360  |
| catcgtgctc atccgcagcc gcaaagtggg gctcatgaac cgcgccgtgc aactgctcat   | 420  |
| cctggcctac gtcatcgggt ggggtgtttgt gtgggaaaag ggctaccagg aaactgactc  | 480  |
| cgtggtcagc tccgttacga ccaaggtcaa gggcgtggct gtgaccaaca cttctaaact   | 540  |
| tggattccgg atctgggatg tggcggatta tgtgatacca gctcaggagg aaaactccct   | 600  |
| cttcgtcatg accaacgtga tctcaccat gaaccagaca cagggcctgt gccccgagat    | 660  |
| tccagatgcg accactgtgt gtaaatacaga tgccagctgt actgccggct ctgccggcac  | 720  |
| ccacagcaac ggagtctcaa caggcagggtg cgtagctttc aacgggtctg tcaagacgtg  | 780  |
| tgagggtggcg gcctggtgcc cgggtggagga tgacacacac gtgccacaac ctgctttttt | 840  |
| aaaggctgca gaaaacttca ctcttttgggt taagaacaac atctggtatc ccaaatttaa  | 900  |
| tttcagcaag aggaatatcc ttcccaacat caccactact tacctcaagt cgtgcattta   | 960  |
| tgatgctaaa acagatccct tctgccccat attccgtctt ggcaaaatag tggagaacgc   | 1020 |
| aggacacagt ttccaggaca tggccgtgga gggaggcatc atgggcatcc aggtcaactg   | 1080 |
| ggactgcaac ctggacagag ccgcctccct ctgcttgccc aggtactcct tccgccgcct   | 1140 |
| cgatacacgg gacgttgagc acaacgtatc tcttggtac aatttcaggt ttgccaagta    | 1200 |
| ctacagagac ctggctggca acgagcagcg cacgctcatc aaggcctatg gcatccgctt   | 1260 |
| cgacatcatt gtgtttggga aggcaggga atttgacatc atccccacta tgatcaacat    | 1320 |
| cggctctggc ctggcactgc taggcatggc gaccgtgctg tgtgacatca tagtcctcta   | 1380 |
| ctgcatgaag aaaagactct actatcggga gaagaaatat aaatatgtgg aagattacga   | 1440 |
| gcagggtctt gctagtgagc tggaccagtg aggcctaccc cacacctggg ctctccacag   | 1500 |
| ccccatcaaa gaacagagag gaggaggagg gagaaatggc caccacatca cccagagaa    | 1560 |
| atctctggaa tctgattgag totccactcc acaagcactc agggttcccc agcagctcct   | 1620 |
| gtgtgttggtg tgcaggatct gtttgccac tcggcccagg aggtcagcag tctgttcttg   | 1680 |
| gctgggtcaa ctctgctttt cccgcaacct ggggtgtcg ggggagcgct ggcccagcgc    | 1740 |
| agtggcactg ctgtggcttt cagggtgga gctggctttg ctcagaagcc tctgtctcc     | 1800 |
| agctctctcc aggacaggcc cagtcctctg aggcacggcg gctctgttca agcactttat   | 1860 |
| gcggcagggg aggccgcctg gctgcagtca ctagacttgt agcaggcctg ggctgcaggc   | 1920 |
| ttccccccga ccattccctg cagccatgcg gcagagctgg catttctcct cagagaagcg   | 1980 |
| ctgtgctaag gtgatcgagg accagacatt aaagcgtgat tttctt                  | 2026 |

<210> 279

<211> 388

<212> PRT  
<213> Homo Sapiens

<400> 279

Met Ala Gly Cys Cys Ala Ala Leu Ala Ala Phe Leu Phe Glu Tyr Asp  
1 5 10 15

Thr Pro Arg Ile Val Leu Ile Arg Ser Arg Lys Val Gly Leu Met Asn  
20 25 30

Arg Ala Val Gln Leu Leu Ile Leu Ala Tyr Val Ile Gly Trp Val Phe  
35 40 45

Val Trp Glu Lys Gly Tyr Gln Glu Thr Asp Ser Val Val Ser Ser Val  
50 55 60

Thr Thr Lys Val Lys Gly Val Ala Val Thr Asn Thr Ser Lys Leu Gly  
65 70 75 80

Phe Arg Ile Trp Asp Val Ala Asp Tyr Val Ile Pro Ala Gln Glu Glu  
85 90 95

Asn Ser Leu Phe Val Met Thr Asn Val Ile Leu Thr Met Asn Gln Thr  
100 105 110

Gln Gly Leu Cys Pro Glu Ile Pro Asp Ala Thr Thr Val Cys Lys Ser  
115 120 125

Asp Ala Ser Cys Thr Ala Gly Ser Ala Gly Thr His Ser Asn Gly Val  
130 135 140

Ser Thr Gly Arg Cys Val Ala Phe Asn Gly Ser Val Lys Thr Cys Glu  
145 150 155 160

Val Ala Ala Trp Cys Pro Val Glu Asp Asp Thr His Val Pro Gln Pro  
165 170 175

Ala Phe Leu Lys Ala Ala Glu Asn Phe Thr Leu Leu Val Lys Asn Asn  
180 185 190

Ile Trp Tyr Pro Lys Phe Asn Phe Ser Lys Arg Asn Ile Leu Pro Asn  
195 200 205

Ile Thr Thr Thr Tyr Leu Lys Ser Cys Ile Tyr Asp Ala Lys Thr Asp  
210 215 220

Pro Phe Cys Pro Ile Phe Arg Leu Gly Lys Ile Val Glu Asn Ala Gly  
225 230 235 240

His Ser Phe Gln Asp Met Ala Val Glu Gly Gly Ile Met Gly Ile Gln  
245 250 255

Val Asn Trp Asp Cys Asn Leu Asp Arg Ala Ala Ser Leu Cys Leu Pro  
260 265 270

Arg Tyr Ser Phe Arg Arg Leu Asp Thr Arg Asp Val Glu His Asn Val  
275 280 285

Ser Pro Gly Tyr Asn Phe Arg Phe Ala Lys Tyr Tyr Arg Asp Leu Ala  
290 295 300

Gly Asn Glu Gln Arg Thr Leu Ile Lys Ala Tyr Gly Ile Arg Phe Asp  
305 310 315 320

Ile Ile Val Phe Gly Lys Ala Gly Lys Phe Asp Ile Ile Pro Thr Met  
325 330 335

Ile Asn Ile Gly Ser Gly Leu Ala Leu Leu Gly Met Ala Thr Val Leu  
340 345 350

Cys Asp Ile Ile Val Leu Tyr Cys Met Lys Lys Arg Leu Tyr Tyr Arg  
355 360 365

Glu Lys Lys Tyr Lys Tyr Val Glu Asp Tyr Glu Gln Gly Leu Ala Ser  
370 375 380

Glu Leu Asp Gln  
385

<210> 280  
<211> 361  
<212> PRT  
<213> Homo Sapiens

<400> 280

Met Ala Gly Cys Cys Ala Ala Leu Ala Ala Phe Leu Phe Glu Tyr Asp  
1 5 10 15

Thr Pro Arg Ile Val Leu Ile Arg Ser Arg Lys Val Gly Leu Met Asn  
20 25 30

Arg Ala Val Gln Leu Leu Ile Leu Ala Tyr Val Ile Gly Trp Val Phe  
35 40 45

Val Trp Glu Lys Gly Tyr Gln Glu Thr Asp Ser Val Val Ser Ser Val  
50 55 60

Thr Thr Lys Val Lys Gly Val Ala Val Thr Asn Thr Ser Lys Leu Gly  
65 70 75 80

Phe Arg Ile Trp Asp Val Ala Asp Tyr Val Ile Pro Ala Gln Glu Glu  
85 90 95

Asn Ser Leu Phe Val Met Thr Asn Val Ile Leu Thr Met Asn Gln Thr  
100 105 110

Gln Gly Leu Cys Pro Glu Ile Pro Asp Ala Thr Thr Val Cys Lys Ser  
115 120 125

Asp Ala Ser Cys Thr Ala Gly Ser Ala Gly Thr His Ser Asn Val Val  
130 135 140

Cys Thr Leu Ile Pro Ala Phe Leu Lys Ala Ala Glu Asn Phe Thr Leu  
145 150 155 160

Leu Val Lys Asn Asn Ile Trp Tyr Pro Lys Phe Asn Phe Ser Lys Arg  
165 170 175

Asn Ile Leu Pro Asn Ile Thr Thr Thr Tyr Leu Lys Ser Cys Ile Tyr  
180 185 190

Asp Ala Lys Thr Asp Pro Phe Cys Pro Ile Phe Arg Leu Gly Lys Ile  
195 200 205

Val Glu Asn Ala Gly His Ser Phe Gln Asp Met Ala Val Glu Gly Gly  
210 215 220

Ile Met Gly Ile Gln Val Asn Trp Asp Cys Asn Leu Asp Arg Ala Ala  
225 230 235 240

Ser Leu Cys Leu Pro Arg Tyr Ser Phe Arg Arg Leu Asp Thr Arg Asp  
245 250 255

Val Glu His Asn Val Ser Pro Gly Tyr Asn Phe Arg Phe Ala Lys Tyr  
260 265 270

Tyr Arg Asp Leu Ala Gly Asn Glu Gln Arg Thr Leu Ile Lys Ala Tyr  
275 280 285

Gly Ile Arg Phe Asp Ile Ile Val Phe Gly Lys Ala Gly Lys Phe Asp  
290 295 300

Ile Ile Pro Thr Met Ile Asn Ile Gly Ser Gly Leu Ala Leu Leu Gly



305 310 315 320

Met Ala Thr Val Leu Cys Asp Ile Ile Val Leu Tyr Cys Met Lys Lys  
325 330 335

Arg Leu Tyr Tyr Arg Glu Lys Lys Tyr Lys Tyr Val Glu Asp Tyr Glu  
340 345 350

Gln Gly Leu Ala Ser Glu Leu Asp Gln  
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<210> 281  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding P2RX4 protein"

<400> 281  
aactgctcat cctggcctac 20

<210> 282  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding P2RX4 protein"

<400> 282  
gtcgtaacgg agctgaccac 20

<210> 283  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding P2RX4 protein"

<400> 283  
ggatgtggcg gattatgtg 19

<210> 284  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<221> Source  
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 <400> 284  
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 <210> 285  
 <211> 20  
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 <220>  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 285  
 agattccaga tgcgaccact 20  
  
 <210> 286  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 286  
 cagaccggtt gaaagctacg 20  
  
 <210> 287  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 287  
 tctgtcaaga cgtgtgaggt g 21  
  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 288  
 ccaaaagagt gaagttttct gc 22

<210> 289  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding P2RX4 protein"

<400> 289  
ttttggttaa gaacaacatc tgg 23

<210> 290  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding P2RX4 protein"

<400> 290  
atatggggca gaagggatct 20

<210> 291  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 291  
cgcttcgaca tcattgtgtt 20

<210> 292  
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<212> DNA  
<213> Artificial Sequence

<220>  
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<400> 292  
tagcagtgcc aggccagag 19

<210> 293  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>

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 <400> 293  
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 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 294  
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 <210> 295  
 <211> 20  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 protein"  
  
 <400> 295  
 ttgtgtggga aaagggctac 20  
  
 <210> 296  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 protein"  
  
 <400> 296  
 ttcgtcatga ccaacgtgat 20  
  
 <210> 297  
 <211> 20  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 protein"

<400> 297  
tcagatgccca gctgtactgc 20

<210> 298  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P2RX4 protein"

<400> 298  
gtggaggatg acacacacgt 20

<210> 299  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P2RX4 protein"

<400> 299  
tccttcccaa catcaccact 20

<210> 300  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P2RX4 protein"

<400> 300  
gaaggcaggg aaatttgaca 20

<210> 301  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
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<400> 301  
gggtcttgct agtgagctgg 20

<210> 302  
 <211> 60  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding P2RX4 protein"

<400> 302  
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<210> 303  
 <211> 14  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Synthetic peptide representing the C Terminus of the sequence according to NP\_002551.2"

<400> 303  
  
 Tyr Arg Glu Lys Lys Tyr Lys Tyr Val Glu Asp Tyr Glu Gln  
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<210> 304  
 <211> 3502  
 <212> DNA  
 <213> Homo Sapiens

<400> 304  
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 tgggcgcgcg ccccgggccgc tgcggtcggg ccgctgggtg gtcggggcgct tgggtccggca 180  
 gttggtcggg gggccagtgg cccgtcgctc gcttctgggc tctcatgttt gaaggtggga 240  
 gggacacggg agcggcccgc acacctgagc cgcccggaga ggagcctcgg ccccgtagcc 300  
 agtaagaaga ggaggaggcc aggcaggcaa aaggagtcag ggcttctgat gctagtcag 360  
 cgctggaagc tgccctggag caaatggacg ggatcattgc aggcactaaa acaggtgcag 420  
 atcttagtga tggtagttgt gagcctggac tggcttcccc ggctcctac atgaaccct 480  
 tcccgggtgct ccatctcatc gaggacttga ggctggcctt ggagatgctg gagcttctc 540  
 aggagagagc agccctcctg agccagatcc ctggcccaac agctgcctac ataaaggaat 600  
 ggtttgaaga gagcttgtcc caggtaaacc accacagtgc tgctagtaat gaaacctacc 660  
 aggaacgctt ggcacgtcta gaaggggata aggagtcctt catattgcag gtgagtgtcc 720

|            |            |            |            |            |             |      |
|------------|------------|------------|------------|------------|-------------|------|
| tcacagacca | agtagaagcc | cagggagaaa | agattcgaga | cctggaagtg | tgtctggaag  | 780  |
| gacaccaggt | gaaactcaat | gctgctgaag | agatgcttca | acaggagctg | ctaagccgca  | 840  |
| catctcttga | gacccagaag | ctcgatctga | tgactgaagt | gtctgagctg | aagctcaagc  | 900  |
| tggttggcat | ggagaaggag | cagagagagc | aggaggagaa | gcagagaaaa | gcagaggagt  | 960  |
| tactgcaaga | gctcaggcac | ctcaaaatca | aagtggaaga | gttggaaaat | gaaaggaatc  | 1020 |
| agtatgaatg | gaagctaaag | gccactaagg | ctgaagtcgc | ccagctgcaa | gaacaggtgg  | 1080 |
| ccttgaaaga | tgcagaaatt | gagcgtctgc | acagccagct | ctcccggaca | gcagctctcc  | 1140 |
| acagtgagag | tcacacagag | agagaccaag | aaattcaacg | tctgaaaatg | gggatggaaa  | 1200 |
| ctttgctgct | tgccaatgaa | gataaggacc | gtcggataga | ggagcttacg | gggctgttaa  | 1260 |
| accagtaccg | gaaggtaaag | gagattgtga | tggtcactca | agggccttcg | gagagaactc  | 1320 |
| tctcaatcaa | tgaagaagaa | ccggagggag | gtttcagcaa | gtggaacgct | acaaataagg  | 1380 |
| accctgaaga | attattttaa | caagagatgc | ctccaagatg | tagctctcct | acagtggggc  | 1440 |
| cacctccatt | gccacagaaa | tactggaaa  | ccagggtcga | gaaaaagctc | tcttgtagtc  | 1500 |
| tagaagactt | gagaagtga  | tctgtggata | agtgtatgga | tgggaaccag | cccttcccg   | 1560 |
| tgtagaacc  | caaggacagc | cctttcttgg | cggagcacia | atatccact  | ttacctggga  | 1620 |
| agctttcagg | agccacgccc | aatggagagg | ctgccaaatc | tcctcccacc | atctgccagc  | 1680 |
| ctgacgccac | ggggagcagc | ctgctgaggc | tgagagacac | agaaagtggc | tgggacgaca  | 1740 |
| ctgctgtggt | caatgacctc | tcatccacat | catcgggcac | tgaatcaggt | cctcagtctc  | 1800 |
| ctctgacacc | agatggtaaa | cggaatccca | aaggcattaa | gaagttctgg | ggaaaaatcc  | 1860 |
| gaagaactca | gtcaggaaat | ttctacactg | acacgctggg | gatggcagag | tttcgacgag  | 1920 |
| gtgggctccg | ggcaaccgca | gggccaagac | tctctaggac | cagggactcc | aagggaacaga | 1980 |
| aaagtgacgc | caatgcccc  | tttgcccagt | ggagcacaga | gcgtgtgtgt | gcatggctgg  | 2040 |
| aggactttgg | cctggctcag | tatgtgatct | ttgccaggca | gtgggtatct | tctggccaca  | 2100 |
| ccttattgac | agccaccctt | caggacatgg | aaaaggagct | aggaattaag | caccactctc  | 2160 |
| acaggaagaa | gcttggttta | gcagtgaaag | ccatcaacac | caaacaggag | gagaagtctg  | 2220 |
| cactgctaga | ccacatttgg | gtgacaaggt | ggcttgatga | tattggctta | cccagtaga   | 2280 |
| aagaccagtt | tcatgaatct | agagttgaca | gacgaatgct | gcaataccta | actgtgaacg  | 2340 |
| atttactctt | cttaaaagtc | accagccaac | tacatcatct | cagcatcaaa | tgtgccattc  | 2400 |
| acgtgctgca | tgtcaacaag | ttcaaccccc | actgcctgca | ccggcgcca  | gctgatgaga  | 2460 |
| gtaacctttc | tccttcagaa | gttgtacagt | ggtccaacca | cagggtgatg | gagtggttac  | 2520 |
| gatctgtgga | cctggcagag | tatgcacca  | atcttcgagg | gagtggagtc | catggaggcc  | 2580 |
| tcattatcct | ggagccacgc | ttcactgggg | acaccctggc | tatgcttctc | aacatcccc   | 2640 |

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 <213> Homo Sapiens

<400> 305

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 20 25 30

Thr Cys Glu Pro Gly Leu Ala Ser Pro Ala Ser Tyr Met Asn Pro Phe  
 35 40 45

Pro Val Leu His Leu Ile Glu Asp Leu Arg Leu Ala Leu Glu Met Leu  
 50 55 60

Glu Leu Pro Gln Glu Arg Ala Ala Leu Leu Ser Gln Ile Pro Gly Pro  
 65 70 75 80

Thr Ala Ala Tyr Ile Lys Glu Trp Phe Glu Glu Ser Leu Ser Gln Val  
 85 90 95



Asn His His Ser Ala Ala Ser Asn Glu Thr Tyr Gln Glu Arg Leu Ala  
100 105 110

Arg Leu Glu Gly Asp Lys Glu Ser Leu Ile Leu Gln Val Ser Val Leu  
115 120 125

Thr Asp Gln Val Glu Ala Gln Gly Glu Lys Ile Arg Asp Leu Glu Val  
130 135 140

Cys Leu Glu Gly His Gln Val Lys Leu Asn Ala Ala Glu Glu Met Leu  
145 150 155 160

Gln Gln Glu Leu Leu Ser Arg Thr Ser Leu Glu Thr Gln Lys Leu Asp  
165 170 175

Leu Met Thr Glu Val Ser Glu Leu Lys Leu Lys Leu Val Gly Met Glu  
180 185 190

Lys Glu Gln Arg Glu Gln Glu Glu Lys Gln Arg Lys Ala Glu Glu Leu  
195 200 205

Leu Gln Glu Leu Arg His Leu Lys Ile Lys Val Glu Glu Leu Glu Asn  
210 215 220

Glu Arg Asn Gln Tyr Glu Trp Lys Leu Lys Ala Thr Lys Ala Glu Val  
225 230 235 240

Ala Gln Leu Gln Glu Gln Val Ala Leu Lys Asp Ala Glu Ile Glu Arg  
245 250 255

Leu His Ser Gln Leu Ser Arg Thr Ala Ala Leu His Ser Glu Ser His  
260 265 270

Thr Glu Arg Asp Gln Glu Ile Gln Arg Leu Lys Met Gly Met Glu Thr  
275 280 285

Leu Leu Leu Ala Asn Glu Asp Lys Asp Arg Arg Ile Glu Glu Leu Thr  
290 295 300

Gly Leu Leu Asn Gln Tyr Arg Lys Val Lys Glu Ile Val Met Val Thr  
305 310 315 320

Gln Gly Pro Ser Glu Arg Thr Leu Ser Ile Asn Glu Glu Glu Pro Glu  
325 330 335

Gly Gly Phe Ser Lys Trp Asn Ala Thr Asn Lys Asp Pro Glu Glu Leu  
340 345 350

Phe Lys Gln Glu Met Pro Pro Arg Cys Ser Ser Pro Thr Val Gly Pro  
355 360 365

Pro Pro Leu Pro Gln Lys Ser Leu Glu Thr Arg Ala Gln Lys Lys Leu  
370 375 380

Ser Cys Ser Leu Glu Asp Leu Arg Ser Glu Ser Val Asp Lys Cys Met  
385 390 395 400

Asp Gly Asn Gln Pro Phe Pro Val Leu Glu Pro Lys Asp Ser Pro Phe  
405 410 415

Leu Ala Glu His Lys Tyr Pro Thr Leu Pro Gly Lys Leu Ser Gly Ala  
420 425 430

Thr Pro Asn Gly Glu Ala Ala Lys Ser Pro Pro Thr Ile Cys Gln Pro  
435 440 445

Asp Ala Thr Gly Ser Ser Leu Leu Arg Leu Arg Asp Thr Glu Ser Gly  
450 455 460

Trp Asp Asp Thr Ala Val Val Asn Asp Leu Ser Ser Thr Ser Ser Gly  
465 470 475 480

Thr Glu Ser Gly Pro Gln Ser Pro Leu Thr Pro Asp Gly Lys Arg Asn  
485 490 495

Pro Lys Gly Ile Lys Lys Phe Trp Gly Lys Ile Arg Arg Thr Gln Ser  
500 505 510

Gly Asn Phe Tyr Thr Asp Thr Leu Gly Met Ala Glu Phe Arg Arg Gly  
515 520 525

Gly Leu Arg Ala Thr Ala Gly Pro Arg Leu Ser Arg Thr Arg Asp Ser  
530 535 540

Lys Gly Gln Lys Ser Asp Ala Asn Ala Pro Phe Ala Gln Trp Ser Thr  
545 550 555 560

Glu Arg Val Cys Ala Trp Leu Glu Asp Phe Gly Leu Ala Gln Tyr Val  
565 570 575

Ile Phe Ala Arg Gln Trp Val Ser Ser Gly His Thr Leu Leu Thr Ala  
580 585 590

Thr Pro Gln Asp Met Glu Lys Glu Leu Gly Ile Lys His Pro Leu His  
595 600 605

Arg Lys Lys Leu Val Leu Ala Val Lys Ala Ile Asn Thr Lys Gln Glu  
610 615 620

Glu Lys Ser Ala Leu Leu Asp His Ile Trp Val Thr Arg Trp Leu Asp  
625 630 635 640

Asp Ile Gly Leu Pro Gln Tyr Lys Asp Gln Phe His Glu Ser Arg Val  
645 650 655

Asp Arg Arg Met Leu Gln Tyr Leu Thr Val Asn Asp Leu Leu Phe Leu  
660 665 670

Lys Val Thr Ser Gln Leu His His Leu Ser Ile Lys Cys Ala Ile His  
675 680 685

Val Leu His Val Asn Lys Phe Asn Pro His Cys Leu His Arg Arg Pro  
690 695 700

Ala Asp Glu Ser Asn Leu Ser Pro Ser Glu Val Val Gln Trp Ser Asn  
705 710 715 720

His Arg Val Met Glu Trp Leu Arg Ser Val Asp Leu Ala Glu Tyr Ala  
725 730 735

Pro Asn Leu Arg Gly Ser Gly Val His Gly Gly Leu Ile Ile Leu Glu  
740 745 750

Pro Arg Phe Thr Gly Asp Thr Leu Ala Met Leu Leu Asn Ile Pro Pro  
755 760 765

Gln Lys Thr Leu Leu Arg Arg His Leu Thr Thr Lys Phe Asn Ala Leu  
770 775 780

Ile Gly Pro Glu Ala Glu Gln Glu Lys Arg Glu Lys Met Ala Ser Pro  
785 790 795 800

Ala Tyr Thr Pro Leu Thr Thr Thr Ala Lys Val Arg Pro Arg Lys Leu  
805 810 815

Gly Phe Ser His Phe Gly Asn Ile Arg Lys Lys Lys Phe Asp Glu Ser  
820 825 830

Thr Asp Tyr Ile Cys Pro Met Glu Pro Ser Asp Gly Val Ser Asp Ser  
835 840 845

His Arg Val Tyr Ser Gly Tyr Arg Gly Leu Ser Pro Leu Asp Ala Pro

850

855

860

Glu Leu Asp Gly Leu Asp Gln Val Gly Gln Ile Ser  
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<400> 306  
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<210> 307  
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<210> 308  
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<210> 309  
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<400> 309  
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 <220>  
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<223> /note="Description of Artificial Sequence: Reverse primer for  
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<220>  
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<210> 325  
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<400> 325  
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<210> 326  
 <211> 20  
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<220>  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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<400> 326  
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<210> 327  
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 <212> DNA  
 <213> Artificial Sequence

<220>  
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<400> 327  
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<210> 328  
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 <211> 2326  
 <212> DNA  
 <213> Homo Sapiens  
  
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 20 25 30

Gln Val Lys Met Trp Ala Gln Ala Glu Lys Glu Ala Gln Gly Lys Lys  
 35 40 45

Gly Pro Gly Glu Arg Pro Arg Lys Glu Ala Ala Ser Gln Gly Leu Leu  
 50 55 60

Lys Gln Val Leu Phe Pro Pro Ser Val Val Leu Leu Glu Ala Ala Ala  
 65 70 75 80

Arg Asn Asp Leu Glu Glu Val Arg Gln Phe Leu Gly Ser Gly Val Ser  
 85 90 95

Pro Asp Leu Ala Asn Glu Asp Gly Leu Thr Ala Leu His Gln Cys Cys  
100 105 110

Ile Asp Asp Phe Arg Glu Met Val Gln Gln Leu Leu Glu Ala Gly Ala  
115 120 125

Asn Ile Asn Ala Cys Asp Ser Glu Cys Trp Thr Pro Leu His Ala Ala  
130 135 140

Ala Thr Cys Gly His Leu His Leu Val Glu Leu Leu Ile Ala Ser Gly  
145 150 155 160

Ala Asn Leu Leu Ala Val Asn Thr Asp Gly Asn Met Pro Tyr Asp Leu  
165 170 175

Cys Asp Asp Glu Gln Thr Leu Asp Cys Leu Glu Thr Ala Met Ala Asp  
180 185 190

Arg Gly Ile Thr Gln Asp Ser Ile Glu Ala Ala Arg Ala Val Pro Glu  
195 200 205

Leu Arg Met Leu Asp Asp Ile Arg Ser Arg Leu Gln Ala Gly Ala Asp  
210 215 220

Leu His Ala Pro Leu Asp His Gly Ala Thr Leu Leu His Val Ala Ala  
225 230 235 240

Ala Asn Gly Phe Ser Glu Ala Ala Ala Leu Leu Leu Glu His Arg Ala  
245 250 255

Ser Leu Ser Ala Lys Asp Gln Asp Gly Trp Glu Pro Leu His Ala Ala  
260 265 270

Ala Tyr Trp Gly Gln Val Pro Leu Val Glu Leu Leu Val Ala His Gly  
275 280 285

Ala Asp Leu Asn Ala Lys Ser Leu Met Asp Glu Thr Pro Leu Asp Val  
290 295 300

Cys Gly Asp Glu Glu Val Arg Ala Lys Leu Leu Glu Leu Lys His Lys  
305 310 315 320

His Asp Ala Leu Leu Arg Ala Gln Ser Arg Gln Arg Ser Leu Leu Arg  
325 330 335

Arg Arg Thr Ser Ser Ala Gly Ser Arg Gly Lys Val Val Arg Arg Val  
340 345 350

Ser Leu Thr Gln Arg Thr Asp Leu Tyr Arg Lys Gln His Ala Gln Glu  
355 360 365

Ala Ile Val Trp Gln Gln Pro Pro Pro Thr Ser Pro Glu Pro Pro Glu  
370 375 380

Asp Asn Asp Asp Arg Gln Thr Gly Ala Glu Leu Arg Pro Pro Pro Pro  
385 390 395 400

Glu Glu Asp Asn Pro Glu Val Val Arg Pro His Asn Gly Arg Val Gly  
405 410 415

Gly Ser Pro Val Arg His Leu Tyr Ser Lys Arg Leu Asp Arg Ser Val  
420 425 430

Ser Tyr Gln Leu Ser Pro Leu Asp Ser Thr Thr Pro His Thr Leu Val  
435 440 445

His Asp Lys Ala His His Thr Leu Ala Asp Leu Lys Arg Gln Arg Ala  
450 455 460

Ala Ala Lys Leu Gln Arg Pro Pro Pro Glu Gly Pro Glu Ser Pro Glu  
465 470 475 480

Thr Ala Glu Pro Gly Leu Pro Gly Asp Thr Val Thr Pro Gln Pro Asp  
485 490 495

Cys Gly Phe Arg Ala Gly Gly Asp Pro Pro Leu Leu Lys Leu Thr Ala  
500 505 510

Pro Ala Val Glu Ala Pro Val Glu Arg Arg Pro Cys Cys Leu Leu Met  
515 520 525

<210> 339  
<211> 21  
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<220>  
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<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding PPP1R16A protein"

<400> 339  
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21

<210> 340  
<211> 21  
<212> DNA

<213> Artificial Sequence  
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 <400> 340  
 gccgtcaggc cgtcctcggt g 21  
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 <211> 19  
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 <400> 341  
 gctgcccga atgacctgg 19  
 <210> 342  
 <211> 19  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 342  
 cggaaatcat caatgcagc 19  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 343  
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 <210> 344  
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<400> 344  
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<210> 345  
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<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding PPP1R16A protein"

<400> 345  
gatgagcaga cgctggactg 20

<210> 346  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
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amplifying the nucleotide sequence encoding PPP1R16A protein"

<400> 346  
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<210> 347  
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<400> 347  
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<210> 348  
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<220>  
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<400> 348  
ggctcgggtgt tccagcagca g 21

<210> 349  
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<213> Artificial Sequence  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 353  
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<210> 354  
 <211> 18  
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 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 354  
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<210> 355  
 <211> 81  
 <212> DNA  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 PPP1R16A protein"

<400> 355  
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 ctgcaaagac tattttttatc c 81

<210> 356  
 <211> 37  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 PPP1R16A protein"

<400> 356  
 ctgacggccc tgcaccagtg ctgcattgat gatttcc 37

<210> 357  
 <211> 31  
 <212> DNA  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 PPP1R16A protein"

<400> 357  
 gactgccatg gccgaccgtg gcatcaccca g 31

<210> 358  
 <211> 30  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PPP1R16A protein"

<400> 358  
 gctcgtggcg cacggggccg acctgaacgc 30

<210> 359  
 <211> 29  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding PPP1R16A protein"

<400> 359  
 gcgccggcag ccgcgggaag gtggtgagg 29

<210> 360  
 <211> 1539  
 <212> DNA  
 <213> Homo Sapiens

<400> 360  
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 ggccatggag ctgaaggtgt ggggtgatgg catccagcgt gtggtctgtg gggctctcaga 120  
 gcagaccacc tgccaggaag tggtcacgac actagcccaa gcaataggcc agactggccg 180  
 ctttgtgctt gtgcagcggc ttcgggagaa ggagcggcag ttgctgccac aagagtgtcc 240  
 agtgggcgcc caggccacct gcggacagtt tgccagcgat gtccagtttg tcctgaggcg 300  
 cacagggccc agcctagctg ggaggccctc ctacagacagc tgtccacccc cggaacgctg 360  
 cctaattcgt gccagcctcc ctgtaaagcc acgggctgcg ctgggctgtg agccccgcaa 420  
 aacactgacc cccgagccag cccccagcct ctacgcccct gggcctgagg ccctgtgac 480  
 acccacacca ggctgctgca cagacctgag gggcctggag ctcagggtgc agaggaatgc 540  
 tgaggagctg ggccatgagg ccttctggga gcaagagctg cgccgggagc agggccggga 600  
 gcgagaggga caggcacgcc tgcaggcact aagtgcggcc actgctgagc atgccgccc 660  
 gctgcaggcc ctggacgctc agggccgtgc cctggaggct gagctgcagc tggcagcgga 720  
 ggcccctggg cccccctcac ctatggcctc tgccactgag cgccctgcacc aggacctggc 780

|                                                                     |      |
|---------------------------------------------------------------------|------|
| tggttcaggag cggcagagtg cggaggtgca gggcagcctg gctctggtga gccgggcccct | 840  |
| ggaggcagca gagcgagcct tgcaggctca ggctcaggag ctggaggagc tgaaccgaga   | 900  |
| gctccgtcag tgcaacctgc agcagttcat ccagcagacc ggggctgcgc tgccaccgcc   | 960  |
| cccacggcct gacagggggcc ctccctggcac tcagggccct ctgcctccag ccagagagga | 1020 |
| gtccctcctg ggcgctccct ctgagtccca tgctggtgcc cagcctaggc cccgaggtgg   | 1080 |
| cccccatgac gcagaactcc tggaggtagc agcagctcct gcccagagt ggtgtcctct    | 1140 |
| ggcagcccag cccagggctc tgtgacagcc tagtgagggc tgcaagacca tcctgcccgg   | 1200 |
| accacagaag gagagttggc ggtcacagag ggctcctctg ccaggcagtg ggaagccctg   | 1260 |
| ggtttggcct caggagctgg ggggtgcagtg ggggactgcc ctagtcttg ccaggtcgcc   | 1320 |
| cagcaccctg gagaagcatg gggcgtagcc agctcggaac ttgccaggcc ccaaaggcca   | 1380 |
| cgactgcctg ttggggacag gagatgcatg gacagtgtgc tcaagctgtg ggcatgtgct   | 1440 |
| tgcttcgccc agaggtcctt cactgtgtgt acacagcaag agcatgtgtg tgccacttcc   | 1500 |
| cctaccccaa cgtgaaaacc tcaataaaact gcccgaaagc                        | 1539 |

<210> 361  
 <211> 373  
 <212> PRT  
 <213> Homo Sapiens

<400> 361

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Leu | Leu | Gly | Leu | Ala | Ala | Met | Glu | Leu | Lys | Val | Trp | Val | Asp | Gly |
| 1   |     |     | 5   |     |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Gln | Arg | Val | Val | Cys | Gly | Val | Ser | Glu | Gln | Thr | Thr | Cys | Gln | Glu |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Val | Ile | Ala | Leu | Ala | Gln | Ala | Ile | Gly | Gln | Thr | Gly | Arg | Phe | Val |
|     |     | 35  |     |     |     | 40  |     |     |     |     |     | 45  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Val | Gln | Arg | Leu | Arg | Glu | Lys | Glu | Arg | Gln | Leu | Leu | Pro | Gln | Glu |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Pro | Val | Gly | Ala | Gln | Ala | Thr | Cys | Gly | Gln | Phe | Ala | Ser | Asp | Val |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Phe | Val | Leu | Arg | Arg | Thr | Gly | Pro | Ser | Leu | Ala | Gly | Arg | Pro | Ser |
|     |     |     | 85  |     |     |     |     |     | 90  |     |     |     |     | 95  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Asp | Ser | Cys | Pro | Pro | Pro | Glu | Arg | Cys | Leu | Ile | Arg | Ala | Ser | Leu |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |

Pro Val Lys Pro Arg Ala Ala Leu Gly Cys Glu Pro Arg Lys Thr Leu  
115 120 125

Thr Pro Glu Pro Ala Pro Ser Leu Ser Arg Pro Gly Pro Ala Ala Pro  
130 135 140

Val Thr Pro Thr Pro Gly Cys Cys Thr Asp Leu Arg Gly Leu Glu Leu  
145 150 155 160

Arg Val Gln Arg Asn Ala Glu Glu Leu Gly His Glu Ala Phe Trp Glu  
165 170 175

Gln Glu Leu Arg Arg Glu Gln Ala Arg Glu Arg Glu Gly Gln Ala Arg  
180 185 190

Leu Gln Ala Leu Ser Ala Ala Thr Ala Glu His Ala Ala Arg Leu Gln  
195 200 205

Ala Leu Asp Ala Gln Ala Arg Ala Leu Glu Ala Glu Leu Gln Leu Ala  
210 215 220

Ala Glu Ala Pro Gly Pro Pro Ser Pro Met Ala Ser Ala Thr Glu Arg  
225 230 235 240

Leu His Gln Asp Leu Ala Val Gln Glu Arg Gln Ser Ala Glu Val Gln  
245 250 255

Gly Ser Leu Ala Leu Val Ser Arg Ala Leu Glu Ala Ala Glu Arg Ala  
260 265 270

Leu Gln Ala Gln Ala Gln Glu Leu Glu Glu Leu Asn Arg Glu Leu Arg  
275 280 285

Gln Cys Asn Leu Gln Gln Phe Ile Gln Gln Thr Gly Ala Ala Leu Pro  
290 295 300

Pro Pro Pro Arg Pro Asp Arg Gly Pro Pro Gly Thr Gln Gly Pro Leu  
305 310 315 320

Pro Pro Ala Arg Glu Glu Ser Leu Leu Gly Ala Pro Ser Glu Ser His  
325 330 335

Ala Gly Ala Gln Pro Arg Pro Arg Gly Gly Pro His Asp Ala Glu Leu  
340 345 350

Leu Glu Val Ala Ala Ala Pro Ala Pro Glu Trp Cys Pro Leu Ala Ala  
355 360 365

Gln Pro Gln Ala Leu  
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<210> 362  
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<220>  
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<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 362  
ctgccaggaa gtggtcac 19

<210> 363  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
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<400> 363  
gccgctgcac aagcaca 17

<210> 364  
<211> 16  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 364  
catggagctg aaggtg 16

<210> 365  
<211> 17  
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<220>  
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<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 365  
ctcaggacaa actggac 17

<210> 366  
<211> 16

<212> DNA  
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 <211> 17  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 369  
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<400> 370  
cacggcctga caggggcc 18

<210> 371  
<211> 15  
<212> DNA  
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<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 371  
gcctaggctg ggcac 15

<210> 372  
<211> 18  
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<220>  
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<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 372  
ctctgagtcc catgctgg 18

<210> 373  
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<400> 373  
gacaccactc tggggc 16

<210> 374  
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<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding RASSF7 protein"

<400> 374  
tgcccagcct agggcc 16

<210> 375  
<211> 17



<212> DNA  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 375  
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 <210> 376  
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 <220>  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 <400> 376  
 gagaggtcct tcactgtgtg tacacagcaa gagcatgtgt gtgccacttc 50  
  
 <210> 377  
 <211> 51  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 RASSF7 protein"  
  
 <400> 377  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 RASSF7 protein"  
  
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 <210> 379  
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 <212> DNA  
 <213> Artificial Sequence  
  
 <220>

<221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding RASSF7 protein"

<400> 379  
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<210> 380  
 <211> 60  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding RASSF7 protein"

<400> 380  
 gaggagctgg gccatgaggc cttctgggag caagagctgc gccgggagca ggcccgggag 60

<210> 381  
 <211> 14  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Epitope of RASSF7"

<400> 381  
 Cys Thr Asp Leu Arg Gly Leu Glu Leu Arg Val Gln Arg Asn  
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<210> 382  
 <211> 1237  
 <212> DNA  
 <213> Homo Sapiens

<400> 382  
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 ggctgagcag cagggccggg agcttgaggc tgagtgtccc gtctgtgga accccttcaa 180  
 caacacgttc cataccccca aaatgctgga ttgctgccac tccttctgcg tggaatgtct 240  
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 gccacagtg ctggcctcag ggcagcctgt cactgacttg ccacaggaca ctgccatgct 360  
 cgccctgctc cgcctggagc cccaccatgt catcctggaa ggccatcagc tgtgcctcaa 420  
 ggaccagccc aagagccgct acttctgctg ccagcctcaa gtctacacgc tggaccttgg 480  
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gccatcctc atccccagcc accactcttt gagggagtgt ttccgcaacc ctcagttccg 600  
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 cttttggacc aagcagttcc tttgggggtgt ggggtgagt ctgttcccag acaagaaacc 720  
 aaaccttttt cggttgctgc tgggtatggt gactacggag cctcatttgg tattgtcttc 780  
 cttttagtggt ttgtttattt tacaatccag ggattgttca ggccatgtgt ttgcttctgg 840  
 gaacaatttt aaaaaaaaaac aaaaaaacga aaagcttgaa ggactgggag atgtggagcg 900  
 acctccgggt gtgagtgtgg cgtcattgaa gggcagagaa gcggttctga ccacagagct 960  
 ccacagcaag ttgtgcaaaa gggctgcaca gtggtatcca ggaacctgac tagcccaaatt 1020  
 agcaagttgc atttctcact ggagctgctt caaaatcagt gcatattttt ttgagttgct 1080  
 cttttactat gggttgctaa aaaaaaaaaa aaaattggga agtgagcttc aattctgtgg 1140  
 gtaaatgtgt gtttgtttct ctttgaatgt cttgccactg gttgcagtaa aagtgttctg 1200  
 tattcattaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 1237

<210> 383  
 <211> 192  
 <212> PRT  
 <213> Homo Sapiens

<400> 383

Met Ala Glu Gln Gln Gly Arg Glu Leu Glu Ala Glu Cys Pro Val Cys  
 1 5 10 15

Trp Asn Pro Phe Asn Asn Thr Phe His Thr Pro Lys Met Leu Asp Cys  
 20 25 30

Cys His Ser Phe Cys Val Glu Cys Leu Ala His Leu Ser Leu Val Thr  
 35 40 45

Pro Ala Arg Arg Arg Leu Leu Cys Pro Leu Cys Arg Gln Pro Thr Val  
 50 55 60

Leu Ala Ser Gly Gln Pro Val Thr Asp Leu Pro Thr Asp Thr Ala Met  
 65 70 75 80

Leu Ala Leu Leu Arg Leu Glu Pro His His Val Ile Leu Glu Gly His  
 85 90 95

Gln Leu Cys Leu Lys Asp Gln Pro Lys Ser Arg Tyr Phe Leu Arg Gln  
 100 105 110

Pro Gln Val Tyr Thr Leu Asp Leu Gly Pro Gln Pro Gly Gly Gln Thr  
 115 120 125

Gly Pro Pro Pro Asp Thr Ala Ser Ala Thr Val Ser Thr Pro Ile Leu  
130 135 140

Ile Pro Ser His His Ser Leu Arg Glu Cys Phe Arg Asn Pro Gln Phe  
145 150 155 160

Arg Ile Phe Ala Tyr Leu Met Ala Val Ile Leu Ser Val Thr Leu Leu  
165 170 175

Leu Ile Phe Ser Ile Phe Trp Thr Lys Gln Phe Leu Trp Gly Val Gly  
180 185 190

<210> 384  
<211> 17  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding RNF183 protein"

<400> 384  
gagaagctgg gctggag 17

<210> 385  
<211> 16  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding RNF183 protein"

<400> 385  
cagccacaca cgggga 16

<210> 386  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 386  
cagctgtgtg ctaagaacaa ag 22

<210> 387  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
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 <400> 387  
 gccctgctgc tcagccatc 19  
  
 <210> 388  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 388  
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 <210> 389  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <210> 390  
 <211> 19  
 <212> DNA  
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 <220>  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <210> 391  
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 <213> Artificial Sequence  
  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 391

caagtcagtg acaggctgc 19

<210> 392  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding RNF183 protein"

<400> 392  
gtctacacgc tggaccttg 19

<210> 393  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
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amplifying the nucleotide sequence encoding RNF183 protein"

<400> 393  
gatgcggaac tgagggttg 19

<210> 394  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding RNF183 protein"

<400> 394  
ctacctgatg gccgtcatc 19

<210> 395  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 395  
ccagcagcaa ccgaaaaag 19

<210> 396  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <210> 397  
 <211> 17  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> Reverse primer for amplifying the nucleotide sequence encoding  
 RNF183 protein  
  
 <400> 397  
 gtgctgctct cccaggg 17  
  
 <210> 398  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <210> 399  
 <211> 23  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding RNF183 protein"  
  
 <400> 399  
 ctgtttctca tatgggtcat tcg 23  
  
 <210> 400  
 <211> 41  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 RNF183 protein"

<400> 400  
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<210> 401  
 <211> 32  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 RNF183 protein"

<400> 401  
 gccacggac actgcatgc tcgccctgct cc 32

<210> 402  
 <211> 37  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 RNF183 protein"

<400> 402  
 ggaccagccc aagagccgct acttcctgcg ccagcct 37

<210> 403  
 <211> 32  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 RNF183 protein"

<400> 403  
 cgctggacct tggccccag cctgggggcc ag 32

<210> 404  
 <211> 28  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 RNF183 protein"

<400> 404  
 gttcctttgg ggtgtgggt gagtgctg 28



<210> 405  
 <211> 60  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding RNF183 protein"

<400> 405  
 cagtggatc caggaacctg actagcccaa atagcaagtt gcatttctca ctggagctgc 60

<210> 406  
 <211> 1413  
 <212> DNA  
 <213> Homo Sapiens

<400> 406  
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 atgtcggtag attacgcggc ggggctgtcg ccgtacgcgg acaagggcaa gtgcggcctc 120  
 ccggagatct tcgaccccc ggaggagctg gagcgggaagg tgtgggaact ggcgaggctg 180  
 gtctggcagt cttccagtgt ggtgttccac acgggtgccg gcatcagcac tgcctctggc 240  
 atccccgact tcagggacaa actggcagag ctccacggga acatgtttgt ggaagaatgt 300  
 gccaaagtga agacgcagta cgtccgagac acagtcgtgg gcaccatggg cctgaaggcc 360  
 acgggccggc tctgcaccgt ggctaaggca agggggctgc gagcctgcag gggagagctg 420  
 agggacacca tcctagactg ggaggactcc ctgcccagacc gggacctggc actcgccgat 480  
 gaggccagca gatccggccc agcgggaacc tgccgctggc taccaagcgc cggggaggcc 540  
 gcctggatcat cgtcaacctg cagcccacca agcagaccg ccatgctgac ctccgcatcc 600  
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 cctgggacgg cccccgtgtg ctggagaggg cgctgccacc cctgccccgc ccgcccaccc 720  
 ccaagctgga gcccaaggag gaatctccca cccggatcaa cggtctatc cccgccggcc 780  
 ccaagcagga gccctgcgcc cagcacaacg gctcagagcc cgccagcccc aaacgggagc 840  
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 aacaggagtg aactccctct gtccccagg cctcccttct gggcccccta cagcccaccc 1260

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<210> 407  
<211> 187  
<212> PRT  
<213> Homo Sapiens

<400> 407

Met Ser Val Asn Tyr Ala Ala Gly Leu Ser Pro Tyr Ala Asp Lys Gly  
1 5 10 15

Lys Cys Gly Leu Pro Glu Ile Phe Asp Pro Pro Glu Glu Leu Glu Arg  
20 25 30

Lys Val Trp Glu Leu Ala Arg Leu Val Trp Gln Ser Ser Ser Val Val  
35 40 45

Phe His Thr Gly Ala Gly Ile Ser Thr Ala Ser Gly Ile Pro Asp Phe  
50 55 60

Arg Asp Lys Leu Ala Glu Leu His Gly Asn Met Phe Val Glu Glu Cys  
65 70 75 80

Ala Lys Cys Lys Thr Gln Tyr Val Arg Asp Thr Val Val Gly Thr Met  
85 90 95

Gly Leu Lys Ala Thr Gly Arg Leu Cys Thr Val Ala Lys Ala Arg Gly  
100 105 110

Leu Arg Ala Cys Arg Gly Glu Leu Arg Asp Thr Ile Leu Asp Trp Glu  
115 120 125

Asp Ser Leu Pro Asp Arg Asp Leu Ala Leu Ala Asp Glu Ala Ser Arg  
130 135 140

Ser Gly Pro Ala Gly Thr Cys Arg Trp Leu Pro Ser Ala Gly Glu Ala  
145 150 155 160

Ala Trp Ser Ser Ser Thr Cys Ser Pro Pro Ser Thr Thr Ala Met Leu  
165 170 175

Thr Ser Ala Ser Met Ala Thr Leu Thr Arg Ser  
180 185

<210> 408  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> Forward primer for amplifying the nucleotide sequence encoding  
 SIRT6 protein  
  
 <400> 408  
 ttgtggaaga atgtgccaag 20

<210> 409  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 409  
 ccttagccac ggtgcagag 19

<210> 410  
 <211> 20  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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<210> 411  
 <211> 20  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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<210> 412  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source

<223> /note="Description of Artificial Sequence: Forward primer for amplifying the nucleotide sequence encoding SIRT6 protein"

<400> 412  
agctgagga caccatccta 20

<210> 413  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for amplifying the nucleotide sequence encoding SIRT6 protein"

<400> 413  
gcaggttgac gatgaccag 19

<210> 414  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for amplifying the nucleotide sequence encoding SIRT6 protein"

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<210> 415  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Reverse primer for amplifying the nucleotide sequence encoding SIRT6 protein"

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atgtaccag cgtgatggac 20

<210> 416  
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<210> 417  
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<223> /note="Description of Artificial Sequence: Reverse primer for amplifying the nucleotide sequence encoding SIRT6 protein"

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<210> 422  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding SIRT6 protein"

<400> 422  
tgtaagacgc agtacgtccg 20

<210> 423  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding SIRT6 protein"

<400> 423  
gacttcaggg acaaactggc 20

<210> 424  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding SIRT6 protein"

<400> 424  
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<210> 425  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding SIRT6 protein"

<400> 425  
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<210> 426  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a  
nucleotide molecule having a nucleic acid sequence encoding SIRT6  
protein"

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<210> 427  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
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protein"

<400> 427  
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<210> 428  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a  
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<400> 428  
gagtctggac catggaggag 20

<210> 429  
<211> 50  
<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a  
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protein"

<400> 429  
gaagtggggg atcagtagag gcttgcaactg cctttggggc tggagggaga 50

<210> 430  
 <211> 2859  
 <212> DNA  
 <213> Homo Sapiens

<400> 430  
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 tttggcattg cgatctctgg aggccgagac cggcccgggt gatccatggt tgtatctgac 180  
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 aacgggggtt ccatggagaa tgccacctcc gcgtttgcc ttcagatact caagacctgc 300  
 accaagatgg ccaacatcac agtgaaacgt ccccgaggga tccacctgcc cgccaccaa 360  
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 gacagcgaag agtttggcgt caagctgggc agtcagatct tcatcaagca cattacagat 720  
 tcgggcctgg ctgcccggca ccgtgggctg caggaaggag atctcattct acagatcaac 780  
 ggggtgtcta gccagaacct gtcactgaac gacaccggc gactgattga gaagtcagaa 840  
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 ccagatgagc aacggtcaga gttgccagg gaaagcagct atgacatcta cagagtgcc 1200  
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 aaaatggtgc agtcccgcgt gggtgactcc ttctacatcc gcactcactt tgagctggag 1560  
 cccagtccac cgtctggcct gggcttcacc cgtggcgacg tcttcacgt gctggacacg 1620  
 ctgcaccccc gccccgggca gagccacgca cgaggaggcc actggctggc ggtgcgcatg 1680



ggtcgtgacc tgcgggagca agagcggggc atcattccca accagagcag ggcggagcag 1740  
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 actcagcggg gccgtgagga cctctcagct ctgacccgac agggccgcta cccgccctac 1920  
 gaacgagtgg tgttgcgaga agccagtttc aagcgcccgg tagtgatcct gggacccgtg 1980  
 gccgacattg ctatgcagaa gttgactgct gagatgcctg accagtttga aatcgagag 2040  
 actgtgtcca ggaccgacag cccctccaag atcatcaaac tagacaccgt gcgggtgatt 2100  
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 ggggcccagg tggacagccg ccacccccag ggacagtggc gacaggacag catgcgaacc 2760  
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 gaagacgggt atgactgggg tccggccact gacctgtga 2859

<210> 431  
 <211> 952  
 <212> PRT  
 <213> Homo Sapiens

<400> 431

Met Asn Leu Cys Gly Leu Met Pro Ile Phe Pro Ala Pro Leu Asp Gln  
 1 5 10 15

Val Ala Asp Met Glu Glu Leu Thr Ile Trp Glu Gln His Thr Ala Thr  
 20 25 30

Leu Ser Lys Asp Pro Arg Arg Gly Phe Gly Ile Ala Ile Ser Gly Gly  
 35 40 45

Arg Asp Arg Pro Gly Gly Ser Met Val Val Ser Asp Val Val Pro Gly  
 50 55 60

Gly Pro Ala Glu Gly Arg Leu Gln Thr Gly Asp His Ile Val Met Val  
65 70 75 80

Asn Gly Val Ser Met Glu Asn Ala Thr Ser Ala Phe Ala Ile Gln Ile  
85 90 95

Leu Lys Thr Cys Thr Lys Met Ala Asn Ile Thr Val Lys Arg Pro Arg  
100 105 110

Arg Ile His Leu Pro Ala Thr Lys Ala Ser Pro Ser Ser Pro Gly Arg  
115 120 125

Gln Asp Ser Asp Glu Asp Asp Gly Pro Gln Arg Val Glu Glu Val Asp  
130 135 140

Gln Gly Arg Gly Tyr Asp Gly Asp Ser Ser Ser Gly Ser Gly Arg Ser  
145 150 155 160

Trp Asp Glu Arg Ser Arg Arg Pro Arg Pro Gly Arg Arg Gly Arg Ala  
165 170 175

Gly Ser His Gly Arg Arg Ser Pro Gly Gly Gly Ser Glu Ala Asn Gly  
180 185 190

Leu Ala Leu Val Ser Gly Phe Lys Arg Leu Pro Arg Gln Asp Val Gln  
195 200 205

Met Lys Pro Val Lys Ser Val Leu Val Lys Arg Arg Asp Ser Glu Glu  
210 215 220

Phe Gly Val Lys Leu Gly Ser Gln Ile Phe Ile Lys His Ile Thr Asp  
225 230 235 240

Ser Gly Leu Ala Ala Arg His Arg Gly Leu Gln Glu Gly Asp Leu Ile  
245 250 255

Leu Gln Ile Asn Gly Val Ser Ser Gln Asn Leu Ser Leu Asn Asp Thr  
260 265 270

Arg Arg Leu Ile Glu Lys Ser Glu Gly Lys Leu Ser Leu Leu Val Leu  
275 280 285

Arg Asp Arg Gly Gln Phe Leu Val Asn Ile Pro Pro Ala Val Ser Asp  
290 295 300

Ser Asp Ser Ser Pro Leu Glu Glu Gly Val Thr Met Ala Asp Glu Met  
305 310 315 320

Ser Ser Pro Pro Ala Asp Ile Ser Asp Leu Ala Ser Glu Leu Ser Gln  
325 330 335

Ala Pro Pro Ser His Ile Pro Pro Pro Pro Arg His Ala Gln Arg Ser  
340 345 350

Pro Glu Ala Ser Gln Thr Asp Ser Pro Val Glu Ser Pro Arg Leu Arg  
355 360 365

Arg Glu Ser Ser Val Asp Ser Arg Thr Ile Ser Glu Pro Asp Glu Gln  
370 375 380

Arg Ser Glu Leu Pro Arg Glu Ser Ser Tyr Asp Ile Tyr Arg Val Pro  
385 390 395 400

Ser Ser Gln Ser Met Glu Asp Arg Gly Tyr Ser Pro Asp Thr Arg Val  
405 410 415

Val Arg Phe Leu Lys Gly Lys Ser Ile Gly Leu Arg Leu Ala Gly Gly  
420 425 430

Asn Asp Val Gly Ile Phe Val Ser Gly Val Gln Ala Gly Ser Pro Ala  
435 440 445

Asp Gly Gln Gly Ile Gln Glu Gly Asp Gln Ile Leu Gln Val Asn Asp  
450 455 460

Val Pro Phe Gln Asn Leu Thr Arg Glu Glu Ala Val Gln Phe Leu Leu  
465 470 475 480

Gly Leu Pro Pro Gly Glu Glu Met Glu Leu Val Thr Gln Arg Lys Gln  
485 490 495

Asp Ile Phe Trp Lys Met Val Gln Ser Arg Val Gly Asp Ser Phe Tyr  
500 505 510

Ile Arg Thr His Phe Glu Leu Glu Pro Ser Pro Pro Ser Gly Leu Gly  
515 520 525

Phe Thr Arg Gly Asp Val Phe His Val Leu Asp Thr Leu His Pro Gly  
530 535 540

Pro Gly Gln Ser His Ala Arg Gly Gly His Trp Leu Ala Val Arg Met  
545 550 555 560

Gly Arg Asp Leu Arg Glu Gln Glu Arg Gly Ile Ile Pro Asn Gln Ser

565

570

575

Arg Ala Glu Gln Leu Ala Ser Leu Glu Ala Ala Gln Arg Ala Val Gly  
 580 585 590

Val Gly Pro Gly Ser Ser Ala Gly Ser Asn Ala Arg Ala Glu Phe Trp  
 595 600 605

Arg Leu Arg Gly Leu Arg Arg Gly Ala Lys Lys Thr Thr Gln Arg Ser  
 610 615 620

Arg Glu Asp Leu Ser Ala Leu Thr Arg Gln Gly Arg Tyr Pro Pro Tyr  
 625 630 635 640

Glu Arg Val Val Leu Arg Glu Ala Ser Phe Lys Arg Pro Val Val Ile  
 645 650 655

Leu Gly Pro Val Ala Asp Ile Ala Met Gln Lys Leu Thr Ala Glu Met  
 660 665 670

Pro Asp Gln Phe Glu Ile Ala Glu Thr Val Ser Arg Thr Asp Ser Pro  
 675 680 685

Ser Lys Ile Ile Lys Leu Asp Thr Val Arg Val Ile Ala Glu Lys Asp  
 690 695 700

Lys His Ala Leu Leu Asp Val Thr Pro Ser Ala Ile Glu Arg Leu Asn  
 705 710 715 720

Tyr Val Gln Tyr Tyr Pro Ile Val Val Phe Phe Ile Pro Glu Ser Arg  
 725 730 735

Pro Ala Leu Lys Ala Leu Arg Gln Trp Leu Ala Pro Ala Ser Arg Arg  
 740 745 750

Ser Thr Arg Arg Leu Tyr Ala Gln Ala Gln Lys Leu Arg Lys His Ser  
 755 760 765

Ser His Leu Phe Thr Ala Thr Ile Pro Leu Asn Gly Thr Ser Asp Thr  
 770 775 780

Trp Tyr Gln Glu Leu Lys Ala Ile Ile Arg Glu Gln Gln Thr Arg Pro  
 785 790 795 800

Ile Trp Thr Ala Glu Asp Gln Leu Asp Gly Ser Leu Glu Asp Asn Leu  
 805 810 815

Asp Leu Pro His His Gly Leu Ala Asp Ser Ser Ala Asp Leu Ser Cys  
820 825 830

Asp Ser Arg Val Asn Ser Asp Tyr Glu Thr Asp Gly Glu Gly Gly Ala  
835 840 845

Tyr Thr Asp Gly Glu Gly Tyr Thr Asp Gly Glu Gly Gly Pro Tyr Thr  
850 855 860

Asp Val Asp Asp Glu Pro Pro Ala Pro Ala Leu Ala Arg Ser Ser Glu  
865 870 875 880

Pro Val Gln Ala Asp Glu Ser Gln Ser Pro Arg Asp Arg Gly Arg Ile  
885 890 895

Ser Ala His Gln Gly Ala Gln Val Asp Ser Arg His Pro Gln Gly Gln  
900 905 910

Trp Arg Gln Asp Ser Met Arg Thr Tyr Glu Arg Glu Ala Leu Lys Lys  
915 920 925

Lys Phe Met Arg Val His Asp Ala Glu Ser Ser Asp Glu Asp Gly Tyr  
930 935 940

Asp Trp Gly Pro Ala Thr Asp Leu  
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<210> 432  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding TJP3 protein"

<400> 432  
ccctcgacca ggtggctgac 20

<210> 433  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding TJP3 protein"

<400> 433  
cctccagaga tcgcaatgc 19

<210> 434  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 434  
 gtatctgacg tggtagctg 19  
  
 <210> 435  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding TJP3 protein"  
  
 <400> 435  
 ggcaaacgcg gaggtggcat tc 22  
  
 <210> 436  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 436  
 cgggggtttcc atggagaatg 20  
  
 <210> 437  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 437  
 gcgggcaggt ggatcctcc 19  
  
 <210> 438  
 <211> 20  
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 <213> Artificial Sequence  
  
 <220>

<221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 438  
 gcaggacgtg cagatgaagc 20  
  
 <210> 439  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding TJP3 protein"  
  
 <400> 439  
 cccgaatctg taatgtgctt g 21  
  
 <210> 440  
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 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 440  
 gtgggctgca ggaaggagat c 21  
  
 <210> 441  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding TJP3 protein"  
  
 <400> 441  
 gaactgccca cgatctctca gc 22  
  
 <210> 442  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 442  
 gatcgtgggc agttcctgg 19

<210> 443  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 443  
gatgtctgca gggggagagg 20

<210> 444  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 444  
caccccgca tgctcagcg 19

<210> 445  
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<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
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<400> 445  
ccgagatggt tctggaatc 19

<210> 446  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
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<400> 446  
gagtccccgg cttcggcgg 19

<210> 447  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>



<221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 cgatcctcca tgctctgact g 21  
  
 <210> 448  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding TJP3 protein"  
  
 <400> 448  
 gtgcagggcgg gcagcccg 18  
  
 <210> 449  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 449  
 gtcttgcttc ctctgcgtc 19  
  
 <210> 450  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding TJP3 protein"  
  
 <400> 450  
 cgagagcagc agacgcggcc 20  
  
 <210> 451  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 451  
 gaggtcagcg gagctgtcg 19

<210> 452  
 <211> 60  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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 protein"  
  
 <400> 452  
 cagggacagt ggcgacagga cagcatgcga acctatgaac gggaagccct gaagaaaaag 60  
  
 <210> 453  
 <211> 42  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding TJP3  
 protein"  
  
 <400> 453  
 gaacagcaca cggccacact gtccaaggac ccccgccggg gc 42  
  
 <210> 454  
 <211> 54  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding TJP3  
 protein"  
  
 <400> 454  
 accaagatgg ccaacatcac agtgaaacgt ccccgaggga tccacctgcc cgcc 54  
  
 <210> 455  
 <211> 54  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding TJP3  
 protein"  
  
 <400> 455  
 cagtgcagc gacagctcgc cattggagga aggcgtgacc atggctgatg agat 54  
  
 <210> 456  
 <211> 54

<212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding TJP3 protein"

<400> 456  
 cgagtggtgt tgcgagaagc cagtttcaag cgcccggtag tgatcctggg accc 54

<210> 457  
 <211> 85  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Partial recombinant amino acid sequence of TJP3"

<400> 457

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Glu | Pro | Pro | Ala | Pro | Ala | Leu | Ala | Arg | Ser | Ser | Glu | Pro | Val | Gln |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Asp | Glu | Ser | Gln | Ser | Pro | Arg | Asp | Arg | Gly | Arg | Ile | Ser | Ala | His |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Gly | Ala | Gln | Val | Asp | Ser | Arg | His | Pro | Gln | Gly | Gln | Trp | Arg | Gln |
|     | 35  |     |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Ser | Met | Arg | Thr | Tyr | Glu | Arg | Glu | Ala | Leu | Lys | Lys | Lys | Phe | Met |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Val | His | Asp | Ala | Glu | Ser | Ser | Asp | Glu | Asp | Gly | Tyr | Asp | Trp | Gly |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |

|     |     |     |     |     |
|-----|-----|-----|-----|-----|
| Pro | Ala | Thr | Asp | Leu |
|     |     |     |     | 85  |

<210> 458  
 <211> 1938  
 <212> DNA  
 <213> Homo Sapiens

<400> 458

|            |            |            |            |            |            |  |     |
|------------|------------|------------|------------|------------|------------|--|-----|
| ggggcgcttc | ctggggccgc | gcgtccaggg | agctgtgccg | tccgcccgtc | cgtctgcccg |  | 60  |
| caggcattgc | ccgagccagc | cgagccgcca | gagccgcggg | ccgcgggggt | gtcgcggggc |  | 120 |
| caaccccagg | atgctcccct | gcgcctcctg | cctaccggg  | tctctactgc | tctgggcgt  |  | 180 |
| gctactgttg | ctcttgggat | cagcttctcc | tcaggattct | gaagagcccg | acagctacac |  | 240 |

|                                                                    |      |
|--------------------------------------------------------------------|------|
| ggaatgcaca gatggctatg agtgggaccc agacagccag cactgccggg atgtcaacga  | 300  |
| gtgtctgacc atccctgagg cctgcaaggg ggaaatgaag tgcatacaacc actacggggg | 360  |
| ctacttgtgc ctgccccgct ccgctgccgt catcaacgac ctacacggcg agggaccccc  | 420  |
| gccaccagtg cctcccgtc aacaccccaa ccctgcca ccaggctatg agcccacga      | 480  |
| tcaggacagc tgtgtggatg tggacgagtg tgcccaggcc ctgcacgact gtcgcccag   | 540  |
| ccaggactgc cataacttgc ctggctccta tcagtgcacc tgccctgatg gttaccgcaa  | 600  |
| gatcggggcc gagtgtgtgg acatagacga gtgccgctac cgctactgcc agcaccgctg  | 660  |
| cgtgaacctg cctggctcct tccgctgcca gtgcgagccg ggcttcacgc tggggcctaa  | 720  |
| caaccgctcc tgtgttgatg tgaacgagtg tgacatgggg gcccacatgc agcagcgctg  | 780  |
| cttcaactcc tatgggacct tccgtgtgcg ctgccaccag ggctatgagc tgcacggga   | 840  |
| tggcttctcc tgcagtgata ttgatgagt tagctactcc agctacctct gtcagtaccg   | 900  |
| ctgcgtcaac gagccaggcc gtttctcctg cactgcca cagggttacc agctgctggc    | 960  |
| cacacgcctc tgccaagaca ttgatgagt tgagctctgt ggcaccagt gctccaggcc    | 1020 |
| ccaaacctgt gtcaacttcc atgggggcta ccgctgcgtg gacaccaacc gctgcgtgga  | 1080 |
| gccctacatc caggctctctg agaaccgctg tctctgcccg gcctccaacc ctctatgtcg | 1140 |
| agagcagcct tcatccattg tgcaccgcta catgaccatc acctcgagc ggagcgtgcc   | 1200 |
| cgtgacgtg ttccagatcc aggcgacctc cgtctacccc ggtgcctaca atgcctttca   | 1260 |
| gatccgtgct ggaaactcgc agggggactt ttacattagg caaatcaaca acgtcagcgc  | 1320 |
| catgctggtc ctgcgccggc cggtgacggg cccccgggag tacgtgctgg acctggagat  | 1380 |
| ggtcaccatg aattccctca tgagctaccg ggccagctct gtactgaggc tcaccgtctt  | 1440 |
| tgtaggggcc tacaccttct gaggagcagg agggagccac cctccctgca gctaccctag  | 1500 |
| ctgaggagcc tgttgtgagg ggcagaatga gaaaggcaat aaaggagaaa agaaagtcct  | 1560 |
| ggtggctgag gtgggcgggt cacactgcag gaagcctcag gctggggcag ggtggcactt  | 1620 |
| gggggggcag gccaaagtta cctaaatggg ggtctctata tggtcaggcc caggggcccc  | 1680 |
| cattgacagg agctgggagc tctgcaccac gagcttcagt caccgcgaga ggagaggagg  | 1740 |
| taacgaggag ggcggactcc aggccccggc ccagagattt ggacttggct ggcttgacag  | 1800 |
| ggtcctaaga aactccactc tggacagcgc caggaggccc tgggttccat tcctaactct  | 1860 |
| gcctcaaact gtacatttgg ataagcccta gtagttccct gggcctgttt ttctataaaa  | 1920 |
| cgaggcaact ggactgtt                                                | 1938 |

<210> 459  
 <211> 443  
 <212> PRT  
 <213> Homo Sapiens

<400> 459

Met Leu Pro Cys Ala Ser Cys Leu Pro Gly Ser Leu Leu Leu Trp Ala  
1 5 10 15

Leu Leu Leu Leu Leu Leu Gly Ser Ala Ser Pro Gln Asp Ser Glu Glu  
20 25 30

Pro Asp Ser Tyr Thr Glu Cys Thr Asp Gly Tyr Glu Trp Asp Pro Asp  
35 40 45

Ser Gln His Cys Arg Asp Val Asn Glu Cys Leu Thr Ile Pro Glu Ala  
50 55 60

Cys Lys Gly Glu Met Lys Cys Ile Asn His Tyr Gly Gly Tyr Leu Cys  
65 70 75 80

Leu Pro Arg Ser Ala Ala Val Ile Asn Asp Leu His Gly Glu Gly Pro  
85 90 95

Pro Pro Pro Val Pro Pro Ala Gln His Pro Asn Pro Cys Pro Pro Gly  
100 105 110

Tyr Glu Pro Asp Asp Gln Asp Ser Cys Val Asp Val Asp Glu Cys Ala  
115 120 125

Gln Ala Leu His Asp Cys Arg Pro Ser Gln Asp Cys His Asn Leu Pro  
130 135 140

Gly Ser Tyr Gln Cys Thr Cys Pro Asp Gly Tyr Arg Lys Ile Gly Pro  
145 150 155 160

Glu Cys Val Asp Ile Asp Glu Cys Arg Tyr Arg Tyr Cys Gln His Arg  
165 170 175

Cys Val Asn Leu Pro Gly Ser Phe Arg Cys Gln Cys Glu Pro Gly Phe  
180 185 190

Gln Leu Gly Pro Asn Asn Arg Ser Cys Val Asp Val Asn Glu Cys Asp  
195 200 205

Met Gly Ala Pro Cys Glu Gln Arg Cys Phe Asn Ser Tyr Gly Thr Phe  
210 215 220

Leu Cys Arg Cys His Gln Gly Tyr Glu Leu His Arg Asp Gly Phe Ser  
225 230 235 240

Cys Ser Asp Ile Asp Glu Cys Ser Tyr Ser Ser Tyr Leu Cys Gln Tyr  
245 250 255

Arg Cys Val Asn Glu Pro Gly Arg Phe Ser Cys His Cys Pro Gln Gly  
260 265 270

Tyr Gln Leu Leu Ala Thr Arg Leu Cys Gln Asp Ile Asp Glu Cys Glu  
275 280 285

Ser Gly Ala His Gln Cys Ser Glu Ala Gln Thr Cys Val Asn Phe His  
290 295 300

Gly Gly Tyr Arg Cys Val Asp Thr Asn Arg Cys Val Glu Pro Tyr Ile  
305 310 315 320

Gln Val Ser Glu Asn Arg Cys Leu Cys Pro Ala Ser Asn Pro Leu Cys  
325 330 335

Arg Glu Gln Pro Ser Ser Ile Val His Arg Tyr Met Thr Ile Thr Ser  
340 345 350

Glu Arg Ser Val Pro Ala Asp Val Phe Gln Ile Gln Ala Thr Ser Val  
355 360 365

Tyr Pro Gly Ala Tyr Asn Ala Phe Gln Ile Arg Ala Gly Asn Ser Gln  
370 375 380

Gly Asp Phe Tyr Ile Arg Gln Ile Asn Asn Val Ser Ala Met Leu Val  
385 390 395 400

Leu Ala Arg Pro Val Thr Gly Pro Arg Glu Tyr Val Leu Asp Leu Glu  
405 410 415

Met Val Thr Met Asn Ser Leu Met Ser Tyr Arg Ala Ser Ser Val Leu  
420 425 430

Arg Leu Thr Val Phe Val Gly Ala Tyr Thr Phe  
435 440

<210> 460

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 460

tgctcttggg atcagcttct 20

<210> 461  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 461  
cctcagggat ggtcagacac 20

<210> 462  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 462  
tgcccaccag gctatgag 18

<210> 463  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 463  
caggcaagtt atggcagtcc 20

<210> 464  
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<212> DNA  
<213> Artificial sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 464  
aacttgctg gctcctatca 20

<210> 465  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 465  
 gtgctggcag tagcggtag 19  
  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 ggcctaaca cogctcct 18  
  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 468  
 tatgggacct tcctgtgtcg 20  
  
 <210> 469  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding EFEMP2 protein"  
  
 <400> 469



gatgcagcgg tactgacaga 20

<210> 470  
<211> 20  
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<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 470  
gtcagtaccg ctgcatcaac 20

<210> 471  
<211> 20  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 471  
cgcaccagac tcacactcat 20

<210> 472  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 472  
gtggagccct acatccaggt 20

<210> 473  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding EFEMP2 protein"

<400> 473  
tccgaggtga tggatcatgta 20

<210> 474  
<211> 50  
<212> DNA  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding  
 EFEMP2 protein"

<400> 474  
 ttcattccatt gtgcaccgct acatgacccat cacctcggag cggagcgtgc 50

<210> 475  
 <211> 20  
 <212> DNA  
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<220>  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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<400> 475  
 gaagagcccg acagctacac 20

<210> 476  
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 <212> DNA  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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<400> 476  
 caggcaagtt atggcagttcc 20

<210> 477  
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 <212> DNA  
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<220>  
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 <223> /note="Description of Artificial Sequence: Probe for detecting a  
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<400> 477  
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<210> 478  
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<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding EFEMP2 protein"

<400> 478  
gtgaacgagt gtgacatggg 20

<210> 479  
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<212> DNA  
<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding EFEMP2 protein"

<400> 479  
atggcttctc ctgcagtgat 20

<210> 480  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding EFEMP2 protein"

<400> 480  
acgcctctgc caagacatt 19

<210> 481  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding EFEMP2 protein"

<400> 481  
atgtcgagag cagccttcatt 20

<210> 482  
<211> 2210  
<212> DNA  
<213> Homo Sapiens

<400> 482  
agccgcggcc tcaactaaaa gtggccattg acctttcaag ctttcgagca gtgatgcaat 60  
agaatagtat ttcaaagaaa aatgcttattc gaaattttgg atccggtttt cccgtgattg 120

|                                                                    |      |
|--------------------------------------------------------------------|------|
| ttaagggttt cttttaaaaa gtaggtcaca tttcaagtag gtcataatttc gggggcgggt | 180  |
| gcgcagacaa ggagatgagt ttccactaag gccagggggc ctccaacggg gttggaggtg  | 240  |
| agaatcccag gtagggtaga ggtgccgaga tccttccgaa tcccagccct ggggcgtcag  | 300  |
| ccctgcaggg aatggcagag acactctccg gactgagga accgaggcca gtcaccaagc   | 360  |
| cccttccggg cgcgcaggcg atcagtgggt gaccgcggct gcgagggact ttgtcatccg  | 420  |
| tcctccagga tctggggaga aagagcccca tcccttctct ctctgccacc atttcggaca  | 480  |
| ccccgcaggg actcgttttg ggattcgcac tgacttcaag gaaggacgcg aacccttctc  | 540  |
| tgaccccagc tcgggcggcc acctgtcttt gccgcggtga cccttctctc atgaccctgc  | 600  |
| ggtgccttga gccctccggg aatggcgggg aaggacgcg gagccagtgg gggaccgcg    | 660  |
| ggtcggcgga ggagccatcc ccgcaggcg cgctctggc gaaggccctg cgggagctcg    | 720  |
| gtcagacagg atggtactgg ggaagtatga ctgttaatga agccaaagag aaattaaaag  | 780  |
| aggcaccaga aggaactttc ttgattagag atagctcgca ttcagactac ctactaacia  | 840  |
| tatctgttaa aacatcagct ggaccaacta atcttcgaat cgaataccaa gacggaaaat  | 900  |
| tcagattgga ctctatcata tgtgtcaaata ccaagcttaa acaatttgac agtgtggttc | 960  |
| atctgatcga ctactatggt cagatgtgca aggataagcg gacaggtcca gaagcccccc  | 1020 |
| ggaacggcac tgttcacctt tatctgacca aaccgctcta cacgtcagca ccatctctgc  | 1080 |
| agcatctctg taggctcacc attaaacaaat gtaccggtgc catctgggga ctgcctttac | 1140 |
| caacaagact aaaagattac ttggaagaat ataaattcca ggtataaatg tttctctttt  | 1200 |
| tttaaacaatg tctcacatag agtatctccg aatgcagcta tgtaaaagag aacaaaaact | 1260 |
| tgagtgtctt ggataactat atggaatgct ttctaagaac agctgaagct aatctaattt  | 1320 |
| aaatttaaca gcttgaagag gtagctaggt gtttaaagtt cctccagata cttttacctg  | 1380 |
| agtgatgctt cccttcctaa ggctgaccaa gacctgtga tccttttaga ttaaaaataa   | 1440 |
| aatgtogcat gtaaaggctg aagtcgcgtt ttatcagaat gccttgctt cttaggttct   | 1500 |
| tttccattat gtcaaaggct caggctccag taggagagaa agaactcctc ataggaatac  | 1560 |
| tgaagaagtg ggaaggaacc aagctgacac aggctcact gcaatttgat atgcctgctg   | 1620 |
| atcagagtct cttgggcatt ttatatatttg cattctgatg tacctaggag ttttgtaaaa | 1680 |
| cagatgatgt atgtgagtat ttatcccat ttatgcaatt aaccaaatac accaaaaaaa   | 1740 |
| gtgaccatga agtcctgtat ttgtcttttt actacatgta ggaactctca tgtgaatgag  | 1800 |
| tactgtagta atccattcta tgggagcctt atttcagaaa tatttcaaac tgggtgcaaat | 1860 |
| ggaaaagact ttctcttttt ctttaaagct aaagacaaga atatcatgct atacaggtgc  | 1920 |
| aactcaatcc ccgttaataa aaaccaatgt aggtataggc attctaccct ttgaaatagc  | 1980 |
| tgtgtcccaa cctgttgcca ttgatttttt ggaaatggct ttagaaatat ccaagttgtc  | 2040 |

cttgaattgt ctaaccatgg acataaacag ttgtctccct tctactgtgt agaatacttt 2100  
 gacttaattt tcttccagat acaggggggat acctgcctgt ttttcaaagt gtttatttac 2160  
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<210> 483  
 <211> 198  
 <212> PRT  
 <213> Homo Sapiens

<400> 483

Met Thr Leu Arg Cys Leu Glu Pro Ser Gly Asn Gly Gly Glu Gly Thr  
 1 5 10 15

Arg Ser Gln Trp Gly Thr Ala Gly Ser Ala Glu Glu Pro Ser Pro Gln  
 20 25 30

Ala Ala Arg Leu Ala Lys Ala Leu Arg Glu Leu Gly Gln Thr Gly Trp  
 35 40 45

Tyr Trp Gly Ser Met Thr Val Asn Glu Ala Lys Glu Lys Leu Lys Glu  
 50 55 60

Ala Pro Glu Gly Thr Phe Leu Ile Arg Asp Ser Ser His Ser Asp Tyr  
 65 70 75 80

Leu Leu Thr Ile Ser Val Lys Thr Ser Ala Gly Pro Thr Asn Leu Arg  
 85 90 95

Ile Glu Tyr Gln Asp Gly Lys Phe Arg Leu Asp Ser Ile Ile Cys Val  
 100 105 110

Lys Ser Lys Leu Lys Gln Phe Asp Ser Val Val His Leu Ile Asp Tyr  
 115 120 125

Tyr Val Gln Met Cys Lys Asp Lys Arg Thr Gly Pro Glu Ala Pro Arg  
 130 135 140

Asn Gly Thr Val His Leu Tyr Leu Thr Lys Pro Leu Tyr Thr Ser Ala  
 145 150 155 160

Pro Ser Leu Gln His Leu Cys Arg Leu Thr Ile Asn Lys Cys Thr Gly  
 165 170 175

Ala Ile Trp Gly Leu Pro Leu Pro Thr Arg Leu Lys Asp Tyr Leu Glu  
 180 185 190

Glu Tyr Lys Phe Gln Val  
195

<210> 484  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding SOCS2 protein"

<400> 484  
agtcaccaag ccccttcc 18

<210> 485  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding SOCS2 protein"

<400> 485  
gctctttctc cccagatcct 20

<210> 486  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding SOCS2 protein"

<400> 486  
gggactgcct ttaccaacaa 20

<210> 487  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding SOCS2 protein"

<400> 487  
tttacatagc tgcattcgga ga 22

<210> 488  
<211> 60  
<212> DNA

<213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding SOCS2 protein"

<400> 488  
 agtgtggttc atctgatcga ctactatggt cagatgtgca aggataagcg gacaggtcca 60

<210> 489  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding SOCS2 protein"

<400> 489  
 gactttgtca tccgtcctcc 20

<210> 490  
 <211> 25  
 <212> DNA  
 <213> Artificial Sequence

<220>

<221> Source

<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding SOCS2 protein"

<400> 490  
 acttgaaga atataaattc caggt 25

<210> 491  
 <211> 2287  
 <212> DNA  
 <213> Homo Sapiens

<400> 491  
 gaatctacaa taagacaaat ttcaaataca gttgctccac tatactgcat aagcagttta 60  
 gaatcttaag cagatgcaaa aagaataaag caaatgggag gaaaaaaaaag gccgataaag 120  
 tttctggcta caatacaaga gacatatcat taccatatga tctaattgtg gtgtcagccg 180  
 gattgtgttc attgagggaa accttatttt ttaactgtgc tatggagtag aagcaggagg 240  
 ttttcaacct agtcacagag cagcacctac cccctcctcc tttcacacc tgcaaactct 300  
 tttacttggg ctgaatatatt agtgtaatta catctcagct ttgagggctc ctgtggcaaa 360  
 ttcccggatt aaaagggttc ctggttgtga aaatacatga gataaatcat gaaggccact 420  
 atcatcctcc ttctgcttgc acaagtttcc tgggctggac cgtttcaaca gagaggctta 480

|                                                                     |      |
|---------------------------------------------------------------------|------|
| tttgacttta tgctagaaga tgaggcttct gggataggcc cagaagttcc tgatgaccgc   | 540  |
| gacttcgagc cctccctagg ccagtggtgc cccttccgct gtcaatgcca tcttcgagtg   | 600  |
| gtccagtggt ctgatttggg tctggacaaa gtgccaaagg atcttcccc tgacacaact    | 660  |
| ctgctagacc tgcaaaaaca caaaataacc gaaatcaaag atggagactt taagaacctg   | 720  |
| aagaaccttc acgcattgat tcttgtcaac aataaaatta gcaaagttag tcttggagca   | 780  |
| tttacacctt tgggtgaagtt ggaacgactt tatctgtcca agaatacagct gaaggaattg | 840  |
| ccagaaaaaa tgcccaaac tcttcaggag ctgcgtgccc atgagaatga gatcaccaaa    | 900  |
| gtgcgaaaag ttactttcaa tggactgaac cagatgattg tcatagaact gggcaccaat   | 960  |
| ccgctgaaga gctcaggaat tgaaaatggg gctttccagg gaatgaagaa gctctcctac   | 1020 |
| atccgcattg ctgataccaa tatcaccagc attcctcaag gtcttcctcc ttcccttacg   | 1080 |
| gaattacatc ttgatggcaa caaaatcagc agagttgatg cagctagcct gaaaggactg   | 1140 |
| aataatttgg ctaagttggg attgagtttc aacagcatct ctgctgttga caatggctct   | 1200 |
| ctggccaaca cgctcatct gagggagctt cacttggaca acaacaagct taccagagta    | 1260 |
| cctggtgggc tggcagagca taagtacatc caggttgtct accttcataa caacaatatc   | 1320 |
| tctgtagttg gatcaagtga cttctgcca cctggacaca acacaaaaa ggcttcttat     | 1380 |
| tgggtgtga gtcttttcag caaccgggc cagtactggg agatacagcc atccaccttc     | 1440 |
| agatgtgtct acgtgcgtc tgccattcaa ctcgaaact ataagtaatt ctcaagaaag     | 1500 |
| ccctcatttt tataacctgg caaaatcttg ttaatgtcat tgctaaaaaa taaataaaag   | 1560 |
| ctagatactg gaaacctaac tgcaatgtgg atgttttacc cacatgactt attatgcata   | 1620 |
| aagccaaatt tccagtttaa gtaattgcct acaataaaaa gaaattttgc ctgccatttt   | 1680 |
| cagaatcatc ttttgaagct ttctgttgat gttaactgag ctactagaga tattcttatt   | 1740 |
| tcactaaatg taaaatttgg agtaaataa tatgtcaata tttagtaaag cttttctttt    | 1800 |
| ttaattttcca ggaaaaata aaaagagtat gagtcttctg taattcattg agcagttagc   | 1860 |
| tcatttgaga taaagtcaaa tgccaaacac tagctctgta ttaatcccca tcattactgg   | 1920 |
| taaagcctca tttgaatgtg tgaattcaat acaggctatg taaaattttt actaatgtca   | 1980 |
| ttattttgaa aaaataaatt taaaaataca ttcaaaatta ctattgtata caagcttaat   | 2040 |
| tggttaatat ccctaaacac aattttatga agggagaaga cattggtttg ttgacaataa   | 2100 |
| cagtacatct tttcaagttc tcagctatct cttctacctc tccctatctt acatttgagt   | 2160 |
| atggtaactt atgtcatcta tgttgaatgt aagcttataa agcacaagc atacatttcc    | 2220 |
| tgactgggtc agagaactga tgtttcaatt taccctctg ctaaataaat attaaaacta    | 2280 |
| tcatgtg                                                             | 2287 |



<210> 492  
 <211> 359  
 <212> PRT  
 <213> Homo Sapiens

<400> 492

Met Lys Ala Thr Ile Ile Leu Leu Leu Leu Ala Gln Val Ser Trp Ala  
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Gly Pro Phe Gln Gln Arg Gly Leu Phe Asp Phe Met Leu Glu Asp Glu  
 20 25 30

Ala Ser Gly Ile Gly Pro Glu Val Pro Asp Asp Arg Asp Phe Glu Pro  
 35 40 45

Ser Leu Gly Pro Val Cys Pro Phe Arg Cys Gln Cys His Leu Arg Val  
 50 55 60

Val Gln Cys Ser Asp Leu Gly Leu Asp Lys Val Pro Lys Asp Leu Pro  
 65 70 75 80

Pro Asp Thr Thr Leu Leu Asp Leu Gln Asn Asn Lys Ile Thr Glu Ile  
 85 90 95

Lys Asp Gly Asp Phe Lys Asn Leu Lys Asn Leu His Ala Leu Ile Leu  
 100 105 110

Val Asn Asn Lys Ile Ser Lys Val Ser Pro Gly Ala Phe Thr Pro Leu  
 115 120 125

Val Lys Leu Glu Arg Leu Tyr Leu Ser Lys Asn Gln Leu Lys Glu Leu  
 130 135 140

Pro Glu Lys Met Pro Lys Thr Leu Gln Glu Leu Arg Ala His Glu Asn  
 145 150 155 160

Glu Ile Thr Lys Val Arg Lys Val Thr Phe Asn Gly Leu Asn Gln Met  
 165 170 175

Ile Val Ile Glu Leu Gly Thr Asn Pro Leu Lys Ser Ser Gly Ile Glu  
 180 185 190

Asn Gly Ala Phe Gln Gly Met Lys Lys Leu Ser Tyr Ile Arg Ile Ala  
 195 200 205

Asp Thr Asn Ile Thr Ser Ile Pro Gln Gly Leu Pro Pro Ser Leu Thr  
 210 215 220

Glu Leu His Leu Asp Gly Asn Lys Ile Ser Arg Val Asp Ala Ala Ser  
225 230 235 240

Leu Lys Gly Leu Asn Asn Leu Ala Lys Leu Gly Leu Ser Phe Asn Ser  
245 250 255

Ile Ser Ala Val Asp Asn Gly Ser Leu Ala Asn Thr Pro His Leu Arg  
260 265 270

Glu Leu His Leu Asp Asn Asn Lys Leu Thr Arg Val Pro Gly Gly Leu  
275 280 285

Ala Glu His Lys Tyr Ile Gln Val Val Tyr Leu His Asn Asn Asn Ile  
290 295 300

Ser Val Val Gly Ser Ser Asp Phe Cys Pro Pro Gly His Asn Thr Lys  
305 310 315 320

Lys Ala Ser Tyr Ser Gly Val Ser Leu Phe Ser Asn Pro Val Gln Tyr  
325 330 335

Trp Glu Ile Gln Pro Ser Thr Phe Arg Cys Val Tyr Val Arg Ser Ala  
340 345 350

Ile Gln Leu Gly Asn Tyr Lys  
355

<210> 493  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Forward primer for  
amplifying the nucleotide sequence encoding DCN protein"

<400> 493  
agctttgagg gctcctgtg

19

<210> 494  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Reverse primer for  
amplifying the nucleotide sequence encoding DCN protein"

<400> 494  
gcaagcagaa ggaggatgat

20

<210> 495  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 495  
 aatgccatct tcgagtggtc 20  
  
 <210> 496  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 496  
 tgcaggtcta gcagagttgt g 21  
  
 <210> 497  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 497  
 aaccgaaatc aaagatggag a 21  
  
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 <212> DNA  
 <213> Artificial Sequence  
  
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 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 498  
 gtccaggtgg gcagaagtc 19  
  
 <210> 499  
 <211> 20  
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<220>  
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 <400> 499  
 aatgccatct tcgagtggtc 20  
  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 500  
 ctgctgattt tgttgccatc 20  
  
 <210> 501  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 501  
 tggcaacaaa atcagcagag 20  
  
 <210> 502  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 502  
 gccattgtca acagcagaga 20  
  
 <210> 503  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 503  
 gggctggcag agcataagta 20

<210> 504  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 504  
 gtccaggtgg gcagaagtc 19  
  
 <210> 505  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence  
  
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 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 505  
 aaccgaaatc aaagatggag a 21  
  
 <210> 506  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence  
  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
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 <400> 506  
 ccaaaggtgt aaatgctcca g 21  
  
 <210> 507  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
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 <400> 507  
 gagatcacca aagtgcgaaa 20  
  
 <210> 508  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 508  
 aaagcccat tttcaattcc 20  
  
 <210> 509  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Forward primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 509  
 aatgcatct tcgagtggc 20  
  
 <210> 510  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Reverse primer for  
 amplifying the nucleotide sequence encoding DCN protein"  
  
 <400> 510  
 aaagcccat tttcaattcc 20  
  
 <210> 511  
 <211> 58  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding DCN  
 protein"  
  
 <400> 511  
 tttaactgtg ctatggagta gaagcaggag gttttcaacc tagtcacaga gcagcacc 58  
  
 <210> 512  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Probe for detecting a  
 nucleotide molecule having a nucleic acid sequence encoding DCN  
 protein"

<400> 512  
ttcccggatt aaaaggttcc 20

<210> 513  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a  
nucleotide molecule having a nucleic acid sequence encoding DCN  
protein"

<400> 513  
aagtgccaaa ggatcttccc 20

<210> 514  
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<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a  
nucleotide molecule having a nucleic acid sequence encoding DCN  
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<400> 514  
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<210> 515  
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<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a  
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protein"

<400> 515  
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<210> 516  
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<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a  
nucleotide molecule having a nucleic acid sequence encoding DCN  
protein"

<400> 516  
atgcagctag cctgaaagga 20

<210> 517  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding DCN protein"

<400> 517  
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<210> 518  
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<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding DCN protein"

<400> 518  
tgaagaacct tcacgcattg 20

<210> 519  
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<213> Artificial Sequence

<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding DCN protein"

<400> 519  
tgtcatagaa ctgggcacca 20

<210> 520  
<211> 20  
<212> DNA  
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<220>  
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<223> /note="Description of Artificial Sequence: Probe for detecting a nucleotide molecule having a nucleic acid sequence encoding DCN protein"

<400> 520  
gttctgattt ggaactgggc 20

<210> 521  
<211> 20



<212> DNA  
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 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 521  
 tcacgggaga agcaggatac 20  
  
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 <221> Source  
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 <400> 522  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 ccagagattg cctgattcct 20  
  
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 <221> Source  
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agctggggga catctgtgt 19

<210> 526  
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<220>  
<221> Source  
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cactcagaaa ctgggcgatt 20

<210> 527  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 527  
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<210> 528  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 528  
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<210> 529  
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<210> 530  
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<212> DNA  
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 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <221> Source  
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<400> 534  
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<210> 535  
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<212> DNA  
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<220>  
<221> Source  
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<400> 535  
ggagatactc gccaggttga 20

<210> 536  
<211> 21  
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<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding CGN"

<400> 536  
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<210> 537  
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<212> DNA  
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<220>  
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<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding CGN"

<400> 537  
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<210> 538  
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<212> DNA  
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<220>  
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<400> 538  
ttagtagaac cagaagaaac catcac 26

<210> 539  
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<212> DNA  
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 <210> 540  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 540  
 ccatatagtc cccactgtag gc 22  
  
 <210> 541  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 ccactctgct ccctgtgtc 19  
  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <210> 543  
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 <212> DNA  
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 <221> Source  
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<400> 543  
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<210> 544  
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<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 544  
acgtcactcg cagtcgtg 18

<210> 545  
<211> 20  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding EPS8L2"

<400> 545  
gcagctcttc tccctcaaca 20

<210> 546  
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<220>  
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nucleotide sequence encoding EPS8L2"

<400> 546  
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<210> 547  
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<220>  
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<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 547  
caagatgagc cccaaggac 19

<210> 548  
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<212> DNA  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 548  
 tgatgacgtt ggagttggaa 20  
  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 549  
 caaggatgag gtcctagagg tg 22  
  
 <210> 550  
 <211> 18  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 550  
 gatgttgcag ggcacgta 18  
  
 <210> 551  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 551  
 tggaaattct ggggtatcgt 20  
  
 <210> 552  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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<210> 553  
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<220>  
<221> Source  
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cctgggaatc aaatatcgaa atag 24

<210> 554  
<211> 21  
<212> DNA  
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<220>  
<221> Source  
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<210> 555  
<211> 25  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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aagaattaac ttttctgcat ttcca 25

<210> 556  
<211> 22  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 556  
cagaacagac acctcagttg gt 22

<210> 557  
<211> 18



<212> DNA  
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 <220>  
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 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding GMIP"  
  
 <400> 557  
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 <210> 558  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 558  
 ccgccacttc tcaatctcag 20  
  
 <210> 559  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 cccagcacca cagtaccc 18  
  
 <210> 560  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 560  
 ctctgtggag ttggaatctc g 21  
  
 <210> 561  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 561  
ctggtggccc atctgttc 18

<210> 562  
<211> 21  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 562  
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<210> 563  
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<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 563  
acagttcaag aagtctagga tgagg 25

<210> 564  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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tggctaaatg actgaaattc acc 23

<210> 565  
<211> 21  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding IKBKE"

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ggacatccct cctctacctc a 21

<210> 566  
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<212> DNA  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 566  
 ggatctcagg cgttccag 18  
  
 <210> 567  
 <211> 20  
 <212> DNA  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 567  
 ctgcctgagg atgagttcct 20  
  
 <210> 568  
 <211> 19  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 568  
 gatgcacaat gccgttctc 19  
  
 <210> 569  
 <211> 20  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 569  
 ccgttacgac caaggtcaag 20  
  
 <210> 570  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 570  
tgacgaagag ggagttttcc 20

<210> 571  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 571  
tctgtcaaga cgtgtgaggt g 21

<210> 572  
<211> 23  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 572  
agtgaagttt tctgcagcct tta 23

<210> 573  
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<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding P2RX4"

<400> 573  
tctcctggct acaatttcag g 21

<210> 574  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding P2RX4"

<400> 574  
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<210> 575  
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<212> DNA  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 gcttccccca aggaatatac a 21  
  
 <210> 576  
 <211> 20  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 576  
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 <210> 577  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <210> 578  
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 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <210> 579  
 <211> 19  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 579  
ctggaggggca aaatcaagc 19

<210> 580  
<211> 20  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding P4HB"

<400> 580  
ttctttcccaa caagcacctt 20

<210> 581  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding PHKG2"

<400> 581  
gcagatccga ctttcagatt tc 22

<210> 582  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding PHKG2"

<400> 582  
gggggtccac acaactctc 19

<210> 583  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding PHKG2"

<400> 583  
ttccagcact gtcaaagacc t 21

<210> 584  
<211> 20

<212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 584  
 aaagaagggg tgctgtaggg 20  
  
  
 <210> 585  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 585  
 aggctatggc aaggaggtc 19  
  
  
 <210> 586  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 586  
 tgcgtaacat caggatctgc 20  
  
  
 <210> 587  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 587  
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 <210> 588  
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 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 588  
 ctggtgtcct tccagacaca 20

<210> 589  
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 <212> DNA  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding PPFIBP2"

<400> 589  
 gaatggaagc taaaggccac t 21

<210> 590  
 <211> 20  
 <212> DNA  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding PPFIBP2"

<400> 590  
 atctttcagg gccacctgtt 20

<210> 591  
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<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding PPFIBP2"

<400> 591  
 aatcttcgag ggagtggagt c 21

<210> 592  
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 <213> Artificial Sequence

<220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding PPFIBP2"

<400> 592  
 cagggtgtcc ccagtga 18

<210> 593  
 <211> 19



<212> DNA  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 ccctcccagt gttgtcctt 19  
  
 <210> 594  
 <211> 18  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 594  
 cccactccc aaggaact 18  
  
 <210> 595  
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 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 595  
 gagtgctgga cgcctctg 18  
  
 <210> 596  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 596  
 ttgaccgcca ggagattg 18  
  
 <210> 597  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding PPPIR16A"

<400> 597  
atgccctatg acctgtgtga t 21

<210> 598  
<211> 19  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding PPPIR16A"

<400> 598  
gatgctgtcc tgggtgatg 19

<210> 599  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding RASSF7"

<400> 599  
cactagccca agcaataggc 20

<210> 600  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding RASSF7"

<400> 600  
cactcttgtg gcagcaactg 20

<210> 601  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding RASSF7"

<400> 601  
cagcctggct ctggtgag 18

<210> 602  
<211> 19

<212> DNA  
 <213> Artificial Sequence  
  
 <220>  
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 <400> 602  
 ggagctctcg gttcagctc 19  
  
 <210> 603  
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 <213> Artificial Sequence  
  
 <220>  
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 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding RASSF7"  
  
 <400> 603  
 tctgcctcca gccagaga 18  
  
 <210> 604  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 604  
 ctccaggagt tctgcgtcat 20  
  
 <210> 605  
 <211> 21  
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 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding RNF183"  
  
 <400> 605  
 tccagagtag tctgcctgac c 21  
  
 <210> 606  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding RNF183"

<400> 606  
catcctcagc cacacacg 18

<210> 607  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding RNF183"

<400> 607  
tccagagtag tctgcctgac c 21

<210> 608  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding RNF183"

<400> 608  
tgtttgttgaa ggggttccag 20

<210> 609  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding RNF183"

<400> 609  
tctgccaccg tgtctacg 18

<210> 610  
<211> 20  
<212> DNA  
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<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding RNF183"

<400> 610  
cggaacact ccctcaaaga 20

<210> 611  
<211> 20

<212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding SIRT6"  
  
 <400> 611  
 agctgagggga caccatccta 20  
  
 <210> 612  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding SIRT6"  
  
 <400> 612  
 atgtacccag cgtgatggac 20  
  
 <210> 613  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding SIRT6"  
  
 <400> 613  
 aggatgtcgg tgaattacgc 20  
  
 <210> 614  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding SIRT6"  
  
 <400> 614  
 agaccagcct cgccagtt 18  
  
 <210> 615  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding SIRT6"

<400> 615  
ggtcagccag aacgtgga 18

<210> 616  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding SIRT6"

<400> 616  
gtggagctct gccagtttgt 20

<210> 617  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding TJP3"

<400> 617  
gtgggcatct tcgtgtcc 18

<210> 618  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding TJP3"

<400> 618  
gaatggcacg tcattcacc 19

<210> 619  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding TJP3"

<400> 619  
atctggacgg cggaagat 18

<210> 620  
<211> 21

<212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding TJP3"  
  
 <400> 620  
 ggtgagggag gtctaggttg t 21  
  
 <210> 621  
 <211> 23  
 <212> DNA  
 <213> Artificial Sequence  
  
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 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding TJP3"  
  
 <400> 621  
 tcatcaagca cattacagat tcg 23  
  
 <210> 622  
 <211> 19  
 <212> DNA  
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 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding TJP3"  
  
 <400> 622  
 ggctagacac cccgttgat 19  
  
 <210> 623  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding EFEMP2"  
  
 <400> 623  
 actcgaggg ggacttttac 20  
  
 <210> 624  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
 nucleotide sequence encoding EFEMP2"

<400> 624  
catgagggaa ttcatggtga 20

<210> 625  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding EFEMP2"

<400> 625  
atcgggatgg cttctcct 18

<210> 626  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding EFEMP2"

<400> 626  
tgatgcagcg gtactgaca 19

<210> 627  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding EFEMP2"

<400> 627  
agtaccgctg catcaacga 19

<210> 628  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding EFEMP2"

<400> 628  
cgcaccagac tcacactcat 20

<210> 629  
<211> 18



<212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 629  
 ggagctcggg cagacagg 18  
  
  
 <210> 630  
 <211> 25  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 630  
 ctaatcaaga aagttccttc tgggtg 25  
  
  
 <210> 631  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 631  
 cagtcaccaa gccccttc 18  
  
  
 <210> 632  
 <211> 19  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 632  
 aagggatggg gctctttct 19  
  
  
 <210> 633  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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<400> 633  
ggagctcggt cagacagg 18

<210> 634  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding SOCS2"

<400> 634  
gttccttctg gtgcctcttt t 21

<210> 635  
<211> 25  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding DCN"

<400> 635  
ggagacttta agaacctgaa gaacc 25

<210> 636  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding DCN"

<400> 636  
cgttccaact tcaccaaagg 20

<210> 637  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<221> Source  
<223> /note="Description of Artificial Sequence: Primer amplifying the  
nucleotide sequence encoding DCN"

<400> 637  
ctgtcaatgc catcttcgag 20

<210> 638  
<211> 20

<212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 638  
 gatcctttgg cactttgtcc 20  
  
 <210> 639  
 <211> 23  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <221> Source  
 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 639  
 caatatcacc agcattcctc aag 23  
  
 <210> 640  
 <211> 20  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
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 <223> /note="Description of Artificial Sequence: Primer amplifying the  
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 <400> 640  
 ctgctgattt tgttgccatc 20